

A Technical Review of Breast Density Reporting in Cancer Screening

Citation: Health New Zealand | Te Whatu Ora. 2025. *A technical review of breast density reporting in cancer screening*.   
Wellington: Health New Zealand | Te Whatu Ora.

Published in May 2025 by Health New Zealand | Te Whatu Ora  
PO Box 793, Wellington 6140, New Zealand

ISBN 978-1-991139-35-1 (online)



This document is available at [tewhatuora.govt.nz](https://www.tewhatuora.govt.nz/)

|  |  |
| --- | --- |
|  | This work is licensed under the Creative Commons Attribution 4.0 International licence. In essence, you are free to: share i.e., copy and redistribute the material in any medium or format; adapt i.e., remix, transform and build upon the material. You must give appropriate credit, provide a link to the licence and indicate if changes were made. |

# Working Group Members

|  |  |  |  |
| --- | --- | --- | --- |
| Name | Agency | Directorate | Team/Title |
| Dr Karen Bartholomew  (Co-Chair) | Health NZ | Te Whatu Ora | Planning, Funding and Outcomes | Director Health Gain Development |
| Dr Jane O'Hallahan  (Co-Chair) | Health NZ | Te Whatu Ora | National Public Health Service | Clinical Lead Screening |
| Dawn Wilson | Te Aho o Te Kahu Cancer Control Agency |  | Kaitohu Mātāmua, Chief Advisor Policy |
| Clare Possenniskie | Ministry of Health | Public Health Agency | Public Health Policy and Regulation, Manager |
| Lisa te Paiho | Health NZ | Te Whatu Ora | National Public Health Service | BreastScreen Aotearoa, National Cancer Screening Programmes, Prevention, Programme Manager |
| Dr Karen McIlhone | Health NZ | Te Whatu Ora | National Public Health Service | Clinicians Screening, Public Health Physician |
| Dr Catriona Murray | Health NZ | Te Whatu Ora | National Public Health Service | Clinicians Screening, Public Health Medicine Registrar |
| Dr Glyn Thomas | Health NZ | Te Whatu Ora |  | Radiologist |
| Dr Rebekah Roos | Health NZ | Te Whatu Ora | National Public Health Service | Clinicians Screening, Principal advisor |
| Tami Xirafakis | Health NZ | Te Whatu Ora | National Public Health Service | BreastScreen Aotearoa, National Cancer Screening Programmes, Prevention, Senior Advisor |
| Mr Adam Stewart | Health NZ | Te Whatu Ora | National Public Health Service | BreastScreen Aotearoa, National Screening Unit, Surgeon & National Clinical Lead |
| Wendy Bennett | Health NZ | Te Whatu Ora | Planning, Funding and Outcomes | Health Gain Development, Scientific and Technical Group Manager |
| Dr Victoria Child | Health NZ | Te Whatu Ora | Planning, Funding and Outcomes | Health Gain Development, Research Analyst |
| Dr Bronwen Chesterfield | Health NZ | Te Whatu Ora | Planning, Funding and Outcomes | Population Health Gain, Public Health Physician |
| Dr CK Jin | Health NZ | Te Whatu Ora | Planning, Funding and Outcomes | Clinical Director, Artificial Intelligence Laboratory |
| Danielle Griffioen | Health NZ | Te Whatu Ora | Hauora Māori Services | Public and Population Health, Pae Ora Programme Manager |
| Isabelle Moody | Health NZ | Te Whatu Ora | Planning, Funding and Outcomes | Project Coordinator, Health Gain Development |

# Early input, review and consultation

The following groups/people contributed advice, expertise and commentary to the working group with early input, review and feedback, advice and consultation:

* Dr Nina Scott (Ngāpuhi, Ngāti Whātua, Waikato), Public Health Physician, interim Chief Medical Officer Hauora Māori Services, NSAC member. Dr Scott supported Māori review at several points in the development of the report and included opportunity for review via the several of the groups below
* Dr Gary Jackson, Public Health Physician, Clinical Director Planning Performance and Health Outcomes, NSAC member
* BreastScreen Aotearoa Māori Monitoring and Equity Group (MMEG)
* BreastScreen Aotearoa Partnership, Action & Equity Rōpū (PAE)
* BreastScreen Aotearoa Pae Whakatere
* BreastScreen Aotearoa Lead Providers/Clinical Directors Unidisciplinary Groups (UDG)
* National Screening Advisory Committee (NSAC)

# Peer Reviewers

|  |  |
| --- | --- |
| Reviewed by | Expertise |
| Professor Mark Elwood | Cancer epidemiologist, University of Auckland; National Screening Advisory Committee (NSAC) member |
| Dr John McMillan | Bioethicist, University of Otago; NSAC member |
| Clare Possenniskie | Manager of Public Health Policy and Regulation, Public Health Agency, Ministry of Health |
| Dr Siniva Sinclair | Pacific Public Health Physician, Population Health and Strategy, Te Whatu Ora |

Contents

[Working Group Members 3](#_Toc199925573)

[Early input, review and consultation 4](#_Toc199925574)

[Peer Reviewers 5](#_Toc199925575)

[Glossary and Abbreviations 10](#_Toc199925576)

[Executive summary 14](#_Toc199925577)

[1 Introduction 17](#_Toc199925578)

[2 Breast Screening in Aotearoa New Zealand 17](#_Toc199925579)

[2.1 BreastScreen Aotearoa 17](#_Toc199925580)

[2.2 Breast Screening Pathway 18](#_Toc199925581)

[2.3 BreastScreen Aotearoa programme metrics 20](#_Toc199925582)

[2.4 BreastScreen Aotearoa and Breast Density 21](#_Toc199925583)

[3 What is Breast Density 22](#_Toc199925584)

[3.1 Breast density distribution in the population 23](#_Toc199925585)

[4 Breast Density Measurement 24](#_Toc199925586)

[4.1 Current State 24](#_Toc199925587)

[4.2 Artificial Intelligence 25](#_Toc199925588)

[5 Breast Density as a Risk Factor for Breast Cancer 27](#_Toc199925589)

[5.1 Effects of Breast Density on Risk of Breast Cancer and Sensitivity of Mammography 27](#_Toc199925590)

[6 Risk Assessment Tools 31](#_Toc199925591)

[7 Supplemental Screening 33](#_Toc199925592)

[7.1 International Supplemental Screening Practice 35](#_Toc199925593)

[7.2 Supplemental Screening Modality Outcomes 37](#_Toc199925594)

[7.3 Breast screening benefits and the potential additional benefit of Breast Density reporting 38](#_Toc199925595)

[7.4 Breast screening harms and the potential additional harms of Breast Density reporting 41](#_Toc199925596)

[8 Breast density reporting 43](#_Toc199925597)

[8.1 Internationally 43](#_Toc199925598)

[8.2 Supplemental Screening Guidelines 45](#_Toc199925599)

[8.3 Ethical and legal considerations 49](#_Toc199925600)

[9 Perspectives on Breast Density Reporting 51](#_Toc199925601)

[9.1 Consumer information 51](#_Toc199925602)

[9.2 Participants 51](#_Toc199925603)

[9.3 Perspectives of Healthcare Professionals 59](#_Toc199925604)

[10 Broader Risk Stratification Approaches 61](#_Toc199925605)

[10.1 Research on Risk Stratification Approaches 62](#_Toc199925606)

[10.2 Limitations and considerations of risk stratification 66](#_Toc199925607)

[11 Discussion 69](#_Toc199925608)

[11.1 Key findings in relation to current knowledge 69](#_Toc199925609)

[11.2 Key Conclusions 70](#_Toc199925610)

[12 References 72](#_Toc199925611)

[13 Appendices 99](#_Toc199925612)

[13.1 Related Considerations 99](#_Toc199925613)

[13.2 Risk stratification in other cancer screening programmes 103](#_Toc199925614)

[13.3 Technical Review Process, Questions and Answers 106](#_Toc199925615)

[13.4 National Health Committee (NHC) screening criteria assessment 112](#_Toc199925616)

[13.5 Mammogram Breast Density Related Screening Recommendations 115](#_Toc199925617)

[13.6 Current risk–based breast cancer screening randomised control trials 119](#_Toc199925618)

[13.7 Project ROSA 126](#_Toc199925619)

List of Tables

[Table 1: Selected Known Risk Factors for Breast Cancer 30](#_Toc199925550)

[Table 2: The Standards NZ Breast Cancer Risk Categories 32](#_Toc199925551)

[Table 3: supplemental screening modalities 34](#_Toc199925552)

[Table 4: Outcomes from Supplemental Screening after standard 2D Mammography in women with dense breasts (or all densities for MRI) 38](#_Toc199925553)

[Table 5: Breast Density reporting status in International screening programmes 44](#_Toc199925554)

[Table 6: Summary of breast density related screening guidelines/recommendations/position statements 46](#_Toc199925555)

[Table 7: Population level trials of risk–based breast screening 63](#_Toc199925556)

[Table 8: NHC Screening Criteria Assessment 112](#_Toc199925557)

[Table 9: Breast density related screening guidelines/recommendations/position statements 115](#_Toc199925558)

[Table 10: Summary of trials comparing risk-based screening with standard non-risk-based screening 119](#_Toc199925559)

[Table 11: Trials comparing different or additional screening modalities with standard screening for higher risk groups 124](#_Toc199925560)

