

## **UK National Screening Committee**

### **Additional screening with ultrasound after negative mammography screening in women with dense breasts**

**27 February 2019**

#### **Aim**

1. To ask the UK National Screening Committee (UK NSC) to make a recommendation, based on the evidence presented in this document, whether or not additional screening with ultrasound after negative mammography screening in women with dense breasts would be beneficial for the women and the screening provides value for money.

#### **Current recommendation**

1. The NHS Breast Screening programme screens women aged 50-70 using mammography every 3 years, with no routine measurement or reporting of mammographic breast density.
2. Some other countries report mammographic breast density to women attending screening, as the dense breast parenchyma may obscure cancer on a mammogram and density may itself be a risk factor for developing cancer. Others offer additional ultrasound testing for women with mammographically dense breasts.
3. This systematic review was commissioned by the UK NSC secretariat to provide a summary of evidence to date on the matter. Thus far there has been no formal approach to modify the programme on the basis of breast density or to add ultrasound; so, this review has been produced as an occasional internal briefing paper on matters of pressing screening interest.

#### **Evidence review**

4. The objectives of this document are to determine the balance of benefits and costs of measuring breast density on mammography, and offering women with dense

breasts supplemental ultrasound screening. The UK NSC criteria for appraising screening programmes state that there should be a validated screening test; there should be robust evidence about the association between the risk factor and serious or treatable disease; and screening should provide value for money. Therefore, this evidence review looked at:

- I. the reliability and validity of available methods to measure mammographic breast density;
  - II. if mammographic breast density is a risk factor for cancers being missed during screening (masking on mammograms/false negatives/interval cancers) and for developing breast cancer; and
  - III. the test accuracy of ultrasound following mammography in comparison to mammography to detect cancer in women with dense breasts.
5. The review also looked at the cost-consequences of adding mammographic density measurements, and then ultrasound for those found to have high mammographic breast density for women attending breast screening in the UK.
6. The systematic review concluded that:
- I. There was a strong consistent association between mammographic breast density and risk of breast cancer. There were consistent findings of reduced sensitivity of mammography and/or increased risk of interval cancers with increasing mammographic breast density. **Criterion 1 met**
  - II. It is difficult to validate the density methods when there is no gold standard applicable to breast density measurement. Ultrasound is not precise because it leads to large numbers of false positives, and while it can detect additional cancers not found on mammography, we do not have evidence as to whether this reduces either interval cancers or mortality, or to what extent identification of additional cancers represents overdiagnosis. **Criterion 4 not met**

- III. There is insufficient evidence for cost-effectiveness of supplemental ultrasound, and the available evidence suggests that it is not currently cost-effective. **Criterion 14 not met**
7. If density assessment followed by supplementary ultrasound screening were undertaken in the current NHS breast screening programme, women could be categorised differently between readers or screening occasions unless a standardized programme-wide method of density assessment were used. Such a programme however would be likely to lead to increased anxiety and resource use (for women identified as at higher risk who might not actually be at higher risk), and to confusion for women whose categorization changed. The evidence in this review suggests that the numbers of false positives and additional biopsies are unlikely to be justified and that there is as yet no clear cost effectiveness evidence to balance the benefits, harms and costs.

### **Consultation**

2. A three month consultation was hosted on the UK NSC website from 19 September to 19 December 2018. Direct emails were sent to the following 18 stakeholders.

#### **Annex A**

3. A sole consultation response was received from Cancer Research UK (**Annex B**).
4. CRUK agreed with the findings of the report including that there was insufficient evidence to support the introduction of ultrasound. The response includes the following information:

“Cancer Research UK is currently supporting a £2.8 million study on risk adaptive breast screening. The study aims to evaluate the feasibility of a risk adaptive approach and will assess a range of automated breast density assessment tools. It will also test the feasibility of different supplemental imaging techniques in a screening setting, including Whole Breast Ultrasound. The study will seek to establish which density score would serve as a threshold in which it would be appropriate and effective to offer additional supplemental imaging tests”.

## Recommendation

8. The Committee is asked to approve the following recommendation:

*Additional screening with ultrasound after negative mammography screening in women with dense breasts should not be recommended.*



| Criteria (only include criteria included in the review)  | Met/Not Met    |
|--|----------------|
| <b>The Condition</b>   |                |
| 1. The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease   | <b>Met</b>     |
| <b>The Test</b>  |                |
| 4. There should be a simple, safe, precise and validated screening test.   | <b>Not Met</b> |
| <b>The screening programme</b>   |                |
| 14. The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (value for money). Assessment against this criteria should have regard to evidence from cost benefit and/or cost effectiveness analyses and have regard to the effective use of available resource. | <b>Not Met</b> |

**List of organisations contacted:**

1. The British Association for Cancer Research
2. British Association of Surgical Oncology
3. Cancer Research UK
4. Faculty of Public Health
5. Macmillan
6. Northern Ireland Cancer Network
7. Royal College of General Practitioners
8. Royal College of Nursing
9. Royal College of Pathologists
10. Royal College of Physicians
11. Royal College of Physicians and Surgeons of Glasgow
12. Royal College of Physicians of Edinburgh
13. Royal College of Radiologists
14. Royal College of Surgeons
15. Royal College of Surgeons of Edinburgh
16. Society and College of Radiographers
17. xxxx xxxx, Consultant Radiologist with a Special Interest in Breast Imaging, NHS
18. xxxx xxxx, NHS England



**December 2018**

**Cancer Research UK response to the UK National Screening Committee consultation: assessing mammographic breast density and the use of ultrasound in breast cancer screening**

**Introduction**

Cancer Research UK welcomes the opportunity to respond to this consultation. Breast cancer is the most common form of cancer in the UK, accounting for 15% of all new cancer cases each year and over 11,500 deaths each year.<sup>i</sup> Currently the Breast Screening Programme invites all women aged 50-70 for screening every three years. The screening programme detects cancer in about 8 out of every 1,000 women screened<sup>ii</sup> and prevents around 1,300 cancer deaths each year.<sup>iii</sup> Yet, for every death prevented through breast screening, 3 women will be overdiagnosed and undergo unnecessary treatment.<sup>iv</sup> Further to this, false negative results mean that 11% of women with breast cancer will have their disease missed at screening.<sup>v</sup> We welcome efforts to improve the current programme, including the investigation into the link between breast density and breast screening. It is vital, however, that national policy is based on the most appropriate and sufficiently robust evidence.

