# Familial Breast Cancer: initial assessment and genetic testing

## Consultation on draft scope
## Stakeholder comments table

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| Surrey and Sussex NHS Healthcare Trust | 002 | 008 | A reference would add validation to this recommendation | Thank you for your comment. The 5-year threshold was chosen based on the UK recommendations for the management of transgender and gender diverse patients with inherited cancer risks consensus paper (see Table 2 section 4 on breast tissue management).<br>We have added the reference to the scope as requested. |
| Surrey and Sussex NHS Healthcare Trust | 004 | 025 | You may wish to rename 'Risk Reducing Therapy (chemoprevention)' in line with UKCCG<br>UKCGG leaflets and guidelines - Cancer Genetics Group | Thank you for your comment. We will consider this as part of the guideline editorial refresh that is carried out during development to bring existing recommendations into current NICE style. |
| Befriend your Boobs | 010 | 008 | You comment that high breast cancer incidence in the south-east, is in affluent Caucasian women.<br>In our Practice population, (1/3 Ashkenazi 1/3 Asian and 1/3 Caucasian black Chinese etc) Women identified as Ashkenazi from a list of possible ethnicities. We confirmed that breast cancer incidence in postmenopausal women accounted for 80% of our breast cancers. But we discovered that there was 1.5 times as much breast cancer, both in premenopausal and in post-menopausal Ashkenazim.<br>It may be that some of your "Caucasians" are mis-identifying and are in fact Ashkenazi Jews skewing the figures for the region.<br><br>Our Study: | Thank you for your comments. This is an interesting point and we have recorded it in section 3.2 of the post scope consultation part of the Equality and health inequalities assessment. |

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| | | | A population -based audit of ethnicity and breast cancer risk in one general practice catchment area in north london, uk: implications for practice<br><br>Hereditary cancer in clinical practice<br><br>2007-09-15 \| Journal article<br><br>DOI: 10.1186/1897-4287-5-3-157 | |
| Breast Cancer Now | General | General | It's positive to see NICE looking to review the population of people eligible for assessment/ genetic testing beyond just strong familial history. It's also positive to see that NICE intends to change the name of the guideline to reflect the fact that a strong familial history is not the only factor that may lead to someone being at an increased risk of inheritable breast cancer. We have recently gathered a substantial amount of data about service provision across England and can provide this dad on request. | Thank you for your comments and support of our plan to widen the scope of the guideline. |

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| Breast Cancer Now | General | General | Whilst we appreciate the need to prioritise, we strongly believe there is a strong case for undertaking a more complete guideline update in this area. Data collected by Breast Cancer Now in response to a UK-wide FOI request has highlighted significant variation across the country in terms of the provision of risk-reducing interventions and screening for women at increased risk can access. The data particularly shows that NICE's current screening guidelines are not being followed by most services. The screening guidelines for women at increased risk have also not been updated since 2014, putting some areas in direct contradiction with more recent expert guidance. Furthermore, the inclusion of both 'offer' and 'consider offering' recommendations in screening guidance is confusing and unclear and allows for further unwarranted variation between services. We would like to see NICE commit to a more complete update of this guidance, in particular reviewing and clarifying its recommendations on screening for this population. | Thank you for your comments. NICE's focus is on developing more relevant, timely, useable and impactful guidance. We discussed your comments with the committee, and they agreed that the existing recommendations were confusing and may be implemented differently across the country.<br><br>At NICE, some recommendations are made with more certainty than others. When using the term "offer", it is referring to recommendations that are based on strong evidence of a benefit and when using the term "consider" it refers to situations where the benefit is less certain. Please see Making Decisions using NICE Guidelines for further information.<br><br>We have not identified new evidence that could change the existing surveillance recommendations, and we will therefore not be carrying out an evidence review on this topic. However, we are planning to editorially refresh all surveillance recommendations as part of the update to make them clearer and more useable and reflect current NICE |

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| | | | | style. This will hopefully reduce any ambiguity and improve implementation.<br><br>We have not identified new evidence that would lead us to update the recommendations on risk reducing interventions apart from risk reducing mastectomy. Variation in provision of these interventions may be more of an implementation issue and we will pass this information onto our implementation team to see if they can explore this issue further. If you are aware of evidence that could lead us to update the other recommendations on risk reduction, then please can you share it with us by submitting a topic suggestion through our topic prioritisation process. See here for information on the prioritisation process and the submission form:<br>• Prioritising our guidance topics<br>• Topic suggestion<br><br>We are aware of the very high-risk screening programme and plan to refer to it in the guideline update. We are not able to update the very high-risk surveillance protocols ourselves but |

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| | | | | any updates to the NICE guideline may result in the very high-risk surveillance protocol being updated by the NHS. |
| Breast Cancer Now | 003 | 006 | We know that testing for BRCA1/2 and other genetic variants can impact treatment options. It would be positive to see NICE providing updated guidance about how quickly genetic testing results should be returned in these circumstances. Any guidance on turnaround times should consider the current 62-day standard for starting treatment from the point of urgent referral. | Thank you for your comments. We will discuss this issue with the committee when we update the genetic testing section of the guideline. |
| Breast Cancer Now | 003 | 010 | We are pleased to see the NICE will be looking at reviewing the guidance for surveillance of some women without a personal history of breast cancer, but evidence collected by Breast Cancer Now via FOI suggests there are significant issues with the consistency of screening and surveillance offerings across the country. We would like to see NICE commit to a full review of this guidance to ensure it is still up to date and in line with best practice. | Thank you for your comment. We have not identified new evidence that could change the existing surveillance recommendations, and we will therefore not be carrying out an evidence review on this topic. However, we are planning to editorially refresh all surveillance recommendations as part of the update to make them clearer and more useable and reflect current NICE style. This will hopefully reduce any ambiguity and improve implementation. We will also include a cross reference to the very high-risk screening programme. |
| Breast Cancer Now | 004 | 027 | Evidence collected by Breast Cancer Now has highlighted that women are not consistently being given the opportunity to have a full and complete conversation | Thank you for your comment. We acknowledge the importance of providing relevant information about chemoprevention. There is currently a recommendation for |

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| | | | with their medical teams about the option of chemoprevention for reducing their risk of breast cancer. Women are regularly not being informed of this as an option or only informed about them via written communications. Women have also reported feeling discouraged from considering them. We would like to see NICE update guidance to support clinicians to have comprehensive discussions with women about chemoprevention as an option and to ensure that the guidance is still in line with current evidence and best practice. There are services that have developed more comprehensive pathways and follow up support for women at increased risk to take and adhere to chemoprevention. The effectiveness of these initiatives should be reviewed as part of this update. | the provision of information for chemoprevention (Recommendation 1.7.20) in the NICE guideline (CG164) section on Chemoprevention for women with no personal history of breast cancer. This recommends that a discussion is held with women at high risk or moderate risk of breast cancer to cover the benefits and risks of chemoprevention, and this process is supported by a decision aid. Therefore, the issue appears to lie with the implementation of this recommendation. The committee thought this could be linked to uncertainty around which healthcare provider should be providing this information in current practice. We will try to clarify this using committee input as part of the guideline editorial refresh that is carried out during development to bring existing recommendations into current NICE style.<br><br>We will not be able to look at the effectiveness of initiatives that provide support for women to take and adhere to chemoprevention as part of this current update. However, if you have evidence to support its inclusion in future work please can you share it with us by submitting a topic suggestion through our topic prioritisation process. See here |

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| | | | | for information on the prioritisation process and the submission form:<br>• Prioritising our guidance topics<br>• Topic suggestion |
| Breast Cancer Now | 005 | 020 | It is positive to see NICE committing to review their guidance on what risk assessment tools are best placed to assess an individual's cancer risk, evidence collected by Breast Cancer Now through FOI requests and expert clinical feedback suggests that the current advice is too vague and there is significant variation in the tools used. However, it is also important to provide clinicians with guidance on the information that should be collected when using these tools to assess risk. Again, evidence collected by Breast Cancer Now suggests that there is significant variation in how different family history units are collecting and inputting risk information into the tools they do use. These two issues combined mean that currently women are being categorised differently based solely on the unit they are being assessed by, without any clinical justification which is not acceptable. | Thank you for your comments and support for these review questions. We are aware that there is variation in practice around the risk tools that are used. We aim to address this with our questions on risk tools to carrier probability and the risk of developing breast cancer. We will bear your comments about the variation in how these tools are used in practice in mind when the committee draft recommendations on this topic. |