List of figures

[Figure 1: BreastScreen Aotearoa screening pathway 20](#_Toc199925620)

[Figure 2: BSA screening coverage rates by ethnicity and deprivation 21](#_Toc199925621)

[Figure 3: BI-RADS Classification of Breast Density 23](#_Toc199925622)

[Figure 4: Pictorial representation of the general population prevalence of breast tissue density for women 24](#_Toc199925623)

[Figure 5: Schematic of algorithmic-based approaches to characterisation of breast density 26](#_Toc199925624)

[Figure 6: Screening intentions after receiving mammogram results. The control group did not receive breast density results. 56](#_Toc199925625)

[Figure 7: Schematic outlining a personalised approach to early detection and prevention of breast cancer 62](#_Toc199925626)

[Figure 8: MyPeBS Screening options 65](#_Toc199925627)

[Figure 9: MyPeBS Risk Categories 65](#_Toc199925628)

[Figure 10: Risk Stratification in screening programmes 103](#_Toc199925629)

[Figure 11: Project ROSA Roadmap five pillars 127](#_Toc199925630)

# Glossary and Abbreviations

|  |  |
| --- | --- |
| AI | Artificial Intelligence |
| BC | Breast Cancer |
| BCSC | Breast Cancer Surveillance Consortium |
| Biopsy | Removal of a sample of tissue from the body for examination under a microscope by a pathologist to assist with the diagnosis of a disease.1 |
| BI-RADS | American College of Radiology’s Breast Imaging-Reporting and Data System. In clinical settings, breast density is typically evaluated using two-view mammograms and classified according to this system. |
| BMI | Body Mass Index |
| BOADICEA | Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm |
| BRCA | The two BRCA (BReast CAncer) genes (BRCA1 and BRCA2) are tumour suppressor genes that help prevent cancers from developing. There is a substantially higher risk of developing breast, ovarian, and other cancers in people who have inherited a mutation in either of these genes.2 |
| BD | Breast density refers to the relative amount of fibrous and glandular tissue compared to fatty tissue that can be visualised and measured by breast mammography. This is not the same as physical firmness of breast tissue. |
| BSA | BreastScreen Aotearoa. |
| Cancer | A general term for a large number of diseases that all display uncontrolled growth and spread of abnormal cells. Also called a malignant tumour. Cancer cells have the ability to continue to grow, invade and destroy surrounding tissue, and leave the original site and travel via the lymph or blood systems to other parts of the body, where they may establish further cancerous tumours.1 |
| CEM | Contrast-Enhanced Mammography – An imaging modality that may be used for breast cancer screening. Combines conventional mammography with iodinated contrast medium and involves an X-ray subtraction technique to improve cancer detection.3 |
| Coverage | Is defined as the proportion of women eligible for screening who have been screened in the previous two-year period. The number of women eligible is derived from Statistics New Zealand Census base populations at the midpoint of the two-year screening period. It bases eligibility on age and does not account for those who may be otherwise ineligible, or who chose not to participate. It also does not include participants undertaking private mammography outside BSA. Therefore, the true participation rates and true overall mammography uptake are unknown. |
| Digital Breast Tomosynthesis (DBT) | An imaging modality that may be used for breast cancer screening. Uses multiple X-ray images to create a 3D breast image.4 |
| False positive | A positive screening test in a person who does not have the condition being screened for. The higher the proportion of false positives, the more people are referred for unnecessary further assessment. A test with a false positive rate of 0% will mean that no one is referred for further assessment unnecessarily.1 |
| False positive rate for screening mammograms | The proportion of women who do not have cancer but are given an abnormal mammogram result (false positives), calculated as the number of false positive results divided by the total number of women screened.1 |
| False negative | A negative screening test in a person who does have the condition being screened for. People with false negative tests are falsely reassured that they do not have the disease in question, and as a result may delay seeking help if symptoms develop later.1 |
| GP | General Practitioner |
| HNZ | Health New Zealand | Te Whatu Ora |
| IBIS | International Breast Cancer Intervention Study |
| Incremental cancer detection rate | The number of additional cancers detected at screening with a particular modality relative to another. This is often stated as a percentage of screens or as a rate per 1000 screens.5 |
| Interval cancer | A cancer that is diagnosed between a negative screen and the time a next screen would have occurred. In Breast Screen Aotearoa, this is a cancer diagnosed within two years of a negative screen. 1 |
| Interval cancer rate | The number of interval cancers diagnosed in a given population during a given period of time. The interval cancer rate is usually expressed per 1000 people per year. The interval cancer rate should be calculated by 12-month intervals from the time of the last screen, and by using the entire time interval from the previous screening.1 |
| Lifetime risk | The likelihood that a particular event will occur during a person’s lifetime, for instance developing a particular type of cancer. 6 This may be expressed as the overall lifetime risk from birth, or the risk within the woman’s remaining lifetime. |
| 5-year risk of cancer | The likelihood that a person who is free of a certain type of cancer will develop that type of cancer within 5 years. |
| Lead Providers (LP) | Lead Providers are organisations that provide breast screening services for BreastScreen Aotearoa.1 |
| Mammogram | A soft tissue X-ray of the breast, which may be used to evaluate a lump, or as a screening test in women with no signs or symptoms of breast cancer.1 |
| MRI | Magnetic Resonance Imaging – An imaging technique that may be used for breast cancer screening. Uses magnetic and radiofrequency fields to produce 3D images. Breast screening using MRI requires intravenous contrast, but does not utilise ionising radiation (X-rays).7 |
| Negative mammogram | A mammogram that has been classified as normal during a routine screening.1 |
| NPHS | National Public Health Service |
| Overdiagnosis | The diagnosis of cancers that would never progress to cause symptoms and/or death during an individual’s lifetime.8 |
| PHA | Public Health Agency |
| Positive predictive value of screening mammogram | The proportion of people having the outcome in question (i.e. a cancer) if the screening test is abnormal, usually expressed as a percentage. The higher the positive predictive value, the more likely it is that the person has the outcome in question (i.e. a cancer) when their test is positive. A screening test with a high positive predictive value is beneficial, since it will reduce the proportion of people having unnecessary further investigations. It is calculated as: the number of women with cancer and an abnormal mammogram result, divided by the total number of women with an abnormal screening mammogram result both with and without cancer.1 |
| Recall for further assessment | A recall for performance of an additional procedure to clarify a perceived abnormality detected at screening.5 |
| Recall rate | The number of women recalled for further assessment as a proportion of all women who were screened.5 |
| Relative risk | The likelihood of a particular event occurring in one group compared with the likelihood of the same event occurring in another group.6 |
| Risk stratification | Risk stratification or risk-based screening involves using a risk assessment process to allocate individuals to different screening protocols on the basis of their risk of cancer. |
| Screening | The examination of asymptomatic people in order to classify them as likely or unlikely to have the disease that is the object of screening. The aim of screening is to detect disease before it is clinically apparent, and for this to improve the outcome for people with the disease.1 |
| Sensitivity | The likelihood that a test will detect a cancer when one is present, The higher the sensitivity, the better the test is at detecting cancer. A test with a low sensitivity will miss a lot of cancers. A test with a sensitivity of 100% will detect all cancers present. It should be calculated for both the screening test alone and for the screening programme (ie, both screening and assessment).1 |
| Specificity | The likelihood that a test will exclude a cancer when one is not present, calculated as the number with true negative screening results (Y) as a percentage of Y plus the number of false positive screening results. The higher the specificity, the better the test is at excluding cancers when they are not present. A test with a low specificity will mean that a lot of people are referred for further assessment unnecessarily. A test with a specificity of 100% will mean that no one is referred for further assessment unnecessarily.1 |
| Supplemental screening | Imaging used in addition to standard screening pathways, for example, undertaking MRI in addition to mammography to improve breast cancer detection. |
| Surveillance | Surveillance is the monitoring of individuals considered at increased risk of a condition and is generally of smaller scale, but increased intensity compared with screening, which effectively identifies high-risk individuals from an average risk population. The differences between surveillance and screening may not be entirely distinct, and screening organisations should work closely with those undertaking surveillance.9 |
| Technical recall | A repeat mammogram because of technical inadequacy of the screening mammogram.5 |
| Underdiagnosis | The failure to detect a cancer that is present, for example due to errors in clinical interpretation or technical constraints. 10 |
| US | Ultrasound - an imaging modality that may be used for breast cancer screening. Uses soundwaves to image tissue, with no radiation or contrast required.4 |
| Wāhine Māori | Māori women |

# Executive summary

Breast density has become an important consideration within population-based breast cancer screening programmes worldwide. The role of breast density reporting and whether supplemental (additional) screening, should (or can) be offered to women with very dense breasts in the public system, is currently being assessed. Women with higher breast density have an increased risk of developing breast cancer (two to five-fold) compared to those with low breast density and are more likely to have a diagnosis missed by mammography.

International data suggests that potentially half of the female population are affected by high breast density and 5-10% of women will have very high density. The publicly funded, national breast screening programme BreastScreen Aotearoa (BSA), does not currently measure or report breast density. The distribution of breast density in the Aotearoa New Zealand female population is relatively unknown, with measurement in an appropriate cohort required to accurately estimate the proportion of women with dense breasts.