**Key points**

- We agree with the National Screening Committee at this stage to not recommend additional breast density measurements or supplemental ultrasound in the Breast Screening Programme.
- It is essential to establish a safe, consistent and reliable method of measuring breast density before its routine use in clinical procedure could be considered. The current lack of a gold standard method must be addressed.
- We agree that evidence suggests breast density increases the risk of developing breast cancer and of cancers being missed during screening. However, we believe that further high-quality and better designed studies need to be conducted in both areas to build the evidence base on both clinical and cost-effectiveness within a screening programme.
- Further studies are also needed to measure the effectiveness of supplementary ultrasound in detecting cancers missed by mammograms, as the existing evidence is of low-quality. Studies must establish to what extent this would represent overdiagnosis as opposed to reducing interval cancers and mortality.
- We also call for future research to focus on the UK screening population, as international evidence may not be representative. Cancer Research UK is currently supporting a £2.8 million study into risk adaptive breast screening, which will help to address this issue.

**Further information**

Overall, we agree that mammographic breast density is an increased risk factor for developing breast cancer. However, many studies in this area are highly heterogeneous and inconsistent, as most primary research in this area consists of case-control studies which are generally lower quality

and subject to biases. Because of the gaps in the evidence, future studies must further investigate the association between breast density and breast cancer risk before supplementary ultrasound screening could be considered within the breast cancer screening programme.

We agree that there is evidence to suggest that high breast density can mask tumours and decrease the sensitivity of mammography. However, we strongly support the call for more high-quality studies to be conducted. This is due to a high variation in methods used to measure breast density, the limitations in the study design, and the fact that this area of research is still in its infancy. Further high-quality evidence is vital to accurately assess the potential benefits that mammographic breast density assessment may bring, including the reduction in interval cancers.

The report makes clear that there is currently no gold standard for measuring mammographic breast density. There are a variety of methods available, from visual through to fully automated, and numerous ways of conducting each method. The disparity in results between and within the different methodologies is striking, and we agree that National Screening Committee (NSC) criterion 4 – that there should be a simple, safe, precise and validated screening test – is not met.

It is essential that a reliable and consistent method for measuring breast density is established to prevent women from being categorised differently by different methods. We do not believe that measuring breast density can be integrated into the screening programme until there is a clear consensus on which method is clinically best. To reach a consensus on the best means of measuring breast density, stronger evidence is needed. We support the call for more UK-based studies that use multiple methodologies across different centres; this will help to build evidence of the clinical effectiveness and the best method of using this within the screening programme.

No good-quality studies were available to review regarding the use of supplemental ultrasound for women with dense breasts. While we commend the authors for updating a previous large-scale review from the USA, it remains the case that there is insufficiently robust evidence available to support a recommendation. With regards to evidence reviewed in this report, the authors raise a critical point: while ultrasound does appear to detect additional cancers, it is not clear whether this reduces either mortality or interval cancers, or to what extent identification of additional cancers represents overdiagnosis.

Cancer Research UK is currently supporting a £2.8 million study on risk adaptive breast screening. The study aims to evaluate the feasibility of a risk adaptive approach and will assess a range of automated breast density assessment tools. It will also test the feasibility of different supplemental imaging techniques in a screening setting, including Whole Breast Ultrasound. The study will seek to establish which density score would serve as a threshold in which it would be appropriate and effective to offer additional supplemental imaging tests.

Given that there is not sufficient evidence to support the policy recommendations, we cannot comment on cost-effectiveness at this time.

## **About us**

Cancer Research UK is the world's largest independent cancer charity dedicated to saving lives through research. It supports research into all aspects of cancer and this is achieved through the work of over 4,000 scientists, doctors and nurses. In 2017/18, we spent £423 million on research in institutes, hospitals and universities across the UK. We receive no funding from the Government for our research and are dependent on fundraising with the public. Cancer Research UK wants to accelerate progress so that three in four people survive their cancer for 10 years or more by 2034. For more information, please contact [xxxx xxxx](#), Policy Advisor, on [xxxx xxxx](#) or [xxxx xxxx](#)





**UK National  
Screening Committee**

<sup>i</sup> Data provided by the Office for National Statistics on request, October 2017; <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/mortality#heading-Zero>

<sup>ii</sup> NHS Breast Screening Programme (NHSBSP). [Breast Screening Results from the NHSBSP 2012/13](#). London: Queen Mary University of London; 2014.

<sup>iii</sup> Independent UK Panel on Breast Cancer Screening. [The benefits and harms of breast cancer screening: an independent review. Lancet 2012; 380; 1778-86.](#)

<sup>iv</sup> Independent UK Panel on Breast Cancer Screening [The benefits and harms of breast cancer screening: an independent review. Lancet 2012; 380; 1778-86.](#)

<sup>v</sup> 6. Lei J, Yang P, Zhang L, Wang Y, Yang K. [Diagnostic accuracy of digital breast tomosynthesis versus digital mammography for benign and malignant lesions in breasts: a meta-analysis. Eur Radiol 2014; 24\(3\): 595-602.](#)