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| Breast Cancer Now | 006 | 014 | As above, whilst it is positive to see NICE reviewing part of the guidance for surveillance of women at increased risk, we would like to see a more complete review of the screening guidance to ensure it is still in line with best practice, and does not allow any for ambiguity in what specific screening should be offered for women at each risk level. | Thank you for your comment. We have not identified new evidence that could change the existing surveillance recommendations, and we will therefore not be carrying out an evidence review on this topic. However, we are planning to editorially refresh all surveillance recommendations as part of the update to make them clearer and more useable and reflect current NICE style. This will hopefully reduce any ambiguity and improve implementation. |
| Breast Cancer Now | General | General | The insights collected by Breast Cancer Now suggest there is significant unmet need regarding the information and emotional support women receive after being informed they are at increased risk. We would like to see NICE reviewing the guidance and resources they recommend services offer for people at increased risk to ensure they are meeting the needs of this population. | Thank you for your comment. We acknowledge the importance of information and emotional support for women after being informed that they are at an increased risk. The current guideline has a section on information and support that covers what information should be provided.<br><br>We will not be reviewing the evidence to update this section of the guideline as part of the current work. However, we will look at the wording that is used as part of the guideline editorial refresh that is carried out during development to bring existing recommendations into current NICE style. We will also include cross reference to the NICE guideline on Patient experience in adult NHS services: improving the |

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| | | | | experience of care for people using adult NHS services which has a recommendation in the information section on advising patients about how to access support services. |
| Breast Cancer Now | General | General | Some of the language held within the current guidelines is outdated and potentially a barrier to access, or unduly restrictive e.g. using 'chemoprevention' and the mastectomy guidelines which currently make no reference to PALB2, NICE should consider looking more broadly at the language used within the guideline to ensure it reflects current best practice. | Thank you for your comment. We will change any outdated language as part of the guideline editorial refresh that is carried out during development to bring existing recommendations into current NICE style. |
| Queen Mary University London | 001, 003 | 012-028 (page 1), 01-018 (page 3) | The draft scope currently seems to exclude the possibility of unselected (all) individuals who have had breast cancer. This is important to consider. A recently concluded NHS England Pilot programme across 15 London hospitals offered unselected testing to all women with breast cancer diagnosis. [redacted] | Thank you for your comments. The committee discussed the information you provided but decided that unselected genetic testing of all people with breast cancer is currently not implementable due to limited testing capacity. Considering the whole healthcare system, the committee noted the need to be equitable across cancer types, and the need to prioritise those at higher risk of carrying pathogenic variants. The carrier probability thresholds at which people with breast cancer are offered genetic testing will be reviewed as part of this update, and the committee agreed that all women with breast cancer should be assessed for eligibility for testing. |

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| | | | [redacted] | |
| Queen Mary University London | 001, 003 | 012-028 (page 1), 01-018 (page 3) | The draft scope is explicit about BRCA1 and BRCA2 but does not mention the other breast cancer genes on the NHS Genomic Test Directory panel. It would be unfortunate to miss the opportunity to update the guideline explicitly to include identification/ascertainment and management of all the other relevant breast cancer genes too – PALB2, RAD51C, RAD51D, CHEK2, ATM. A number of women even with moderate risk genes or just a family history of breast cancer with some other risk factors will exceed the current NICE risk thresholds for preventive or screening interventions.<br><br>The scope seems to exclude women at increased risk based on modifiable risk factors, mammographic density and a polygenic risk score. A number of women can be at increased risk just from this? | Thank you for your comments. The 'Activities, services or aspects of care covered by the guideline update' includes the headings from the current CG164 guideline, which is why they only mention BRCA1, BRCA2 and TP53. However, these are likely to change during the update. The committee will review evidence and make recommendations related to all relevant breast cancer predisposition genes, not just BRCA1 and BRCA2. The committee will also consider cross-referencing to the National genomic test directory for information on which genes to test during development.<br><br>The scope population referred to people who may be at increased risk of developing breast cancer because of ancestry with a high prevalence of BRCA1 or BRCA2 mutations. This has been expanded to cover everyone with |

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| | | | | ancestry with a high prevalence of pathogenic variants associated with breast cancer.<br><br>The committee were unable to include people in the scope based on modifiable risk factors and mammographic density alone, as the focus of the guideline is people who are predisposed to breast cancer due to heritable factors. The committee recognised that modifiable risk factors and breast density may alter the risk of developing breast cancer for people with a genetic predisposition to breast cancer. They will bear this in mind when we review the evidence on tools for predicting the risk of developing breast cancer.<br><br>PRS were not included specifically in the current scope but was raised by a number of stakeholders. Women who have polygenic risk predisposing them to developing breast cancer are not excluded from the current guideline provided they meet other scope inclusion criteria (for example, having a personal or family history of breast cancer).<br><br>We will examine the evidence to determine whether additional work on PRS is possible at this time and what it would entail, or whether this is a topic that should be |

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| | | | | monitored and included in the future when more evidence is available. |
| Queen Mary University London | 005 | 010-018 | The scope states under the question regarding Assessing carrier probability -<br>"a personal history of breast cancer that is suspected to be heritable"<br>This does not reflect the opportunity for reviewing unselected testing. As number (up to 60%) of CSG carriers are missed if we are looking just for suspicion of heritability. | Thank you for your comment. Taking your comment into account, we have amended the review question and scope to include all adults with a personal history of breast cancer for parts of the guideline associated with assessment of carrier probability. |
| Queen Mary University London | 005 | 019-026 | Assessing the risk of developing breast cancer-<br>Why restrict this to BRCA1, BRCA2. | Thank you for your comments. This was restricted to BRCA1 and BRCA2 to reflect the higher incidence of BRCA variants in some populations, such as Ashkenazi Jews. Following committee discussion, this has now been widened to include people from an ancestry with a high prevalence of pathogenic variants associated with breast cancer. |
| Queen Mary University London | 001, 003 | 012-028 (page 1),<br><br>001-018 (page 3) | The scope seems to miss out on the need and opportunity to address how PRS can be used to modify risk of moderate risk genes as well as contribute to personalised risk prediction without the presence of cancer susceptibility genes. This will identify additional | Thank you for your comments. The committee acknowledged that PRS could play a role in determining the level of surveillance or preventative interventions that people are offered, especially for those with pathogenic variants in moderate risk genes who may be pushed into a different risk |

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| | | | individuals who fulfil current risk thresholds for screening or preventive interventions. | category by also having a particular level of polygenic risk, and in families with strong family history where no monogenic cause has been identified. However, they noted that polygenic risk scores (PRS) are not available currently on the NHS, although some people may have this test carried out privately and bring the results to their NHS risk assessments.<br><br>PRS were not included specifically in the current scope, but we will examine the evidence presented by several stakeholders during this consultation to determine whether additional work on PRS is possible at this time and what it would entail, or whether this is a topic that should be monitored and included in the future when more evidence is available. |
| Queen Mary University London | 006 | 010-011 | Overlap with NICE Guideline NG241 (this has already been addressed there also) with respect to –<br>"ancestry with a high prevalence of BRCA1 or BRCA2 mutations be offered genetic testing?" | Thank you for your comments. The review questions for carrier probability thresholds have now been amended following your comment and other stakeholder suggestions. The populations have been simplified to people with or without a personal history of breast cancer. The rationale for this was that only a specific population would have their carrier probability assessed, as specified in the review |

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| | | | | question for tools for assessing carrier probability, and that it was not necessary to have a narrow population to assess the threshold at which testing should be offered. We will bear in mind your comment about the overlap with the NG241 ovarian cancer guideline for people with ancestry with a high prevalence of BRCA1 or BRCA2 variants when we come to develop the review protocols for the carrier probability assessment reviews. |
| Queen Mary University London | 006 | 019-025 | We would like to highlight our recent publications which are relevant to this, for consideration by the committee–<br>1. Wei, X.; Mansour, L.; Oxley, S.; Fierheller, C.T.; Kalra, A.; Sia, J.; Ganesan, S.; Sideris, M.; Sun, L.; Brentnall, A., et al. Defining Lifetime Risk Thresholds for Breast Cancer Surgical Prevention. JAMA Oncol 2025, 10.1001/jamaoncol.2025.2203, doi:10.1001/jamaoncol.2025.2203.<br>Wei, X.; Sun, L.; Slade, E.; Fierheller, C.T.; Oxley, S.; Kalra, A.; Sia, J.; Sideris, M.; McCluggage, W.G.; Bromham, N., et al. Cost-Effectiveness of Gene-Specific Prevention Strategies for Ovarian and Breast Cancer. | Thank you for your comments. We will take these publications into account during development if they meet the inclusion criteria for the reviews as defined in the review protocols. |