Mammographic breast density refers to the relative amount of fibrous and glandular tissue compared to fatty tissue within the breast. Measurement can be assessed from mammographic images visually by a radiologist or through automated reporting software based on algorithms and artificial intelligence (AI).

Screening programmes that incorporate breast density reporting are increasing. It has been mandated in the United States of America, is reported in most Canadian territories and is recommended by the European Society of Breast Imaging (EUOSBI), with at least 9 European countries reporting breast density. New South Wales, Western and South Australia report breast density in their screening programmes, with the Royal Australian and New Zealand College of Radiologists (RANZCR) recommending “mandating the reporting of breast density in both screening and diagnostic settings” in December 2023.

Supplemental screening in the context of breast screening refers to imaging used in addition to standard screening protocols that is undertaken to improve breast cancer detection. Internationally and in Aotearoa, supplemental breast screening has been recommended for women deemed to be at high risk of developing breast cancer. However, there are no universally agreed guidelines on screening type or timing, and women with dense breasts alone are generally not considered to reach a high enough level of risk.

Supplemental screening options including Magnetic Resonance Imaging (MRI), ultrasound and contrast enhanced mammography (CEM) have been shown to increase the detection of cancer compared to standard mammography. All methods are associated with varying risks and benefits. MRI has the greatest sensitivity for detection but comes with an increased false positive rate and is a costly procedure. Ultrasound is not as sensitive as MRI and has a similar false positive rate, however, it is a less invasive and less costly procedure. CEM is nearly as effective as MRI for cancer detection, with less false positives and is a simpler, lower cost method, however, is not routinely available and like MRI, uses intravenous contrast dye.

Studies investigating supplemental screening for women with dense breasts have shown increased cancer detection rates, detection of cancers earlier and decreased rates of interval cancers, however, whether this results in any additional lives saved is currently unknown.

Patient information about breast density is becoming increasingly available. Online information generally outlines the facts of breast density measurement but lacks discussion on the harms and benefits. Countries that do report on breast density usually provide notifications directly to patients. Overseas evidence suggests that women want to know their breast density, although this can be associated with anxiety and does vary across populations and healthcare contexts.

Risk-based screening protocols use risk assessment to provide personalised screening pathways that vary depending on the identification of risk. Those deemed to be at high-risk may receive more or different interventions than those at low risk. Modelling data supports the use of risk-based breast cancer screening protocols, including risk assessment tools and screening technologies, to provide personalised screening protocols that use resources efficiently and improve programme outcomes.

There are various methods for breast cancer risk stratification, with a number of tools available utilising different criteria (personal risk factors, family history, genetic testing), of which 3 include breast density. Population-based clinical trials are underway that are designed to assess the benefits and harms of supplemental screening for women with dense or extremely dense breasts and to investigate risk based screening that includes reduced screening for some very low risk groups.

In Aotearoa New Zealand there is significant inequity in breast cancer outcomes and screening coverage by ethnicity, with Māori women particularly impacted. Breast density reporting is available to women who have health insurance or pay for screening out-of-pocket through private providers. Studies have shown that women with dense breasts do not receive the same outcome benefits from current breast screening programmes as those with less dense breasts. There are a number of ethical considerations with the topic of breast density; one key issue is that failing to address the increased risk of breast cancer in women with dense breasts may be creating and perpetuating inequities for these women.

### KeyConclusions

Breast density is an independent risk factor for breast cancer development and increased breast density can make it more difficult to identify breast tumours by mammogram. As such density should be considered when evaluating a women’s risk of breast cancer.

Women with higher-than-average risk of breast cancer may benefit from supplemental breast screening, however, currently there is no consensus on how best to manage women with dense breasts.

These factors need to be assessed in the context of the current BreastScreen Aotearoa screening programme with further consideration of introducing risk-based screening in the future.

Incorporation of breast density notification into an existing screening programme is ethically complex. Issues to review include equitable care, patient autonomy, physician trust, duty of care and uncertainties relating to measurement and clinical management pathways for women with dense breasts.

Consideration needs to be given to the best way to measure breast density within the BSA programme, including the possible use of AI versus visual assessment by radiologists and what the additional costs for these would be. The prevalence of breast density amongst women in Aotearoa New Zealand needs to be ascertained to understand the potential programme impacts, benefits and costs, including the potential number of women who may be offered supplemental screening.

Further evidence from international trials is required regarding the impact of supplementary screening for women with high breast density on breast cancer outcomes (e.g. mortality) and to provide guidance on risk stratification options, screening modality and interval.

Aotearoa New Zealand specific cost-effectiveness modelling would greatly assist in providing information regarding health system and economic implications of various policy options, including alternate ways to achieve marginal improvements to breast cancer outcomes (e.g. alternate age ranges, modalities (e.g. Digital Breast Tomosynthesis (DBT)), screening intervals, and interventions to improve current programme participation).

The current BSA workforce capacity needs to be assessed with regards to BreastCare nurses and Medical Imaging Technologists (mammographers) potentially needing to explain breast density results and recommendations for supplemental screening with women. As does the funding and workforce enhancements that would be needed to undertake further ultrasound/screening assessments.

The capacity of the wider health system to fulfil supplementary ultrasound or MRI requirements also needs to be assessed. Currently, CEM is not routinely available in Aotearoa New Zealand and there is limited availability of DBT. If supplemental screening is not available to women with dense breasts through the public health system, it will not be accessible to many due to cost. This is likely to further disadvantage some groups of women already facing inequities, for example, wāhine Māori with dense breasts and those living in areas of socioeconomic disadvantage.

A more detailed assessment of whole system capacity issues and potential impacts on the BSA programme in the context of current projects and existing coverage inequities for Māori and Pacific women is also required. This knowledge is necessary to produce robust local guidelines and recommendations for women with dense breasts.

1. Introduction

Breast density has been increasingly recognised as a key consideration in breast cancer screening. There is clear evidence that high breast density is both an independent risk factor for breast cancer and reduces the sensitivity of mammography for screening. As a result, population-based screening programmes internationally have been assessing the role of breast density reporting in their programmes and whether additional screening or surveillance, should (or can) be offered to women with very dense breasts. These considerations have included risk stratification, programme and workforce issues but, importantly, the views of consumers themselves.

Currently, breast density is not measured or reported as part of the BreastScreen Aotearoa (BSA) programme. The National Public Health Service (NPHS) has identified breast density as a key topic requiring further in-depth consideration in the Aotearoa New Zealand context. To this end, a joint working group was established with members from across Health New Zealand | Te Whatu Ora (HNZ) and including Te Aho o te Kahu the Cancer Control Agency and the Public Health Agency (PHA) in Manatū Hauora. A number of literature reviews were undertaken to address questions and points of interest identified by the working group (further details in Appendices 13.2) with resulting summaries synthesised into this technical review.

1. Breast Screening in Aotearoa New Zealand
   1. BreastScreen Aotearoa

Initiated in 1998, BreastScreen Aotearoa (BSA) is Aotearoa New Zealand’s publicly funded, national breast screening programme that offers free mammography nationally for eligible women aged 45–69 years biennially. 1

* On 1 October 2024, the eligible age range for BSA was extended in Nelson-Marlborough. Those in this region who turned 70 on or after 1 October 2024, and those who are 74 (before they turn 75) are now eligible. HNZ is aiming to progressively extend the age range for free breast screening across the rest of Aotearoa New Zealand from October 2025.
* Eligibility criteria include women who;
* have not had mammography within the previous 12 months,
* are not pregnant or breastfeeding,
* are free from breast cancer (women previously diagnosed with breast cancer are eligible for screening at least five years after diagnosis),
* are asymptomatic
* are eligible for public health services in Aotearoa New Zealand.

Individuals considered at increased risk for breast cancer compared with those of “average population risk”, or who present with symptoms or signs of breast cancer are managed through pathways outside of the BSA programme.1 High-risk people with BRCA mutations are discussed further in section 11.1.

In HNZ the NPHS is responsible for the national management and oversight of BSA, and its service providers. Te Aho o Te Kahu provides strategic leadership for cancer control in New Zealand and works closely with NPHS to support their programme. There are eight regional Lead Providers (LP) who provide breast screening services for BSA. This includes all steps along the screening pathway, workforce recruitment and retention, and quality assurance. In addition, there are eleven Screening Support Service Providers who work in partnership with Lead Providers in their districts to support services directly to priority population groups – identified as Māori, Pacific, under screened and unscreened women. Both service providers are accountable to the NPHS and are responsible for ensuring their services are delivered according to the BSA National Policy and Quality Standards.1 Screening is provided at fixed and mobile sites with further assessment usually provided at centralised locations within each district.1