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| | | | *JAMA Netw Open* **2024**, *7*, e2355324, doi:10.1001/jamanetworkopen.2023.55324. | |
| Antegenes Ltd | Question 1 | general | A proposal based on research and clinical practice is to add **a polygenic risk score** component to the assessment of hereditary breast cancer risk.<br><br>In the context of familial breast cancer, current scientific evidence clearly shows the need to also take into account the impact of the breast cancer polygenic risk score on breast cancer risk and the resulting preventive measures.<br>The international evidence base for the clinical use of the breast cancer polygenic risk score, together with a description and justification of its application, has been published in a recent review: https://doi.org/10.3390/cancers17071056 .<br>This includes also the link and application in the context of the current NICE Guidance for Familial Breast Cancer, and is particularly relevant for the assessment of familial and hereditary breast cancer risk. | Thank you for your comments and the information provided about polygenic risk scores (PRS).<br>The committee discussed how PRS could be used in current practice and acknowledged that they could play a role in determining the level of surveillance or preventative interventions that people are offered, especially for those with pathogenic variants in moderate risk genes who may be pushed into a different risk category by also having a particular level of polygenic risk, and in families with strong family history where no monogenic cause has been identified. However, they noted that polygenic risk scores (PRS) are not available currently on the NHS, although some people may have this test carried out privately and bring the results to their NHS risk assessments. This could link to the first of the clinical scenarios you suggest.<br><br>PRS have not been specifically mentioned in the current scope. However, separately from this current piece of work, we will examine the evidence you presented and other |

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| | | | We therefore propose that, in the context of these guidelines, **the testing and use of the polygenic risk score** be considered as an important component of inherited breast cancer risk.<br><br>Tests for the breast cancer polygenic risk score and their clinical application are already being implemented in healthcare in the United Kingdom.<br><br>Additional explanation:<br>Secondary prevention through mammography screening has been shown to reduce breast cancer mortality by approximately 20-30%. In the UK, the NHS Breast Screening Programme invites women aged 50 to 71 for mammography every three years. However, this age-based approach does not account for individual variations in breast cancer risk, overlooking younger women at higher risk and older women who may benefit from more intensive screening. In the UK, approximately 20% of breast cancer cases are diagnosed in women under the age of 50. The traditional one-size-fits-all | related stakeholder comments from this consultation to determine whether additional work on PRS is possible at this time and what this would entail, or whether this is a topic that should be monitored and included in the future when more evidence is available. To note, the use of PRS would likely be limited to certain groups of people, for example those already attending hereditary cancer clinics, because population screening is the remit of the UK National screening committee and NICE is unable to make recommendations in this area. |

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| | | | approach to breast cancer screening does not account for individual variations in risk factors such as genetic predisposition, family history, breast density, and lifestyle factors. An alternative to age-based screening is risk-based screening, where individual risk assessments guide screening recommendations.<br><br>It has been shown that hereditary factors account for approximately one-third of overall breast cancer risk. Therefore, genetic predisposition followed by a genetic risk assessments are an extremely important component in risk-based, or personalised, breast cancer prevention.<br><br>A significant proportion of breast cancer risk variation is attributed to common single-nucleotide polymorphisms (SNPs) located outside high- and moderate-risk genes. These SNPs have been identified through genome-wide association studies (GWAS. **A polygenic risk score (PRS)** represents the cumulative impact of multiple breast cancer susceptibility SNPs. While individual SNPs may confer only a modest risk, their combined | |

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| | | | effect can be considerable. A breast cancer PRS reflects the cumulative impact of these susceptibility variants, which have been shown to effectively stratify individual breast cancer risk.<br><br>**Utilising Breast Cancer Polygenic Risk Scores in Clinical Practice**<br>Based on published research evidence, breast cancer PRSs have become an increasingly relevant tool in the landscape of breast cancer risk-stratified prevention and screening. The evidence-based clinical use of the breast cancer polygenic risk score is reflected in published clinical guidelines, which outline different clinical use scenarios:<br>1) Management of healthy women with a family history of cancer in hereditary cancer clinics.<br>2) Individual personalised breast cancer prevention and screening in healthcare services.<br>3) Breast cancer screening programs to make screening more precise and effective. | |

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| | | | Reference: Padrik P, Tõnisson N, Hovda T, Sahlberg KK, Hovig E, Costa L, et al. Guidance for the Clinical Use of the Breast Cancer Polygenic Risk Scores. Cancers. 2025;17(7):1056. https://doi.org/10.3390/cancers17071056 . | |
| Antegenes Ltd | 001 | 015 | We propose explicitly including women identified as being at increased risk on the basis of polygenic risk, quantified using validated polygenic risk scores (PRS), either alone or integrated into multifactorial risk prediction models. Increased polygenic risk is clearly a distinct component of heritable risk and should be considered in heritable risk estimation. | Thank you for your comment. We aware of PRS and how they can be integrated into risk prediction models such as CanRisk. PRS are not available or routinely used to guide management options in the NHS at this time, although some people choose to have their PRS done privately. We are therefore not going to include people with an elevated PRS as a specific scope population at this time. However, as mentioned above, we will do some more investigative work around the use of PRS outside of this guideline update. |
| Antegenes Ltd | 002 | 018 | Women from the age of 30, with or without a family history of breast cancer, who may have an increased heritable risk due to elevated polygenic risk. | Thank you for your comments. The committee have decided not to include people with an elevated PRS as a specific scope population at this time. However, as mentioned above, we will do some more investigative work around the use of PRS outside of this guideline update. |
| Antegenes Ltd | 003 | 007 | Breast cancer polygenic risk score (PRS) testing. | Thank you for your comment. This page refers to the headings of the current sections of the guideline that may be |

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| | | | | updated in the current piece of work. We have therefore not made your requested change. |
| Antegenes Ltd | 005 | 026 | Individuals with no personal history of breast cancer, with or without a family history of the disease, who are at high polygenic risk as assessed by polygenic risk score testing. | Thank you for your comments. The committee have decided not to include people with an elevated PRS as a specific scope population at this time. However, as mentioned above, we will do some more investigative work around the use of PRS outside of this guideline update. |
| Antegenes Ltd | 006 | 012 | Who should be offered polygenic risk assessment using polygenic risk score testing, and at what age.<br><br>We propose clarifying that "heritable risk" includes not only monogenic risk (e.g., BRCA1/2) but also polygenic risk as quantified by validated PRS tools. These account for a significant share of familial clustering in breast cancer and are now suitable for routine use. This will also ensure consistency with the growing evidence base and evolving international guidance. | Thank you for your comments. The committee have decided not to include people with an elevated PRS as a specific scope population at this time. However, as mentioned above, we will do some more investigative work around the use of PRS outside of this guideline update. |

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| Prevent Breast Cancer | general | general | We would recommend including Polygenic Risk Scores (PRS) within the Initial Assessment and Genetic Testing guidelines for Familial Breast Cancer.<br><br>PRS have an important role in women with a significant family history, but who then test negative for BRCA 1 and BRCA2. In this circumstance PRS becomes an important predictor of risk, and should be included in the clinical pathway.<br><br>For women with a family history who then test positive for a high-risk gene mutation the addition of PRS may modify the risk level, either up or down, and thus still have a bearing on clinical decision making. | Thank you for your comments. The committee acknowledged that PRS could play a role in determining the level of surveillance or preventative interventions that people are offered, especially for those with pathogenic variants in moderate risk genes who may be pushed into a different risk category by also having a particular level of polygenic risk, and in families with strong family history where no monogenic cause has been identified. However, they noted that polygenic risk scores (PRS) are not available currently on the NHS, although some people may have this test carried out privately and bring the results to their NHS risk assessments.<br><br>PRS were not included specifically in the current scope but was raised by several stakeholders. We will investigate whether additional work on PRS is possible at this time and what this would entail, or whether this is a topic that should be monitored and included in the future when more evidence is available. |
| The UK Charity for Triple | 002 | 010 | The draft scope should be expanded to include people who have received a diagnosis for Triple Negative Breast Cancer and for TNBC to be a specific | Thank you for your comment. We consider triple negative breast cancer to be a feature associated with heritable breast cancer in line with the testing criteria in National genomic test |

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| Negative Breast Cancer | | | consideration with respect to the guidelines. This aligns with the NHS 10 Year Health Plan priority emphasis on disease prevention, as the incidence of BRCA 1 is several times higher in those with TNBC. Prevention is disproportionately important in TNBC because of the higher rate of relapse and death compared to other breast cancer subtypes. This should include the availability of PARP inhibitor Olaparib, which improves invasive and distant free survival in those with germline mBRCA. | directory R208. Therefore, people with triple negative breast cancer are included in the scope. To make this clearer we have amended the scope population wording to say "clinical or pathological features". The Early and locally advanced breast cancer guideline (NG101) has been recently updated to include TA866 on olaparib for people with BRCA-mutation-positive HER2-negative breast cancer. |
| St George's University Hospitals NHS Foundation Trust | 003 | 004 | Section 1.5.2 of current guidelines recommend "Pre-test counselling (preferably 2 sessions) should be undertaken [2004]. This is outdated and not in line with current clinical practice. Pre-test counselling in a specialist Genetics service is typically 1 visit. In the mainstream setting (genetic testing being offered by a cancer treatment team rather than a specialist genetics service) this pre-test counselling may be particularly short and brief with the intention that positive patients will have an onward referral to Clinical Genetics. | Thank you for your comments. As part of planned review work we expect to be able to address this issue with the committee during development and amend the recommendations as required. |

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| | | | Consider removing (preferably 2 sessions) from the guidance | |
| St George's University Hospitals NHS Foundation Trust | 003 | 006 | Acknowledgement and support of mainstream testing is important to add to this section. | Thank you for your comments. As part of planned review work we expect to be able to address this issue with the committee during development and amend the recommendations as required. |
| St George's University Hospitals NHS Foundation Trust | 003 | 010 | Section 1.6.5 is far too vague in the current guidelines. When should additional surveillance be "considered". In my clinical experience, the majority of women coming through a family history service want as much screening as they can get, independent of their risk and independent of capacity within the screening services. As moderate and high risk individuals are not screened under NHS BSP, it is important to have clear guidance on when we should refer to screening outside of the 40-49 and 40-59 guidance. This should not be a "patient choice" situation. This entire section only adds ambiguity and uncertainty and opens a clinical service up to patient complaints if they are motivated to pursue additional | Thank you for your comments. At NICE, the term 'consider' relates to a weak recommendation where the committee has concluded based on the evidence that there is a closer balance between benefits and harms, and some people would not choose an intervention whereas others would. For further information see chapter 9 of Developing NICE guidelines: the manual.<br><br>We are planning to editorially refresh all surveillance recommendations as part of the update to bring existing recommendations into current NICE style, make them clearer and more useable. This will hopefully reduce any ambiguity and improve implementation. |

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| | | | screening and denied this. If there are specific clinical scenarios to be considered, such as breast density, then this should be specified. | |
| St George's University Hospitals NHS Foundation Trust | 003 | 012 | Clarification around "lifetime risk" and "remaining lifetimes risk" continue to cause confusion amongst both genetics and surgical teams. We have some surgery services that will not consider mastectomy in a patient who has a lifetime breast cancer risk >30%, but remaining breast cancer risk <30% due to having outlived some of their risk. The current wording of 1.7.33 could be more clear. | Thank you for your comments. We will consider this issue during development when we review the evidence for risk reducing mastectomy. |
| Association of Breast Surgery | General | General | Throughout the document reference is given to BRCA1 or BRCA 2 mutations. Given the panel of moderate and high penetrance genes which are looked at as part of modern genetic testing is this now relevant?<br><br>Panel testing is guided by the NHS genomic testing directory with criteria laid out in R208/R444/R215 and R216 and includes more than BRCA1/2 and should be reflected in this update. | Thank you for your comments. The scope document currently lists headings from the current CG164 guideline, which refer specifically to BRCA1 and BRCA2. The guideline is not limited to BRCA1 and BRCA2 pathogenic variants. During development, the committee will consider cross-referring to the National genomic test directory instead of listing individual genes to test for. |

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| Association of Breast Surgery | 006 | 014 | Many units continue to use the B1/B2 classification set out by the RMH and ICR, rather than an individual risk that aligns with moderate risk group.<br><br>We are aware of a number of units that take the moderate risk group based on percentage risk and then decide if MMGS are 40-49 or 40-59 based on the B1/B2 criteria.<br><br>Should there be a sub-classification of the Moderate risk group to aid in this decision making? | Thank you for your comment. The committee were aware of the classification set out by the RMH and ICR and understand that this historically has been based on NICE guidelines. They acknowledged that there is variation in practice around the risk tools that are used. We will take your comments into account and explore this issue further with the committee in the development stage of the guideline when we review risk prediction tools. |
| Association of Breast Surgery | 006 | 017 | We are very aware that there is significant resource pressure on services to provide risk reducing surgery and reconstruction (esp autologous reconstructions). When considering the cost effectiveness the impact of implant surgery and further lifelong need for revisions should carefully be considered with clear recommendations that this revision surgery is considered from the outset and thus built into any modelling. | Thank you for your comments. We will consider them during development when we review the evidence for risk reducing mastectomy. |

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| | | | It should be made clear that this surgery is not a single episode and that all patients starting this pathway should be eligible for all forms of reconstruction revisions that are deemed appropriate in the future.<br><br>Given the pressure on services to deliver risk reducing surgery consideration should be given to the outcome it is hoped surgery can achieve. Aside from BRCA 1 mutation carriers there is limited evidence that surgery changes overall survival and this may need to be reflected. Should there be prioritisation based not only on lifetime risk but also on the where there is evidence survival is impacted. | |
| Yorkshire Cancer Research | 003 | 006 | Yorkshire Cancer Research agree that the 'Genetic testing for BRCA1, BRCA2 and TP53 mutations within 4 weeks of diagnosis of breast cancer' section should be considered for updating. It is vital that testing is carried out as soon after diagnosis as possible to be able to best inform treatment decisions. Timely testing can also ensure that people understand their risk of developing | Thank you for your comments. We plan to discuss this issue with the committee during development and amend the recommendations as required. |

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| | | | other cancers and can initiate cascade testing (see below). | |
| Yorkshire Cancer Research | General | General | There is no specific mention within the scope document of cascade testing. Yorkshire Cancer Research recommend that the guideline update should review the evidence for cascade testing both male and female relatives after discovering a genetic mutation. This could enable a better understanding of carrier probability and improve the early detection of various cancer types. | Thank you for your comment. As part of the planned work we will be looking at updating the sections of the guideline covering genetic testing and carrier probabilities for referral for genetic testing. Cascade testing is an important part of current practice, and this will be reflected as part of this work. |
| Yorkshire Cancer Research | 003 | 004 | The evidence around population based genetic screening is currently growing. For example, Yorkshire Cancer Research are currently funding PROTECT-C, a research study offering genetic testing to women, regardless of whether they or their families have had cancer. Increased evidence generation in this area could be critical for understanding carrier probability and enable more women to make informed decisions about their health. Studies such as this will provide a greater depth of understanding on population level rates of | Thank you for your comments. Population-based screening is managed by the UK National Screening Committee (UK NSC). For this guideline, genetic testing is focused on the identification of people with gene variants that predispose them to developing breast cancer based on their family history, ancestry with a high prevalence of pathogenic variants associated with breast cancer or having clinical or pathological features associated with heritable breast cancer rather than population-based screening, which is outside of the scope of this work and NICE's remit. |

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| | | | BRCA carriers. This guidance update should engage with population level studies and consider the value of recommending further research in this area. | |
| Yorkshire Cancer Research | General | General | There is no mention within this scope of the use of PARPi as a risk reduction strategy. In a recent position statement, Yorkshire Cancer Research along with six other organisations have called for research to explore the viability of whether poly (ADP-ribose) polymerase (PARP) inhibitors can be used as a chemo preventative treatment for people at high risk of hereditary cancers as part of a drive toward a future of precision cancer prevention. At this stage there is limited evidence for the use of PARPi within primary prevention. However, given the emerging evidence in terms of secondary prevention, the updated guideline should back this call for more research into the use of PARPi in risk reduction. | Thank you for your comments. We are currently unable to recommend PARP inhibitors as part of this guideline, as they are not currently licensed for chemoprevention.<br><br>NICE guidelines make research recommendations for topics where we have carried out an evidence review and found gaps in the evidence or limited evidence. See the Guideline manual section 9.5 for more information. We are dependent on some research being available for us to review before we would consider looking at a topic and we only make research recommendations on topics where we have reviewed the available evidence. |
| Yorkshire Cancer Research | 003 | 020 | Yorkshire Cancer Research recommends that 'Family history-taking and initial assessment in primary care' is added to the scope of this guidance update to consider broadening the information gathered for referral | Thank you for your comments. The committee do not plan to review evidence on ancestries with a high prevalence of pathogenic variants associated with breast cancer. However, as part of refreshing the guideline, the committee may |

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| | | | decisions to include other Founder populations alongside those with Jewish ancestry. | consider how these recommendations can be amended to include other at-risk populations such as those specified in R208 of the National genomic test directory. |
| UK Cancer Genetics Group | General | General | We are grateful to the committee for undertaking this essential work to update the out-of-date cg164 familial breast cancer guidelines. Our over-arching comment though is that there is a real tension between the NICE framework for updating a guideline, and the fact that the rapidly transforming field of genetic risk assessment creates the possibility that this scope will not deliver a workable meaningful document for clinical practice and without change and horizon scanning, this work will already be out of date by the time it is published.<br><br>Key considerations in this are<br><br>1. The increasing standardised use of multi-data risk assessment tools (e.g. CanRisk) entering ubiquitous clinical use where family history is only 1 component of the assessment. | Thank you for your comments and support for this update. We acknowledge the issues you raise around the difficulties in maintaining a guideline that covers a rapidly changing area of practice. We are constantly looking for methods and processes that will allow us to update our guidelines in a timely manner. We will bear these points in mind as we develop review protocols and carry out this update to the familial breast cancer guideline.<br><br>1. We acknowledge the increase in use of multi-data assessment tools such as CanRisk and we will be reviewing CanRisk in this update.<br><br>2 and 3. We have expanded the guideline population to include those people who could have an increased risk of breast cancer due family history, ancestry with a high prevalence of breast cancer predisposing pathogenic variants |