* 1. Breast Screening Pathway

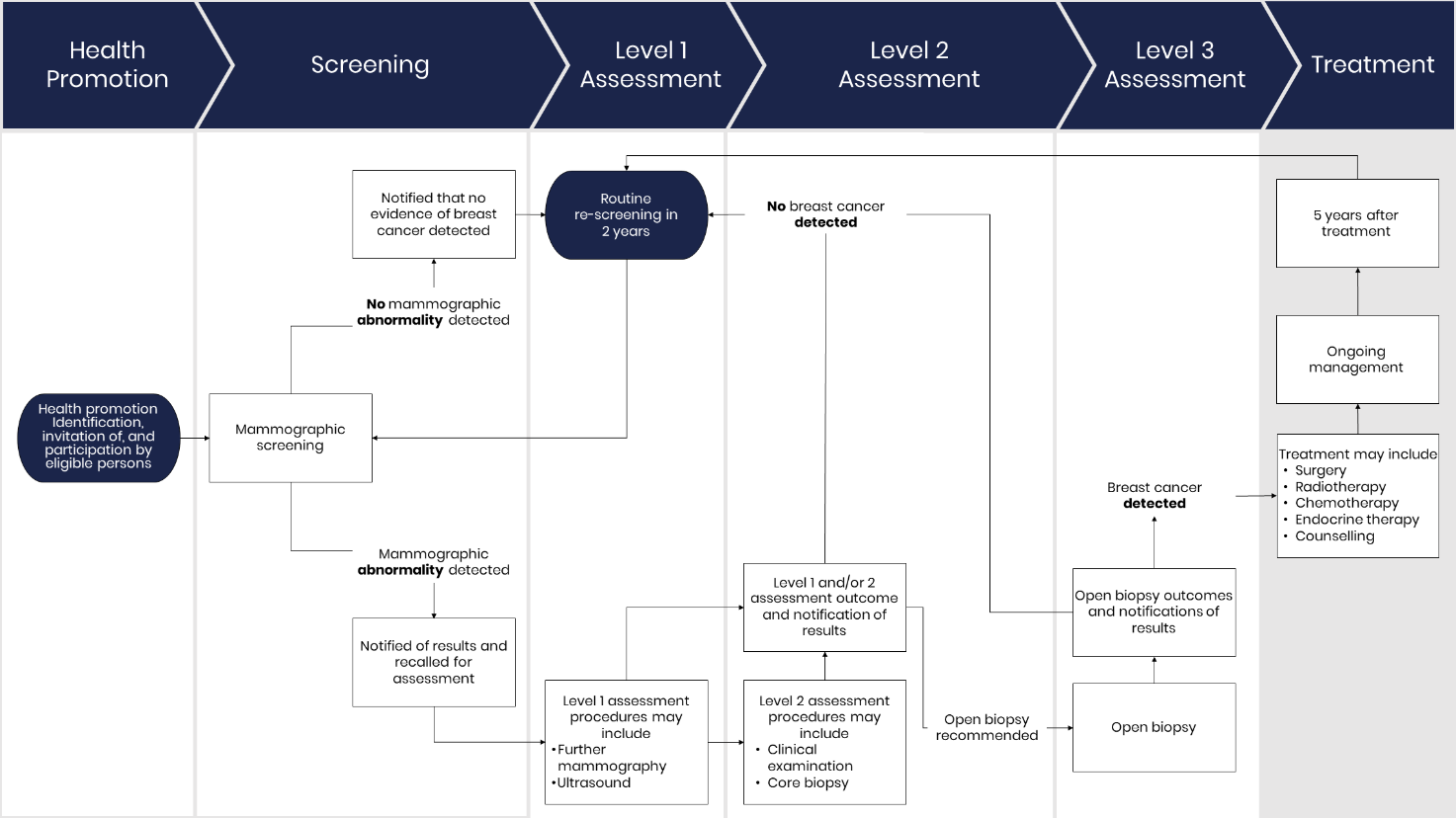
The breast screening pathway is described in Figure 1. It has multiple steps, including:

* Engagement with whānau, communities and service providers and screening promotion.
* Identification and enrolment of eligible women – historically, women were required to enrol themselves with BSA by telephone or online. In February 2025, a new system incorporating a population-based register was introduced that will invite women by email, text or letter to confirm enrolment and book appointments. The register is designed to capture a wider cohort of women and is estimated to reach an additional 135 000 participants.11
* Once enrolled, women are invited to an appointment for a mammogram at a local site and provided with support to access services where necessary.
* Screening mammograms are offered regionally at lead provider sites (fixed and mobile services).
* Mammograms are double-read independently by two accredited programme radiologists. Where there is discordance in these reads, a third read is undertaken. Artificial Intelligence (AI) is not currently used in the programme.
* For those with a negative mammogram (a mammogram that has been classified as normal during a routine screening, with no mammographic abnormality detected), a results letter will be sent to the individual and to their primary care provider (where consent for this has been given). These individuals will be recalled for routine screening in a further two years.
* If an abnormality is identified on mammography, the individual will be recalled for assessment.
* There are three levels of assessment testing where women may undergo some or all of the following procedures. Level 1. Further mammogram and/or ultrasound (US), Level 2. Clinical breast exam and/or needle biopsy (fine needle aspiration, core or vacuum assisted), Level 3. Excision or open surgical biopsy, or wire localisation open biopsy.
* If possible, provisional results will be given at the assessment otherwise final results are communicated after all clinical review processes are complete. If the result is no evidence of cancer, eligible women will be recalled to routine screening in a further two years.

Women with a diagnosis of cancer will be given counselling and information about treatment options and will be referred to a treatment service. After treatment for breast cancer, follow-up usually includes funded annual mammograms for five years. After five years, women are encouraged to re-enter the programme with BreastScreen Aotearoa for standard screening if still within the eligible age range. 1,12

Note: Breast screening is available at private providers outside of BSA, however BSA does not have visibility/monitoring of mammograms taken outside of the programme.

Figure 1: BreastScreen Aotearoa screening pathway



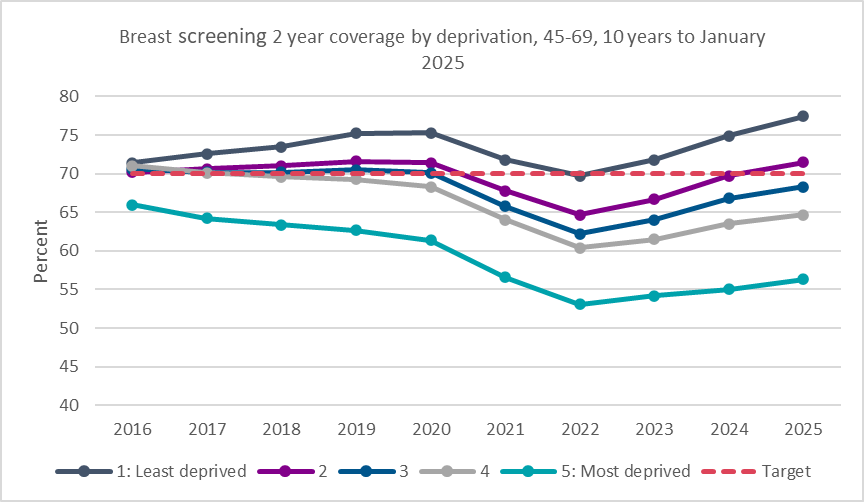
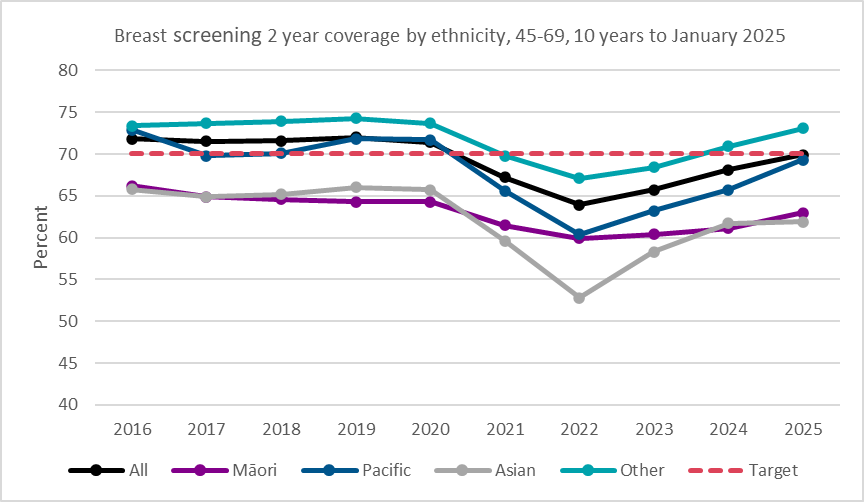
Source; Adapted from BreastScreen Aotearoa National Policy and Quality Standards 2013. Wellington: Ministry of Health.1

* 1. BreastScreen Aotearoa programme metrics

In a linkage study on the impact on mortality from breast screening in Aotearoa New Zealand, based on a participation rate of 71%, women who screened through BSA had a 34% reduction in mortality from breast cancer compared with women who did not screen after adjusting for age at death, ethnicity, and screening selection bias. This study demonstrated that mortality reduction was equitable for wāhine Māori and Pacific women compared with non-Māori, non-Pacific women, based on achieving specified participation rates.13,14

BSA screens approximately 270,000 women per annum with a target coverage rate of 70%. In the two years to January 2025, BSA screened 70% of the eligible population, with differing coverage rates by ethnicity and socioeconomic deprivation (see figure 2 below). Only 63% of eligible 45-69 year old wāhine Māori, 62% of Asian and 69% of Pacific women were screened compared to 73% of European/other women. Looking at coverage rate by deprivation status, only 56% of women living in the most deprived areas were screened compared to 77% of eligible women aged 45-69 years in the least deprived areas.15 The COVID-19 pandemic had a significant impact on screening rates and inequities for Māori, Pacific and Asian women were exacerbated. Equity focused recovery plans are in place to address these as a priority.16

Figure 2: BSA screening coverage rates by ethnicity and deprivation



Data source: BreastScreen Aotearoa interactive coverage data tool accessed April 202515

As per Figure 1, following mammography women are referred for assessment if there are concerns raised in the results. Nearly 10% (9.9%) of women aged 50-69 years having an initial screen and 3.5% of those having a subsequent screen through BSA were recalled for assessment in the two years to July 2022.17 Of all women recalled for assessment, 12.8% of those following an initial screen and 18.8% following a subsequent screen were diagnosed with cancer (this is the positive predictive value – the number of women with cancer and an abnormal mammogram result, divided by the total number of women with an abnormal screening mammogram result both with and without cancer1). These figures vary by ethnicity, with the rates of referral for assessment and of cancer detection in those referred being higher for Māori and Pacific women. Of all the women screened aged 50-69 years, 7.3% of those having their initial and 2.6% of those having subsequent screens were recalled for assessment but did not have cancer (false positive rate).