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| | | | 2. The rapid drive to offer breast cancer risk assessment outside of the context of clinically ascertained self-presenting families through the creation of neighbourhood hubs and population health pillars where breast cancer risk assessment does not rely on family history as an entry point.<br><br>3. The rapid increase in ubiquitous tumour/circulating tumour DNA and/or germline genetic testing for breast cancer patients under treatment-focussed indications, leading to increasing identification of germline pathogenic variants outside of the family history context.<br><br>4. The widening of NHS-funded breast cancer gene testing to the NHS England National Genomic Test Directory (and equivalent practice in Devolved Nations), broadening testing beyond *BRCA1* and *BRCA2* and *TP53*, making focus only on these genes narrow and leaving a significant knowledge gap for the other genes. | or because they have clinical or pathological features associated with heritable breast cancer.<br><br>4. The guideline is not limited to BRCA1, BRCA2 and TP53 pathogenic variants. During development, the committee will consider cross-referring to the National genomic test directory instead of listing individual genes to test for.<br><br>5. PRS are not routinely used in the NHS at this time. Therefore, we are not currently able to add people with a known PRS who do not meet other inclusion criteria (such as breast cancer, a known pathogenic variant in a breast cancer predisposition gene, or a family history of breast cancer) to the scope population. We acknowledge developments in this area and will examine the evidence to determine whether additional work on PRS is possible at this time and what this would entail, or whether this is a topic that should be monitored and included in the future when more evidence is available. |

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| | | | 5. The inevitable near-future inclusion of polygenic risk scores into integrated breast cancer risk assessments for unaffected individuals with and without a monogenic cancer predisposition, which will inform their genetic risk beyond family history.<br><br>6. The parallel NICE work to advise on stratified screening based on breast density, which if not aligned to this work would lead to women being given 2 different breast cancer risk assessments based on two different assessments leading to significant confusion for breast screening services. CanRisk can already incorporate genetic risk and breast density alongside other factors into a single risk assessment. We should focus patient centred care to deliver single integrated risk assessments, not produce multiple different new updated guidelines for breast cancer risk assessment and screening. | 6. We will assess the impact of the work of the National screening committee that is looking at additional screening based on breast density on our guideline when it is available. Population screening is the remit of the UK National screening committee and NICE is unable to make recommendations in this area. |

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| | | | We strongly advise the committee to consider these contexts in designing the scope of this review or there is the potential for a lot of panel resource and time to be taken up producing something unfit for clinical purpose. | |
| UK Cancer Genetics Group | General | General | Please can you italicise gene names? The use of italics for gene names enables them to be distinguished from the protein they produce and makes this document scientifically accurate. i.e. *BRCA1* = gene, BRCA1 = protein.<br><br>For affected individuals, please define if "breast cancer" extends to precancerous lesions (ductal carcinoma in situ) and, if so, of what grade (low, intermediate or high).<br><br>A distinction between bilateral risk-reducing mastectomy in unaffected individuals and contralateral risk-reducing mastectomy in currently or previously affected individuals is required. | Thank you for your comments. We have now removed reference to BRCA1 and BRCA2 mutations from the scope population and review questions and replaced them with 'ancestry with a prevalence of pathogenic variants associated with breast cancer'. We have retained this term in the scope where we refer to the existing headings in the guideline but they will be changed in the guideline as we carry out the update. We are unable to italicise gene names due to accessibility issues and in case the formatting is lost during editing. However, we will state when we mean a gene to make this clearer, for example, BRCA gene.<br><br>The scope has now been amended to clarify that a personal history of breast cancer refers to high grade DCIS and invasive breast cancer, which is in line with National genomic test directory R208. |

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| | | | | The committee will consider whether the reviews will stratify people with and without a personal history of breast cancer or treat bilateral or contralateral mastectomy as separate interventions when developing review protocols. We will remind them of your comment at this time. |
| UK Cancer Genetics Group | 001 | 023 | Will you define high prevalence more numerically? There are multiple different founder variants outside of the Ashkenazi Jewish community – not all of them have the same frequency. Some more specific guidance on what constitutes the prevalence of a clinically significant founder variant would be helpful. See "ancestry with a high prevalence of *BRCA1* or *BRCA2* mutations"<br><br>Are other genes with recognised founder variants out of scope e.g. *TP53* founder variants? | Thank you for your comments. We have amended the scope population to refer to "ancestry with a high prevalence of pathogenic variants associated with breast cancer" without listing any specific genes. This will allow consideration of evidence for a wider population, and we will confirm with the committee which genes should be included in addition to BRCA1 and BRCA2 at this time. However, the committee do not plan to review evidence on ancestries with a high prevalence of pathogenic variants associated with breast cancer and will therefore not be able to define high prevalence more numerically. |
| UK Cancer Genetics Group | 001 | 024 | "*because they have features associated with heritable breast* cancer" – does this mean clinical features of breast cancer associated syndromes? Or pathological features of a tumour (such as triple negative status), or will it also refer to those who have a higher risk of breast | Thank you for your comment. The scope has now been amended to clarify that this relates to clinical or pathological features associated with heritable breast cancer. |

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| | | | cancer due to polygenic risk which is also potentially heritable? What is your definition of "features?" | |
| UK Cancer Genetics Group | 002 | 010 | "*For the consideration of referral for genetic testing only*" – Given there are multiple different types of genetic test available now in the assessment of breast cancer risk (somatic testing on tumour, polygenic risk score testing) – you need to define that you mean germline genetic testing throughout this document if that is the type of test to which you are referring. | Thank you for your comment. We have edited the scope to clarify that genetic testing refers to germline testing. |
| UK Cancer Genetics Group | 002 | 020 | The comment regarding the "*equality and health inequalities assessment impact*" is noted but the hyperlink provided is not functional. Within the document as written there is little mention of strategies to improve equity of access in underserved groups. | Thank you for your comment and highlighting the error in the hyperlink that we will fix in the final published version.<br><br>We have added your comment to section 3.2 of the post-scope consultation Equality and health inequalities assessment (EHIA). When the committee review the evidence and make recommendations in the areas we are updating we will revisit the equality issues noted in the EHIA and consider whether any of the issues that have been raised can be mitigated by making additional recommendations. |

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| UK Cancer Genetics Group | 003 | 001 | Regarding "*Family history and carrier probability*" we presently do not work, and will not be working, in clinical pathways that use family history in isolation from other risk factors when we calculate carrier probability using integrated data models. Using family history in isolation in this document means it is already out of date | Thank you for your comments. These headings are from the current NICE CG164 guideline. We plan to address this issue with the committee during development and amend the recommendations as required. |
| UK Cancer Genetics Group | 003 | 003 | Genetic testing – the focus specifically on *BRCA1, BRCA2, TP53* risk is already out of date. Where germline genetic testing is indicated, most patients with breast cancer are offered a panel of genes, including *PALB2,* amongst others – it would be helpful to be inclusive for breast cancer genes tested in NHS practice, aligned with NHSE National Genomic Test Directory. | Thank you for your comments. These headings are from the current NICE CG164 guideline. We plan to address this issue with the committee during development and amend the recommendations as required. During development, the committee will consider cross-referring to the National genomic test directory instead of listing individual genes to test for. |
| UK Cancer Genetics Group | 003 | 006 | We note the recommendations for testing within 4 weeks of diagnosis of breast cancer; the turnaround time of laboratory testing (6-8 weeks) should be noted and considered in recommending timing of testing where result is required more expediently to guide immediate treatments/interventions. A comment on rapid testing pathways/use of technology-enhanced tools in consenting pathways would be welcomed. | Thank you for your comments. We will discuss this issue with the committee during development when we update the section on genetic testing. |

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| UK Cancer Genetics Group | 004 | 009 | Regarding secondary care, it should be noted that there is variability nationally with respect to care of presymptomatic women – certain regions have dedicated family history clinics, others rely on referral to routine breast surgical clinics, and in some regions, lack of access to dedicated services in secondary care results in increased (often inappropriate) referrals to clinical genetics. | Thank you for your comments. The care and management approach in secondary care section of the guideline is not within the scope of this update. However, we will bear your comment in mind when we make recommendations on carrier probability assessment and genetic testing. |
| UK Cancer Genetics Group | 005 | 014 | Assessing carrier probability: "a personal history of breast cancer *that is suspected to be heritable*" – all individuals with breast cancer should have appropriate consideration of whether they are likely to be carriers of a pathogenic variant in a breast cancer gene – this is how you decide the likelihood of heritability – you don't start with an assumption that some are heritable and some are not and then try to estimate carrier probability. This feels like an old-fashioned assumption that only individuals with some form of family history may carry pathogenic variants. All cancer patients should be universally assessed for carrier likelihood to determine if they require testing at the agreed NHS thresholds. | Thank you for your comments. We discussed this point with the committee and have now amended the carrier probability questions to remove reference to the suspicion of the breast cancer being heritable.<br><br>The committee will take into implementation into account when they make recommendations relating to testing thresholds and we will raise the issue you have highlighted about testing people at lower likelihood of carrying pathogenic variants in high-risk genes with them at this time.<br><br>We will consider whether any potential changes to the thresholds in this guideline might impact other related cancer |