In 2016 to 2017, for women aged 50-69 years, the interval cancer rate in the first 12 months after a screen was 6.3 per 10,000 women screened for initial screens and 5.1 per 10,000 women screened for subsequent screens. For the 12 to 24 months after a screen, the interval cancer rate was 14.5 per 10,000 women and 10.1 per 10,000 women for initial and subsequent screens.18

BSA monitor and report regularly on a range of clinical and programme indicators that are published on the Health New Zealand | Te Whatu Ora website ([BreastScreen Aotearoa programme monitoring reports – Health New Zealand | Te Whatu Ora](https://www.tewhatuora.govt.nz/health-services-and-programmes/breastscreen-aotearoa/breastscreen-aotearoa-programme-monitoring-reports/)).

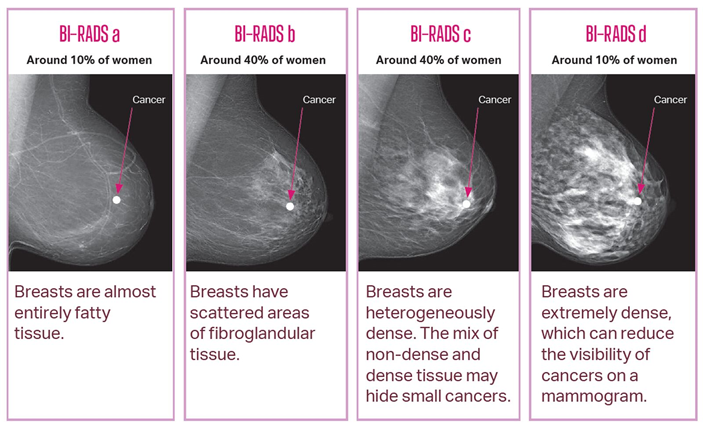
* 1. BreastScreen Aotearoa and Breast Density

BSA does not currently measure, calculate or report breast density. BSA providers report that increasing numbers of participants are requesting their breast density information. A position statement on breast density was written and published on their website in 2019.19 The evidence review at that time concluded that for women with dense breasts who otherwise have an average risk of breast cancer, there was insufficient evidence to recommend additional imaging. The position statement advises that women with dense breasts at an otherwise average risk of breast cancer can be managed within BSA by regular mammography every two years. Women at high risk of breast cancer, for example those with very strong family history of breast cancer, or those with gene mutations, should be referred for additional care outside the BSA programme.

1. What is Breast Density

Breast density refers to the relative amount of fibrous and glandular tissue compared to fatty tissue that can be visualised and measured by breast mammography.20,21 This is not the same as physical firmness of breast tissue. 22 Breast density is usually classified according to the American College of Radiology’s Breast Imaging-Reporting and Data System (BI-RADS). The BI-RADS atlas provides standardised breast imaging terminology and a classification system for mammography, ultrasound and magnetic resonance imaging (MRI) of the breast. It includes a specific scale for breast density. This scale includes four categories, ranging from Category A (almost entirely fatty breasts), Category B (scattered areas of fibroglandular density), Category C (heterogeneously dense) to Category D (extremely dense breasts). Breast composition is defined by mammographic visually estimated content of fibroglandular-density tissue within the breasts and categorised accordingly. The female population distribution of 10% fatty, 40% scattered, 40% heterogeneous and 10% extremely dense breasts reflects the historical assignment from clinical practice and is due to the observation that a few coalescent areas of dense tissue may be present in breasts with as little as 10% dense tissue, whereas primarily fatty areas may be present in breasts with as much as 90% dense tissue. The fifth BI-RADS edition does not indicate ranges of percent dense tissue, instead it emphasises text descriptions which are currently believed to be more important clinically. This allows for subjective assessment of the volume of dense tissue and the relative possibility of masking, compromising the sensitivity of mammography. In the case of scattered density with a focally dense area, this may be categorised as heterogeneously dense. As the density category increases, the sensitivity for identification of non-calcified lesions decreases and larger lesions can be obscured. If breasts are not of apparently equal density the denser breast is used for categorisation. 23

Figure 3: BI-RADS Classification of Breast Density



Source: Breast Screen South Australia24

Breast tissue density influences breast cancer management in two ways: firstly, high breast density is an independent risk factor for the development of breast cancer; secondly, high breast density can obscure potential lesions on mammograms, thereby reducing the diagnostic sensitivity of imaging tests. This masking effect makes it more challenging to detect tumours, as dense tissue and cancer both appear white on a mammogram, complicating the differentiation process.25

* 1. Breast density distribution in the population

Breast density is determined mainly by genetics and decreases with age, with a particularly marked decrease in density during menopause after which it stabilises.26 It is also affected by factors such as parity, body mass index (BMI) and some medications e.g. menopausal hormone therapy and the oestrogen activity blocker tamoxifen. Breast density has been shown to decrease with increasing parity, increasing BMI and tamoxifen use, whereas breast density has been shown to increase with exposure to menopausal hormone therapies.27–30 The association of these factors with density and risk of breast cancer development is further discussed in section 5.

Approximately 6-10% of women over the age of 40 have extremely dense breasts (equivalent to BI-RADS D category), and 40-45% have heterogeneously dense breasts (equivalent to BI-RADS C category). The remainder of women have fibroglandular or fatty breasts which are considered non-dense. 31–33

Figure 4: Pictorial representation of the general population prevalence of breast tissue density for women

Diagram showing the prevalence of breast tissue density.
1 in 10 women have extreme density.
4 in 10 women have heterogeneous density.
4 in 10 women have scattered fibroglandular tissue.
1 in 10 women have fatty breast tissue.

Ethnic differences in breast density are unclear, with unique patterns demonstrated across some ethnic groups in different screening populations34–36. A study in Aotearoa New Zealand conducted in the Northern Region, demonstrated that wāhine Māori (over 50 years) have higher absolute breast density and Asian women (all ages) have lower absolute breast density relative to New Zealand European/Other women. However, assessing volume percent breast density (the percentage of the total breast volume that is dense) there was no significant differences for wāhine Māori and Asian women had higher percent density compared to New Zealand European/Other. The sample contained fewer Māori and Pacific women and more Asian women than the general population at the time (2013) and there was a lack of additional data to assess the potential effects of confounding.37 Further study is required to understand the true prevalence of breast density for Aotearoa New Zealand women.

It has also been suggested that there is a positive association between socioeconomic status and breast density, though this has largely been attributed to lower BMI in higher socioeconomic groups.34,38,39

1. Breast Density Measurement
   1. Current State

In clinical settings, breast density is typically evaluated using two-view mammograms and classified according to the BI-RADS system described earlier. Mammographic visual assessment of breast density can be highly subjective and varies between observers as well as in the same observer over time. The highest discordance is between adjacent categories, more so between the least dense categories (A/B) than the high dense categories (C/D).40 This variability can lead to inconsistent diagnostic categorisation and treatment planning. Dual reading, where each mammogram is read by two radiologists can improve consistency and has been recommended.41,42

* 1. Artificial Intelligence

Artificial intelligence (AI) has been viewed as a potential solution to mammogram reader variability, providing more objective and standardised measurements, aiding clinical decision making. Historically, AI measurement was physics-based, calculating the total dense volume and total breast volume to provide volumetric percentage density. Two commercial companies, Volpara and Quantra, have pioneered and developed such algorithms which demonstrated fair to substantial agreement with BI-RADS reporting. With the advancements of AI in the early 2010s, a number of deep learning-based algorithms have been developed or incorporated into existing algorithms. These deep learning-based algorithms are capable of identifying intricate patterns in imaging data that are often not visible to the human eye and report improved accuracy over the previous physics-based algorithms from internal test results.43,44

The algorithmic-based approach to characterisation of breast density is not new, with many commercial products available. Figure 5 demonstrates the available algorithms and three broad approaches, either physics-based, machine learning-based or deep learning-based, described further below.25

### Physics-based

The physics-based method relies on direct calculations derived from the properties of the breast tissues captured in mammograms. This approach involves measuring the total dense volume (fibroglandular tissue) and the total breast volume based upon different X-ray attenuation characteristics of fat, connective tissue and epithelial tissue of the breast. From these measurements, a volumetric percentage is calculated which correlates to the BI-RADS breast density classification. This method is grounded in physics, offering a systematic approach to assess breast density by quantifying the actual composition of the breast. 45