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| | | | Consideration should be given to the workload associated with lowering (if applicable) of probability at which testing should be offered – not just in terms of numbers needed to test but in variant analysis and reporting, given that offering testing to people at lower likelihood of carrying variants in high-risk genes *BRCA1/BRCA2* is likely to inadvertently increase the yield of identification of variants in moderate risk genes routinely tested as part of breast cancer susceptibility panels - workload associated with variant interpretation in these genes is disproportionate to clinical utility (https://www.ukcgg.org/information-education/exceptional-variantsgene-specific-variant-reporting/).<br><br>Although beyond the scope of this document, it should be noted that changing thresholds for germline testing in patients with breast cancer may impact recommendations for testing across other related cancers (e.g. prostate, pancreatic etc), and indeed, | guidelines and decide what action to take during the guideline development stage. |

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| | | | unrelated cancers/testing of other cancer susceptibility genes. | |
| UK Cancer Genetics Group | 005 | 019 | "*Assessing the risk of developing breast cancer*" – why are you restricting which tools are best for assessing risk to these specific groups? Given the high likelihood of universal breast cancer risk assessment being incorporated into preventative and community health it would be helpful if you are doing this work to future proof for this by just stating which risk tools work for breast cancer risk prediction across the population both with and without a family history. Otherwise, we will likely be end up with a third guideline for breast cancer risk assessment using the same integrated data models at some point or just have a gap in the field – which would be a shame when population assessment for breast cancer risk is so inevitable. | Thank you for your comments. We have been unable to amend the review question as you requested because<br><br>It is outside of NICE's remit to make population-level recommendations as this would be classed as screening. |
| UK Cancer Genetics Group | 006 | 007 | "*At what carrier probability should people with breast cancer who have features associated with heritable breast cancer as well as or in addition to a family history of breast,* ***ovarian*** *or a related cancer….be offered genetic testing*" | Thank you for your comment. The focus of this guideline will be heritable breast cancer, but we are aware of the related recommendations in the ovarian cancer guideline and will try to avoid contradictions between the 2 guidelines. We are also aware of the issues around implementation of the ovarian |

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| | | | NICE released NG241 guidelines for familial ovarian cancer in March 2024 (Overview \| Ovarian cancer: identifying and managing familial and genetic risk \| Guidance \| NICE) – it would be important to make sure that these guidelines do not contradict each other and are in alignment to ensure equity amongst individuals with the same likelihood of carrying a pathogenic variant in the same gene – however, if NICE were to align and accept the carrier probability levels in guidelines NG241 to these updated guidelines for familial breast cancer, it would need to be aware that at the current time it is impossible that the NHS could either fund this increase in testing or manage the increased demand for clinical genetics services (Roe et al. 2025 Impact of NICE Guideline NG241 'Ovarian Cancer: identifying and managing familial and genetic risk' on a regional NHS family history and clinical genetics service \| Journal of Medical Genetics. | cancer guideline recommendations and plan to discuss implementation with the committee during the guideline development process |

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| | | | It would be very helpful for the committee to address this situation. | |
| UK Cancer Genetics Group | 006 | 012 | "*Surveillance and strategies for early detection of breast cancers*" – this is likely out of scope but we want to state on record that the absence of national funding or infrastructure to deliver moderate and high risk breast screening which fall outside of the national breast screening programme means that this is inequitable and poorly delivered across the UK – any increase in this without accompanying resource and infrastructure will exacerbate these inequalities.<br><br>Consideration of surveillance in women aged 50-59 who carry a (likely) pathogenic variant in *CHEK2/ATM/RAD51C/RAD51D* with an estimated very high 10-year breast cancer risk would also be welcome – at present, surveillance for carriers of such variants with very high estimated breast cancer risks is provided via the VHR programme but only up until age 50. | Thank you for your comments. This is an important point and we will take into account equity, resource use and implementation when updating the guideline. However, we cannot change funding allocations or infrastructure. We have added the point you raise to the section 3.2 of the Equality and health inequalities assessment that accompanies this work.<br><br>We are not able to directly amend the VHR programme as this is produced by the NHS but we appreciate that NICE recommendations feed into it and we will be exploring this issue in the development stage of the guideline. |

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| UK Cancer Genetics Group | 006 | 016 | "*Risk-reducing surgery*" – please specify which genes are in scope here? Are these all breast cancer susceptibility genes for which testing is currently available in the National genomic Test Directory? This should be risk-based not gene-based, since we have integrated data models which will account for the genotype. A personalised risk assessment is what should inform decisions regarding surgical prophylaxis – not population-based risks.<br><br>Effectiveness/cost effectiveness analyses should also consider possible alternative options (e.g. chemoprevention). This is particularly relevant for carriers of variants in *ATM/CHEK2*, which predominantly confer a risk of ER-positive breast cancer, and for whom the survival benefit (if any) of risk-reducing surgery is uncertain.<br><br>Guidance on lower and upper ages at which risk-reducing surgery should be considered (medical co-morbidities notwithstanding) would also be welcomed, | Thank you for your comments. In the review question on risk-reducing mastectomy we have included specific pathogenic gene variants as well as risk thresholds, previous cancer history, and age as potential groups we may want to make have as subgroups when we carry out our analyses. This could help inform recommendations about who would benefit most from risk reducing mastectomy. By including age as a potential factor of interest we may be able to provide the guidance you request about lower and upper ages.<br><br>We will discuss your comments further with the committee when we develop the review protocols. If the specific pathogenic variant category is included in a subgroup analyses, then it would be limited to the genes specified by the committee, but the main analyses will look at people have an increased risk irrespective of the pathogenic variants that underly this risk. We will raise your point about people with ATM/CHEK2 pathogenic variants during protocol development as these may be a subgroup of interest for our analyses. |

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| | | | considering the ages at which breast cancer surveillance starts and ends. At present, there are some women for whom risk-reducing surgery would be considered because of an estimated lifetime cancer risk but for whom enhanced screening is not yet available because of their age. | We do not plan to update the recommendations on chemoprevention at this time as we are not aware of any new evidence that would likely change the current recommendations. However, we will take your point about using this as a comparator in any cost-effectiveness analyses into account when we carry out the work on risk-reducing mastectomy. |
| OUTpatients Charity | 002 | 005, 007, 015, 016 | Trans men are men and trans women are women, so if you are referring cisgender men and women then that needs to be stated rather than just "men" and "women". | Thank you for your comment. The language used in the scope aligns with the NICE style guide where we don't refer to cis gender, but we do use trans . The editorial team at NICE have notified us that they don't use cisgender as NICE style is to use additive language to describe people groups for example, "trans men" and "trans women". This also aligns with other organisations such as the NHS when talking about "cis men" and "cis women". |
| OUTpatients Charity | 001<br>002 | 007-009<br>016-018 | The evidence is particularly solid around 5 years of oestrogen-based hormone therapy being the cut off for acquiring breast cancer risk. This is somewhat unevidenced based advice from UCSF (https://transcare.ucsf.edu/guidelines/breast-cancer-women ) and reiterated by the Radiological Society of | Thank you for your comments. The 5-year threshold was chosen based on the UK recommendations for the management of transgender and gender-diverse patients with inherited cancer risks consensus statement paper (see Table 2 section 4 on breast tissue management). |

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| | | | North America (https://pubmed.ncbi.nlm.nih.gov/31782932/ ). However, de Blok et al (https://pubmed.ncbi.nlm.nih.gov/31088823/ ) studying breast cancer in trans people without conclude " exposure to hormone treatment before breast cancer diagnosis was relatively short in trans women, at a median of 18 years" and that one of their cases had BRCA1 which may shorten this median. [redacted] One assumes that the risk is dependent on degree of breast development, rather than oestrogen exposure as models of BRCA-related cancer seem to be less sensitive to this, and therefore its simply about developing the breast duct structures in the first place. (https://www.medrxiv.org/content/10.1101/2025.09.15.25335324v1 ) I would therefore consider saying "or have had a significant degree of breast development". | We discussed your point about the risk relating to the degree of breast development with the committee and they agreed with it. However, they decided against amending the scope population as requested because they were unclear what constituted a significant degree of development and how inclusion of people on this basis this could be implemented in practice. In contrast using the 5-year threshold as a proxy for breast development is easily implementable. |

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| OUTpatients Charity | 003 | 010 | As opposed to just "women", should be "cisgender women, trans men, non-binary people who were assigned female at birth and trans women who have had at least 5 years of oestrogen-based hormone therapy or had a significant degree of breast development." | Thank you for your comment. The language used in the scope aligns with the NICE style guide where we don't refer to cis gender, but we do use trans . The editorial team at NICE have notified us that they don't use cisgender as NICE style is to use additive language to describe people groups for example, "trans men" and "trans women". This also aligns with other organisations such as the NHS when talking about "cis men" and "cis women".<br>The 5-year threshold was chosen based on the UK recommendations for the management of transgender and gender-diverse patients with inherited cancer risks consensus statement paper (see Table 2 section 4 on breast tissue management).<br><br>We discussed your earlier point about the risk relating to the degree of breast development with the committee and they agreed with it. However, they decided against amending the scope population as requested because they were unclear what constituted a significant degree of development and how inclusion of people on this basis this could be implemented in practice. In contrast using the 5-year |

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| | | | | threshold as a proxy for breast development is easily implementable. |
| OUTpatients Charity | 003 | 012 | As opposed to just "women", should be "cisgender women, trans men, non-binary people who were assigned female at birth and trans women who have had at least 5 years of oestrogen-based hormone therapy or had a significant degree of breast development." | Thank you for your comment. The language used in the scope aligns with the NICE style guide where we don't refer to cis gender, but we do use trans . The editorial team at NICE have notified us that they don't use cisgender as NICE style is to use additive language to describe people groups for example, "trans men" and "trans women". This also aligns with other organisations such as the NHS when talking about "cis men" and "cis women".<br><br>The 5-year threshold was chosen based on the UK recommendations for the management of transgender and gender-diverse patients with inherited cancer risks consensus statement paper (see Table 2 section 4 on breast tissue management).<br><br>We discussed your earlier point about the risk relating to the degree of breast development with the committee and they agreed with it. However, they decided against amending the scope population as requested because they were unclear |

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| | | | | what constituted a significant degree of development and how inclusion of people on this basis this could be implemented in practice. In contrast using the 5-year threshold as a proxy for breast development is easily implementable. |
| OUTpatients Charity | 003 | 014 | "Hormone replacement therapy" is not a risk reduction or treatment strategy. This should probably be "endocrine chemoprevention". Hormone replacement therapy could be within the scope of the guideline but needs its own section under "Potenial Risk Factors". | Thank you for your comments. The guideline will undergo an editorial refresh during development to bring existing recommendations into current NICE style, and we will consider these points as we restructure the guideline. |
| OUTpatients Charity | 004 | 015 | As opposed to just "women", should be "cisgender women, trans men, non-binary people who were assigned female at birth and trans women who have had at least 5 years of oestrogen-based hormone therapy or had a significant degree of breast development." | Thank you for your comment. The language used in the scope aligns with the NICE style guide where we don't refer to cis gender, but we do use trans . The editorial team at NICE have notified us that they don't use cisgender as NICE style is to use additive language to describe people groups for example, "trans men" and "trans women". This also aligns with other organisations such as the NHS when talking about "cis men" and "cis women".<br>. The 5-year threshold was chosen based on the UK recommendations for the management of transgender and gender-diverse patients with inherited cancer risks |

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| | | | | consensus statement paper (see Table 2 section 4 on breast tissue management).<br><br>We discussed your earlier point about the risk relating to the degree of breast development with the committee and they agreed with it. However, they decided against amending the scope population as requested because they were unclear what constituted a significant degree of development and how inclusion of people on this basis this could be implemented in practice. In contrast using the 5-year threshold as a proxy for breast development is easily implementable. |
| OUTpatients Charity | 004 | 016 | As opposed to just "women", should be "cisgender women, trans men, non-binary people who were assigned female at birth and trans women who have had at least 5 years of oestrogen-based hormone therapy or had a significant degree of breast development." | Thank you for your comment. The language used in the scope aligns with the NICE style guide where we don't refer to cis gender, but we do use trans . The editorial team at NICE have notified us that they don't use cisgender as NICE style is to use additive language to describe people groups for example, "trans men" and "trans women". This also aligns with other organisations such as the NHS when talking about "cis men" and "cis women". |

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| | | | | The 5-year threshold was chosen based on the UK recommendations for the management of transgender and gender-diverse patients with inherited cancer risks consensus statement paper (see Table 2 section 4 on breast tissue management).<br><br>We discussed your earlier point about the risk relating to the degree of breast development with the committee and they agreed with it. However, they decided against amending the scope population as requested because they were unclear what constituted a significant degree of development and how inclusion of people on this basis this could be implemented in practice. In contrast using the 5-year threshold as a proxy for breast development is easily implementable. |
| OUTpatients Charity | EIA | Page 008 | Sexual orientation and Gender Reassignment are separate characteristics and require separate sections | Thank you for your comment. We have corrected this error in the Equality and health inequalities assessment, which accompanies the scope. |
| OUTpatients Charity | EIA | Page 008 | "There are also known issues with NHS IT systems, where it is not currently possible to add people who are registered as male on their medical records to the very | Thank you for your comment. We have added this information to section 3.2 of the updated Equality and health inequalities assessment, which accompanies the scope. |

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| | | | high risk (VHR) screening programme." – This should come at the end, after sections regarding trans men and trans women, as the issue of male registration can affect either.<br><br>In addition, timely access to genetic counselling and appropriate screening affects decision making about gender affirming interventions, including gender affirming male chest reconstruction (and whether all breast tissue is removed or not), risk reducing bilateral salpingoophorectomy (which lowers oestrogen further than testosterone therapy alone) and whether to access oestradiol therapy (trans women and non-binary people who were assigned male at birth). (https://pubmed.ncbi.nlm.nih.gov/39516684/, https://www.sciencedirect.com/science/article/abs/pii/B9780323885348000080, https://link.springer.com/article/10.1007/s40142-021-00201-6 ) | |

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| British Society of Breast Radiology | General | General | Surveillance will rely heavily on imaging and representation from screening and symptomatic services should be present | Thank you for your comments. We will consider whether we need to recruit additional committee members to provide this expertise. |
| British Society of Breast Radiology | 005 | 019 | Image based risk prediction tools with AI are being developed in research areas. The review may wish to assess evidence in this area | Thank you for your comment. It would be helpful if you could clarify if you are referring to AI technologies being used alongside imaging in surveillance or to AI technologies being used in predicting risk? This issue is not currently covered by the scope of this piece of work. However, if you have evidence to support its inclusion in future work please can you share it with us by submitting a topic suggestion through our topic prioritisation process. See here for information on the prioritisation process and the submission form:<br>• Prioritising our guidance topics<br>• Topic suggestion |
| British Society of Breast Radiology | 006 | 012 | Along with surveillance strategies the type of surveillance and if using MRI the increasing use for fast/or shortened MRI protocols, contrast enhanced mammography and automated breast ultrasound would be of relevance to review | Thank you for your comment. This issue is not currently covered by the scope of this piece of work. However, if you have evidence to support its inclusion in future work please can you share it with us by submitting a topic suggestion through our topic prioritisation process. See here for |

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| | | | | information on the prioritisation process and the submission form:<br>• Prioritising our guidance topics<br>• Topic suggestion |
| British Society of Breast Radiology | 006 | 021 | Costs of radiologist and radiographic staffing would also be affected by any change in guidelines and will need factored as part of any economic assessment | Thank you for your comment, we will take relevant costs into account when we make recommendations. The updated guideline will also be accompanied by a resource impact assessment. |
| NHS England | 006 | 003 - 011 | Agree that carrier probability for genetic testing in affected and unaffected people needs to be included in scope.<br><br>However the scope document makes reference to just BRCA1 and BRCA2 genes for testing. But if a person is offered germline genetic testing for inherited breast cancer as per eligibility criteria in the NHS National Genomics Test Directory, they will get a test for a panel of genes that includes more than BRCA1 and BRCA2. The current gene content includes: BRCA1, BRCA2, PALB2, ATM, CHEK2, RAD51C and RAD51D. The scope should include reviewing genetic testing for all the | Thank you for your comments. We do not plan to review which pathogenic variants should be tested for, and the committee will include a cross-refer to the National genomic test directory during development of the update of the genetic testing section of the guideline.<br><br>The review questions your comment refers to limit ancestry to people with ancestry with a high prevalence of BRCA1 or BRCA2 varaints. We have amended the scope population to refer to "ancestry with a high prevalence of pathogenic variants associated with breast cancer" without listing any specific genes. This will allow consideration of evidence for a wider population, and we will confirm with the committee |

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| | | | genes and making recommendations on both the carrier probability and the genes to test.<br><br>Stating that carrier probability will only be reviewed for people who have features associated with heritable breast cancer as well as or in addition to family history of breast, ovarian or a related cancer or ancestry with a high prevalence does not need to be specified in this context as the calculation of carrier probability takes all these into account.<br><br>Suggest text is amended to the following, changes are highlighted in blue:<br><br>"At what carrier probability should people with breast cancer ~~who have features associated with heritable breast cancer as well as or in addition to a family history of breast, ovarian or a related cancer or ancestry with a high prevalence of BRCA1 or BRCA2 mutations~~ be offered genetic testing and what genes should be tested?" | which genes should be included in addition to BRCA1 and BRCA2 at this time.<br><br>We have taken your suggestions into account and have now updated the carrier probability questions as suggested. |