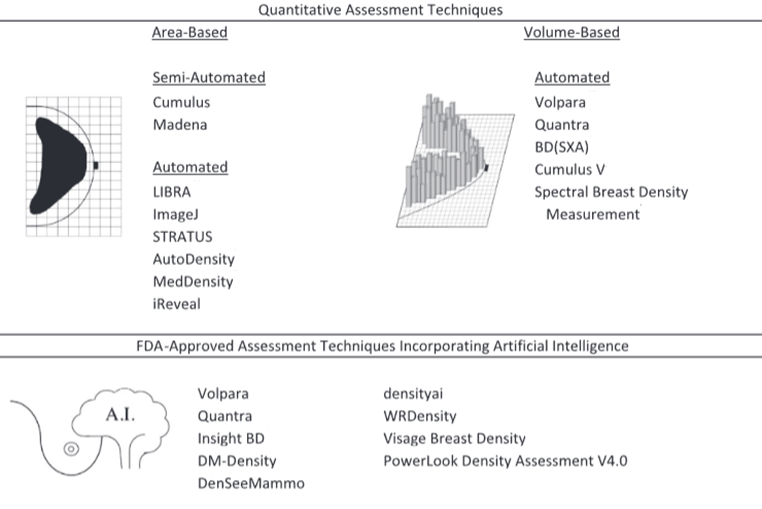
### Machine learning-based

Limited information exists around the use of machine learning approaches for the classification of breast density. Quantra describes the use of a support vector machine (SVM) algorithm within their white paper.46 In general, a machine learning-based approach is similar to a deep learning-based approach, requiring large datasets with images and the corresponding grades. The main difference between machine learning-based approach and deep learning-based algorithms is that the features used for prediction will need to be identified and created by human subject matter experts in order for algorithm development.

### Deep learning-based

In contrast, the deep learning-based approach represents a more advanced AI technology that uses neural networks to analyse images. These algorithms allow the system to learn from a vast quantity of data, identifying subtle patterns and features within mammographic images. These features do not need to be created and are learnt during the training process. This method has proven to be effective in improving the accuracy and reliability of computer vision algorithms with the technology being well utilised in other healthcare use cases.47,48 Within breast density assessment, algorithms have been developed using deep learning techniques. Based on internal test results, deep learning-based algorithms have surpassed the performance of traditional physics-based algorithms 43,44. However, deep learning-based algorithms for breast density assessment are a recent development and the increased performance has not been translated into real world evidence.

Figure 5: Schematic of algorithmic-based approaches to characterisation of breast density



Source: Chalfant and Hoyt, 202225

Due to commercial sensitivity, it is difficult to determine how each vendor has developed their current product. While vendors do share information about the initial algorithm development, details on subsequent ongoing development are often limited.45 It is likely that vendors employ a variety of methods within their tools. These methods might include integrating multiple algorithms to pool results for more accurate outcomes or using different algorithms as quality control mechanisms to cross-verify and enhance the reliability of the final output.

The output produced by these AI tools is typically the volumetric breast density value, a numerical value that ranges from 0 to 100, where a score of 100 indicates extremely high breast density. Each vendor would choose specific thresholds to represent the different BI-RADS classification and report the results as either the raw numeric value or classified into groupings. Additional metrics of total breast volume and fibroglandular volume is also presented to the end user.46,49 Providing both volumetric breast density and absolute dense volume is important to ensure that breast size and area of dense volume can be considered, as is allowed for with the BI-RADS classification system. Studies have shown that absolute measures of dense tissue area or volume have greater predictive power of breast cancer risk than percentage or mammographic visual categorisation, though all measures are associated with increased risk of breast cancer.50

In terms of technical integration, the AI systems are designed to analyse raw Digital Imaging and Communications in Medicine (DICOM) images. DICOM is the global standard for storing and transmitting medical imaging information and related data. Once the AI has processed these images, the results are transferred into the Picture Archiving and Communication System (PACS). PACS is a medical imaging technology which provides storage and convenient access to each patient’s images from multiple modalities. Within the PACS, these AI-generated results can be stored in two formats:

1. Standalone Structured Report: is a detailed report that outlines the findings of the AI analysis in a structured format. It includes the breast density score along with other relevant diagnostic information derived from the AI’s interpretation of the mammogram. This format allows radiologists and other medical staff to quickly understand the AI's assessments in a comprehensive, organised manner.
2. Secondary Capture Image: Alternatively, the information might be saved as a Secondary Capture Image, which is a snapshot or image that contains the result. This is particularly useful for visual reference and comparison, providing a direct, illustrative representation of the findings that can be reviewed alongside the original mammograms.
3. Breast Density as a Risk Factor for Breast Cancer
   1. Effects of Breast Density on Risk of Breast Cancer and Sensitivity of Mammography

Breast density has been shown to be an independent risk factor for the development of breast cancer and high breast density can obscure potential lesions on mammograms, thereby reducing the diagnostic sensitivity of imaging tests.25

The radiographic appearance of the breast varies among women because of differences in tissue composition.51 Extensive mammographic density can make breast cancer more difficult to detect as tumours can be obscured by the appearance of normal dense tissue.52 The sensitivity of mammography to detect cancer is inversely proportional to the degree of breast density, with up to 50% of cancers missed in mammograms on women with extremely dense breasts.53,54

Cancers detected in women with dense breasts have been shown to be larger, more aggressive55 and are more frequently advanced with vascular or lymphatic invasion and spread to lymph node s.56 Interval cancers appear to occur more frequently in women with dense breast tissue, with different risk estimates reported.52,54 Contemporary evidence suggests extreme breast density carries around a two-fold increase in risk of interval cancers compared with women with lower density breasts.57 A recent large British study reported twice the overall rate of interval cancers in women with the highest 10% breast density (Volpara measure) compared to the overall rate.54 Mortality reduction from participation in the Dutch breast cancer screening programme was shown to be lower in women with dense breasts (>75% density)58. A Swedish study where 13% of women were classified as having dense breasts also demonstrated increased breast cancer mortality compared to other densities (after adjusting for other risk factors including stage), and this was considered mainly due to higher incidence of disease and partly poorer survival.59 There is no consistent evidence currently that women with dense breasts once diagnosed have worse outcomes for equivalent subtypes compared with women with non-dense breasts.60,61

The exact mechanism responsible for development of cancer in dense breasts is unclear, however, there is substantial evidence to demonstrate the increased risk is independent and not due to missed identification alone, although the degree of independence is debated.21 There is a consistent association over time of increased risk of breast cancer in women with high breast density. Studies of mammograms taken years before a breast cancer diagnosis show an increased association with cancer development long before it would be visible by mammogram.52,62,63 Dense breasts have a greater proportion of stromal and epithelial tissue, which is where breast cancers arise, therefore, it is surmised that with a greater amount of this tissue comes a greater chance of cancer.64 A linear trend of increased risk has been demonstrated when density is measured quantitatively.54,65 Breast density may be considered as a continuum, with levels of breast cancer risk that can be variously categorised and thresholds debated.

Baseline density and changes over time have also been shown to be independently associated with the risk of breast cancer development. Women whose mammographic density is maintained or increases over time have been shown to have a higher risk of breast cancer than those for whom it decreases regardless of menopausal status. 66,67 The bodies hormonal milieu can modulate breast density and breast cancer risk, which has been demonstrated by a reduction in breast density and subsequent breast cancer risk when taking the oestrogen blocker tamoxifen.68–70 The use of post-menopausal hormone therapy, in particular, oestrogen plus progestin, has been shown to be associated with higher breast cancer risk among women with high breast density compared to post-menopausal women with high breast density that do not take hormone therapy. However, the relationship between hormone therapy and breast cancer risk appears to be additive and not fully mediated by a change in breast density. Women with low breast density have a lower risk of breast cancer, regardless of age, menopausal status and hormone therapy use.71

Obesity is another risk factor for breast cancer development. Obesity is consistently associated with an increased risk of breast cancer in post-menopausal women, however, the relationship in premenopausal women is not as clear with studies reporting both negative and positive associations.72 Breast density and BMI are inversely correlated and appear to act as confounders to each other. 73

There are also numerous studies showing associations between breast density and various subtypes of breast cancer, particularly for oestrogen receptor (ER)-positive disease. These relationships are important for the consideration of biological mechanisms responsible for tumour development and could be used to further develop risk prediction models and influence screening strategies.74

The magnitude of risk attributed to dense breast tissue varies from 2-6 fold across studies, which may be due to different ways of measuring and comparing density. The comparison group is important and risk will vary depending on this. For example, a meta-analysis of 42 studies using different density grading methods and comparing extreme densities found a 4-6 fold higher risk in women with >75% density compared with women with <5% density.65 The best estimates are likely to be those comparing between a clinically defined high-risk group and all women or all women excluding the high-risk group. A recent meta-analysis of studies using the Breast Imaging Reporting and Data System (BI-RADS) density scale concluded that women with high breast density (density D) have a two-fold risk of breast cancer relative to density B, scattered fibroglandular tissue. 57 A two-fold increased cancer risk with high breast density compared to average density was also supported by an analysis of six American studies that all used the same density calculations75.