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| | | | "At what carrier probability should people without a personal history of breast cancer~~, but with a family history of cancer suggestive of heritable breast cancer or ancestry with a high prevalence of BRCA1 or BRCA2 mutations~~ be offered genetic testing and what genes should be tested? | |
| NHS England | General | General | The Guideline refers to two groups of people, those with:<br>• a personal history of breast cancer that is suspected to be heritable or<br>• no personal history of breast cancer but a family history of breast, ovarian or a related cancer, or ancestry with a high prevalence of BRCA1 or BRCA2 mutations.<br><br>Please could the group of people that do not have a personal history of breast cancer but have ancestry with a high prevalence of BRCA 1 or BRCA2 mutations be reviewed as a distinct and separate group to the people who do not have a personal history of breast cancer but have a relevant family history. | Thank you for your comments. The scope includes the populations that will be included in the guideline, but it will be determined at the protocol development stage which populations will be separated into subgroups based on the committee's advice and expertise. We will raise your request with the committee at this time.<br><br>We have amended the scope population to refer to "ancestry with a high prevalence of pathogenic variants associated with breast cancer" without listing any specific genes. This will allow consideration of evidence for a wider population, and we will confirm with the committee which genes should be included in addition to BRCA1 and BRCA2 at this time. |

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| | | | Could the review not restrict ancestry to just BRCA1 or BRCA2 high prevalence but check if there are any other groups where ancestry has high prevalence for the other genes that are tested for inherited breast cancer i.e. PALB2, ATM, CHEK2, RAD51C and RAD51D. | |
| NHS England | General | General | Terminology has changed and instead of using the term "mutations", should use pathogenic variants. | Thank you for your comment. We have changed "mutations" to "pathogenic variants" in the scope populations and review questions and will use this terminology going forward. We have retained this term in the scope where we refer to the existing headings in the guideline but they will be changed in the guideline as we carry out the update. |
| NHS England | General | General | The scope includes economic aspects but should also include review of recommendations in relation to equity for all people who could benefit from genetic testing for the breast cancer predisposing genes (currently BRCA1, BRCA2, PALB2, ATM, CHEK2, RAD51C and RAD51D) and enhanced screening / prophylactic surgeries. | Thank you for your comments. The committee will consider any equity issues during development of the recommendations. Equity issues that have been identified at the scoping stage have been reported in the Equality and health inequalities assessment. |

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| NHS England | 003 | 005 | What is meant by "mutation test"? Please define. Does this mean genetic testing in general and does this mean that NICE will review and recommend what genes should be tested in each clinical scenario that is being reviewed? Or does this mean that NICE will review variants (i.e. mutations) that should be tested? | Thank you for your comments. These headings are from the current NICE CG164 guideline. We plan to refresh the guideline and these heading will likely change. We do not plan to review which pathogenic variants should be tested for, and the committee will include a cross-refer to the National genomic test directory during development of the update of the genetic testing section of the guideline . |
| NHS England | General | General | People with a learning disability and autistic people experience significant health inequalities such as those as highlighted in LeDeR reports (Learning from Lives and Deaths of people with learning disability and autistic people) https://www.kcl.ac.uk/research/leder and so it is important that consideration is given to their particular needs and to ensuring equality of access, experience and outcomes in healthcare services.<br>· We suggest including a reference to making reasonable adjustments to care on the basis of disability. This is a legal requirement in the Equality Act 2010 and is important to help you make the right diagnostic and treatment decisions for an individual. You can ask the person and their carer or family member what | Thank you for your comments. The points you raise about making reasonable adjustments have been added to section 3.2 of the updated Equality and Health Inequalities Assessment, which accompanies the scope.<br><br>The NICE guideline on Patient experience in adult NHS services includes recommendations about knowing the patient as an individual that cover taking the requirements of the Equality Act 2010 into account and making sure NHS services are equally accessible and supportive for everyone using them. The updated guideline will include cross reference to this guideline. |

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| | | | reasonable adjustments should be made. Adjustments aim to remove barriers, do things in a different way, or to provide something additional to enable a person to receive the assessment and treatment they need. Possible examples include; allocating a clinician by gender, taking blood samples by thumb prick rather than needle, providing a quiet space to see a patient away from excess noise and activity. Resources are available such as NHS England » Sensory-friendly resource pack and NDTi \| Green Light Toolkit 2022.<br>· Ensuring information and advice is in formats that is accessible and can easily be understood is essential In line with the NHS England » Accessible information standard<br>· Be aware of diagnostic overshadowing: This occurs when the symptoms of physical ill health are mistakenly either attributed to a mental health or behavioural problem or considered inherent to the person's learning disability or autism diagnosis. People with a learning disability or autistic people have the same illnesses as everyone else, but the way they | |

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| | | | respond to or communicate their symptoms may be different and not obvious. More information can be found in this guidance:. NHS England » Clinical guide for front line staff to support the management of patients with a learning disability and autistic people – relevant to all clinical specialties | |
| NHS England | General | General | The NHS Cancer Programme welcomes the development of this guideline as it addresses an area of unmet need within cancer diagnosis. | Thank you for your comments and for your support of this update. |
| NHS England | General | General | We support this scope including consideration of people with ancestry with a high prevalence of BRCA1 or BRCA2 mutations, which includes the Ashkenazi Jewish population. This guideline may support onwards policy decisions, including the inclusion of this cohort on the National Genomic Testing Directory. | Thank you for your comments and for your support of this update. |
| NHS England | General | General | We encourage NICE to provide clarity on the limitations of risk prediction models. For example, cancer patients on endocrine therapy will have a different risk of future cancers than those who do not. | Thank you for your comments. We will consider this during development when we review the evidence for the risk prediction models. |
| NHS England | General | General | This scope should set a clear position on where the diagnosis of ductal carcinoma in situ (DCIS) fits within | Thank you for your comment. We have added a definition of breast cancer that includes high grade DCIS. |

# Familial Breast Cancer: initial assessment and genetic testing

## Consultation on draft scope
## Stakeholder comments table

## 22/09/2025 – 03/10/2025

***Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.***

| Stakeholder | Page no. | Line no. | Comments<br>Please insert each new comment in a new row | Developer's response<br>Please respond to each comment |
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| | | | guidance on breast cancer diagnosis. For example, high grade DCIS can count as a cancer diagnosis when using the Manchester score, but some models outline DCIS as an exception. This should be clarified. | |
| NHS England | General | General | This scope should also consider a combination of family history and the diagnosis of an equivalence B3 lesion in terms of risk and the management of this risk. | Thank you for your comment. We have added definitions for breast cancer (to include high grade DCIS and invasive breast cancer) and family history to the scope, however the committee agreed that B3 lesions should not be covered. |
| Royal College of Pathologists | General | General | No comments. | Thank you for reviewing the scope. |
| National Hereditary Breast Cancer Helpline | 003 | 003 | 3 Genetic testing<br>there is no mention of<br>1. Polygenic risk score testing (PRS)<br>2. Testing of breast cancer genes beyond BRCA1/2 and TP53 notably no mention of CHEK2,ATM, PALB2 which are found on population based screening more than the other three combined<br>3. R208 breast cancer test screens 7 genes and many women prior to 2020 only had testing for | Thank you for your comments.<br><br>1. PRS are not available currently on the NHS, although some people may have this test carried out privately and bring the results to their NHS risk assessments. PRS were not included specifically in the current scope, but we will examine the evidence presented by stakeholders as part of this consultation to determine whether additional work on PRS is possible at this time and what this would entail, or whether this is a topic that should be monitored and included |

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| | | | BRCA1/2 is there a need to offer restesting to this group for the additional genes if original testing was negative?<br><br>Please note the clinical utility of CHEK2 and ATM have been called into question by an expert group for ESMO https://pubmed.ncbi.nlm.nih.gov/40523834/. Multiple papers show that PRS may be more useful for risk assessment than testing additional genes in women with a family history particularly if not due to BRCA1/2 but may also provide more accurate assessment even for high risk genes. These two element are vital for this review and it would be a major oversight not to include | in the future when more evidence is available.<br><br>2. The section on genetic testing in the scope document refers to the headings used in the current CG164 guideline, which specifically refer to BRCA1 and BRCA2. But the guideline is not limited to looking at BRCA1 and BRCA2 pathogenic variants. During development, the committee will consider cross-referring to the National genomic test directory instead of listing individual genes to test for.<br><br>3. We will discuss your point about retesting with our committee during development.<br><br>We will not be reviewing the specific genes that are included in the gene testing panels, but plan to cross refer to the National genomic test directory to future proof the genetic testing section of the guideline.<br><br>PRS were not included specifically in the current scope, but we will examine the evidence presented in stakeholder comments from this consultation to determine whether |

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| | | | | additional work on PRS is possible at this time and what this would entail, or whether this is a topic that should be monitored and included in the future when more evidence is available. |