As a comparison to selected other known risk factors for breast cancer (summarised below), presence of high penetrance genetic mutations, for example BRCA1/2, afford a greater than 5 fold increase in risk, whereas, moderate-penetrance mutations are associated with a relative risk of between 1.5 and 5. 76

Table 1: Selected Known Risk Factors for Breast Cancer

|  |  |  |
| --- | --- | --- |
| Risk Factor | | Relative Risk |
| Gender | Female vs Male | 100.810 |
| Age | Older age (40-64 years vs 15-39 years) | 9.410 |
| Genetic germline mutation carriers | High penetrance  (BRCA1/2, TP53, STK11, CD1, PTEN) | ≥5 and ≤1276–78 |
| Moderate penetrance  (ATM, CHECK2, PALB2, BRIP1, RAD51, C/D) | ≥1.5 and ≤576,78 |
| Low penetrance  (CASP8, FGFR2, H19, MAP3K1, LSP1, TNRC9) | ≥1.01 and ≤1.576 |
| Familial related | One or more breast cancer affected first-degree relatives vs. none | 1.7079 |
| Age of breast cancer affected first-degree relatives (younger than 50 years) | 1.3–479,80 |
| Personal history | Systemic therapy for prior breast cancer and breast carcinoma in situ (BCIS) | >581,82 |
| Benign breast lesions | 1.17-3.9383,84 |
| Prior irradiation exposure | 2.7-2085,86 |
| Breast density | High mammographic breast density | 2.0-5.065,87 |
| Hormonal related | Recent and long-term hormone replacement therapy | 1.17–2.3088 |
| Oral contraception (less than one year vs. more than 10 years) | 1.09–1.3889 |
| Parity related | Age of first childbirth (over 35 years vs. before 21 years) | 1.3–2.290 |
| Lifestyle related | Alcohol consumption (intake-dependent) vs. none | 1.32–1.4691 |
| Physical activity (low vs. high level of activity) | 1.12–1.2392,93 |
| Obesity (BMI > 30 kg/m2 vs. BMI <23 kg/m2)  Pre-menopausal  Post-menopausal | 0.54–0.9894  1.12–1.2994 |

Adapted from Tsarouchi et al. 202310

1. Risk Assessment Tools

Risk assessment is central to a population level approach to cancer screening to ensure that the benefits afforded by screening outweigh the harms to those participating. Participants with greater risk are more likely to benefit, with the most basic level of risk stratification being age and sometimes gender.95 Risk tools can produce risk estimates for individuals and be used to assign individuals to risk groups. The size of each risk group is an important consideration to enable planning of resources for risk-based screening protocols, and to help ensure relatively stable and accurate risk assessment and advice over time.96 Numerous breast cancer risk models have been developed for different purposes. These mainly incorporate classical risk factors such as clinical, demographic or pharmacological exposures but may also include family history, genetic risk markers or polygenic risk scores and imaging related parameters to varying degrees.97 The heterogeneity in model inputs, development and improvements to versions make direct comparisons complex. There is no single benchmark or performance metric that identifies a model as suitable for guiding personalised screening as this depends on the purpose of the tool. Models need to be robustly assessed in terms of discrimination, calibration and potential clinical utility in the target population.98

A 2023 review of studies comparing 11 breast cancer risk assessment tools found that no tool was consistently well-calibrated across multiple studies. Most tools were capable of identifying groups with higher rates of observed cancers across different settings but not lower risk groups. Tools that were recalibrated to the risk profiles of the population in which they were applied demonstrated an improvement in fit.99 The most commonly assessed tool, the Breast Cancer Risk Assessment Tool (BCRAT or Gail Model) was developed by the National Cancer Institute in the USA. It uses personal medical, reproductive and family history to estimate absolute breast cancer risk over the next 5 years (up to age 90). Currently, three models, IBIS (Tyrer-Cuzick), BOADICEA (Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm) and BCSC (Breast Cancer Surveillance Consortium) are known to include breast density measurement in the calculation of risk. 100 AI algorithms that were developed to improve accuracy of breast cancer detection on mammography have also been shown to have comparable or better risk prediction than standard tools.101 The Mirai model is an AI deep learning-based approach that uses full mammographic images in addition to traditional risk factors to predict 5 year breast cancer risk. This model was shown in retrospective studies to have improved risk prediction compared to the IBIS model across a number of international datasets.102,103 The combination of a mammographic AI algorithm for cancer detection (Transpara) and clinical risk factors, including breast density measurement has been shown in one study to improve long-term risk prediction (including overall invasive cancers, screen-detected, advanced, and nonadvanced cancers).104 However, the addition of clinical factors to AI image prediction does not always result in significantly improved risk prediction.101 A number of clinical trials (see Research on Risk Stratification Approaches) are allocating women to risk-based screening protocols based on their predicted risk of breast cancer estimated with risk assessment tools, including those that incorporate breast density.

How breast cancer risk thresholds are set is complex, varies from country to country and remains inconsistent, with high-risk definitions ranging from 20-30% lifetime risk.105 The thresholds set by different countries have been developed based on evidence and local context. Risk can be expressed as a lifetime risk from birth, remaining lifetime risk and risk for a fixed horizon e.g 5 years. As breast cancer incidence and mortality change with age and over time so too do risk estimates. Studies suggest that breast cancer risk stratification models will likely be more accurate when based on predicted short term risk compared with risks based on predicted lifetime and remaining lifetime, particularly for younger women.106,107

NICE clinical guidelines indicate that a 30% lifetime risk is equivalent to an 8% chance of developing breast cancer between the ages of 40 and 50.108 The “Standards of Service Provision for Breast Cancer Patients in New Zealand 2013” (the Standards NZ) provide the Cancer Australia risk thresholds as good practice points. Women are considered high-risk when their calculated lifetime risk is 25% or higher and recommend annual MRI.109 The Royal Australian College of General Practitioners recommends supplemental ultrasound or MRI for asymptomatic women with a risk of breast cancer three times above the population average, and the Australian government guidelines recommend annual MRI and mammography before age 50 for women with 30% or greater lifetime risk of breast cancer, and annual mammography for those with a 17 to 30% lifetime risk. 110,111

Table 2: The Standards NZ Breast Cancer Risk Categories

|  |  |  |  |
| --- | --- | --- | --- |
| Risk | High | Moderate | Average |
| Lifetime risk (up to 75 years) | >25%  1 in 2 to 1 in 4 women | 12-25%  1 in 4 to 1 in 8 women | 9-12%  1 in 8 to 1 in 11 women |
| Percent of female population | less than 1% | 4% | 95% |

Based on Cancer Australia risk categories109

The Australian website, eviQ, is a free web-based resource of evidence-based protocols and information intended to be used by health professionals at the point of cancer care delivery. It has been developed for the Australian context but has been considered appropriate for use in Aotearoa New Zealand. It has produced guidelines on surveillance for individuals who are BRCA1 or BRCA2 carriers, or otherwise considered at high-risk. Individual risk assessment using CanRisk or equivalent validated tools is recommended, which can be accessed through the eviQ website.112

CanRisk is a validated and internationally endorsed tool developed through Cambridge University to calculate cancer risks for individuals, including mutation carrier probabilities. It is designed to provide formats that assist healthcare professionals to communicate results to individuals. It uses the clinically validated BOADICEA model to calculate breast (and ovarian) cancer risks using individual level information including personal risk factors, family history, genetic testing, and mammographic density where known. BOADICEA was developed as a comprehensive risk stratification tool for the general population and those considered at higher risk of breast or ovarian cancer.113

In the late 1980s an Aotearoa New Zealand specific breast cancer risk calculator tool was developed.114,115 The relative risks for selected predictors were combined with baseline breast cancer incidence rates and non-breast cancer mortality rates to calculate individual probabilities of developing breast cancer within 5 years. The model predicts risk in women aged 25-54 and is designed for use in unscreened asymptomatic women. The lifetime risk of female breast cancer in Aotearoa New Zealand is 1 in 9 and the calculated individual risk varies based on factors including age, ethnicity, age at menarche, age at menopause, parity, oral contraceptive use, family history of breast cancer, and history of thyroid or breast disease. Breast density is not incorporated into this model and the model is not recommended for women with a strong family history of breast or ovarian cancer or a BRCA gene mutation.116 Whether this calculator is used clinically in Aotearoa New Zealand is unknown. The Standards NZ recommend the use of iPrevent (a web based decision support tool that estimates breast cancer risk utilising the IBIS and BOADICEA models), BCRAT/The Gail Model or the IBIS tool for calculation of breast cancer risk.109

1. Supplemental Screening

Supplemental imaging in breast screening is imaging used in addition to standard screening pathways. It is a term most often used in the context of breast density where it is used to improve sensitivity for breast cancers. Supplemental imaging is distinct from technical recalls when a radiologist is not satisfied with the quality of mammograms, or as additional imaging undertaken as part of any recall to assessment, determined following reading of standard screening mammograms – these would be considered part of the standard screening pathway. A number of potential supplementary screening strategies (alternate modalities and alternate intervals) have been considered internationally. The following table outlines a range of potential supplemental screening modalities:

Table 3: supplemental screening modalities

|  |  |  |  |
| --- | --- | --- | --- |
| Modality | Description | Sensitivity | Comment |
| Additional Mammogram e.g annual | Creates a 2D breast image using multiple X-rays. Uses ionising radiation and breast compression.117 | 25-59% mainly in high-risk populations118 | Not generally recommended due to low sensitivity.21 Repeated exposure to radiation not recommended for younger women due to increased cancer risk associated with radiation.119 |
| Ultrasound (US) | Uses soundwaves to image tissue, no radiation or contrast required.4 | 80%-83% mainly in high-risk populations42,120 | Improved cancer detection compared to standard mammography.121 Suggested in addition to mammography122,123 or alternate annually.124 |
| Contrast-Enhanced Mammography (CEM) | An X-ray subtraction technique, requires iodinated intravenous contrast and involves radiation exposure.3 Not widely available in New Zealand. | 91%-96% in patients with suspicious breast lesions on prior imaging125–127 | Similar sensitivity to MRI in women with dense breasts.128 Suggested supplemental screen for high-risk women (lifetime risk ≥ 25%).129 |
| Digital Breast Tomosynthesis (DBT) | Uses multiple X-ray images to create a 3D breast image.4 Limited availability in Aotearoa New Zealand. | 88% (average risk of cancer) 130,131 | Modestly improved cancer detection compared to standard mammography. Suggested alternative for routine mammographic screening but no mortality results available yet. 132 |
| Contrast-enhanced Magnetic Resonance Imaging (MRI) or abbreviated MRI | Uses magnetic and radiofrequency fields to produce 3D images. Requires intravenous contrast.7 Abbreviated MRI protocols are shorter in duration133 and is available in a number of private providers in New Zealand. | 81-100% mainly in high-risk populations118,134 | Most sensitive imaging modality, preferably identifies more aggressive/invasive cancer.135 Used in high-risk groups as both screening and supplemental screening tool.136 |

* 1. International Supplemental Screening Practice

Current guidelines for supplemental breast screening are limited to women deemed to be at high-risk of developing breast cancer. Therefore, the lack of consensus and lack of use of formal risk assessment protocols can be a barrier to implementing supplemental screening, with appropriate and consistent application required to identify those who may be recommended for supplemental screening.

Guidelines on the imaging type used for supplemental screening vary, mainly due to the availability of resources. Since discovery of the BRCA1/2 gene mutations for breast cancer susceptibility in the mid-1990s, MRI has been used as a screening tool for women with high breast cancer risk. MRI was first recommended for women with a lifetime breast cancer risk of ≥20% by the American Cancer Society in 2007137. Breast MRI does not use ionising radiation but does require intravenous injection of contrast medium. Studies have demonstrated superiority of MRI over mammography for cancer detection in women with higher risk136,138. A recent meta-analysis of cancer detection rates for high-risk women in diagnostic studies using MRI, mammography or both demonstrated that a combination was best for identification of cancers.139

However, MRI is not always appropriate due to contraindications (e.g. metalware, pacemakers), claustrophobia, availability and cost.140–142 Abbreviated MRI is a more efficient, tailored protocol specifically aimed to detect the presence or absence of cancer, that is as effective diagnostically as standard MRI, whilst reducing cost and improving accessibility.143

Standard mammography, that creates 2D images from multiple x-rays, is not generally recommended as a supplemental screening method due to low sensitivity in high-risk women118 and the harmful risk of radiation exposure for younger women.119 However, a Canadian retrospective study comparing the interval cancer rates of annual vs biennial screening for women with dense breasts demonstrated a reduction in interval cancers for those screened annually.144 Thus, suggesting that women with dense breasts may benefit from an annual screening programme.

Contrast-enhanced digital mammography (CEM) is a simpler, lower cost alternative to MRI that utilises intravenous contrast injection in combination with X-ray image subtraction. It has been shown to be more sensitive than mammography and ultrasound for detecting breast cancer, including in a screening population 145–147 and has similar sensitivity to MRI with respect to cancer detection and tumour size estimation.148 CEM has been reported to improve cancer diagnosis in dense breasts compared with mammography.128 This could be a good alternative for those that cannot undergo MRI, however, radiation exposure may exclude use for younger women and at present it is not widely available in Aotearoa New Zealand.

Breast ultrasonography (US) uses sound waves to image tissue, it is widely available (although with capacity issues within the public healthcare system in Aotearoa New Zealand) with no radiation or intravenous contrast required. Initial clinical studies showed no value in the use of ultrasound to detect cancers in asymptomatic women with a negative mammogram. However, by the mid-1990s improvements in technology resulted in the detection of cancers missed on mammograms.149 It was subsequently demonstrated to identify small sized, node negative tumours not visible on mammography149–151 and increase cancer detection rates in women with dense breasts,122 however, at a rate much lower than MRI but with similar specificity (as described in Table 4 Outcomes from Supplemental Screening after standard 2D Mammography in women with dense breasts (or all densities for MRI)).

Digital Breast Tomosynthesis (DBT) or 3D mammography uses multiple X-ray images to create a 3D breast image. A reduction in the superimposition of imaging fields allows for visualisation of abnormalities that may be obscured by overlapping tissue. Increased visibility allows for better identification of tissue architecture, minimising overdiagnosis and reducing recall rates for assessment.152–154 Support for the use of DBT in routine screening has been demonstrated in a number of studies showing improved and earlier cancer detection and improved specificity. 33,155,156 DBT was initially utilised in addition to digital mammography and improvements in cancer detection and specificity were observed.152,157,158 However, it has been suggested to be better utilised for routine screening rather than for supplemental or high-risk screening. A study investigating the effectiveness of DBT screening showed benefit for women with heterogeneously dense breasts but none for women with extremely dense breasts.154 DBT is available in a number of private providers in New Zealand, with limited availability outside of this.

* 1. Supplemental Screening Modality Outcomes

Any modality of breast screening has benefits and harms to the patient. In the context of supplemental screening three metrics have been described in the literature to quantify and compare modalities – the incremental cancer detection rate, recall rate and interval cancer rate.

The incremental cancer detection rate is the number of additional cancers detected at screening with a particular modality relative to another. This is often stated as a percentage of screens or as a rate per 1000 screens.5

The recall rate is the number of women recalled for further assessment as a proportion of all women who were screened. A recall may be a consequence of the screening mammogram, for (i) a repeat mammogram because of technical inadequacy of the screening mammogram (technical recall) or (ii) clarification of a perceived abnormality detected at screening, by performance of an additional procedure (recall for further assessment).5 The additional false positive recall rate is the percentage of women recalled who were found to not have cancer.

An interval cancer is a primary breast cancer diagnosed in a woman who had a result in a screening test, with or without further assessment, that was negative for malignancy, either (i) before the next invitation to screening was due or (ii) within a period equal to a screening interval for a woman who has reached the upper age limit for screening. This may be expressed as a rate, which is the number of interval cancers diagnosed within a defined period since the last negative result in a screening examination, per 1000 women with negative results.5

A comparison of supplemental screening outcomes with regards to cancer detection predominantly in women with dense breasts (all densities for MRI) was summarised by Berg et al 2023100 (see Table 4 below). With regards to cancer detection MRI has the highest rate of incremental detection at between 6-20 per 1000 screens, with CEM the next best improvement at 7-13 per 1000 screens. Supplemental screening with ultrasound and DBT provides a modest improvement in cancer detection. All methods of screening are associated with false positive recalls, which decrease with subsequent rounds. In women with dense breasts ultrasound and MRI screening results in an average recall rate of 8-11% with first screens, which decreases to between 2% and 5% with subsequent screens.159,160 Overall, CEM has an average recall rate of 6.5%.

Table 4: Outcomes from Supplemental Screening after standard 2D Mammography in women with dense breasts (or all densities for MRI)

|  |  |  |  |
| --- | --- | --- | --- |
| Method | Incremental Cancer Detection Rate per 1000 | False Positive Recall Rate | Interval Cancers Reduced |
| US\* (first round) | 2–3161 | 8%–12%123,161,162 | Yes |
| US (subsequent rounds) | 1–3123,162,163 | 2%–5%123,162,163 | Yes |
| Contrast-enhanced mammography (CEM) | 7–13146,164–166 | 6.5%146,164–166 | Unknown |
| DBT | 1.2-1.4 152,154 | Unknown | Unknown |
| MRI or abbreviated MRI (first round) | 10–20123,159,167–169 | 9%123,159,167–169 | Yes |
| MRI  (subsequent rounds) | 6–7169,170 | 2%169,170 | Yes |

\*US – ultrasound

Adapted from Berg et al. 2023100

* 1. Breast screening benefits and the potential additional benefit of Breast Density reporting

Population-based mammography screening programmes have been shown to decrease breast cancer mortality, although estimates vary in magnitude and across age groups. 171–173 However, identifying mortality benefit from mammography can be challenging174 and there are known issues in breast screening programmes with estimation of overdiagnosis, false positive results and false negative results or interval cancers171,175. Screening programmes can also reduce morbidity with early diagnosis enabling less extensive surgical procedures (e.g. breast conserving surgery), and avoidance of adjuvant therapy, and more recently lower intensity radiotherapy.176–179 The potential benefits and risks of reporting breast density are dependent firstly on the standard screening programme plus the addition of density measurement and any subsequent screening modality. These issues are further discussed below.

### Benefits

#### Mortality

The benefits of breast density reporting and resultant supplemental screening are currently difficult to quantify, particularly given that overall breast cancer survival is high compared to other cancer types180. It should be noted that overall breast cancer mortality in New Zealand is 16% higher than Australia.181 Due to the time required to evaluate mortality data, no randomised controlled trials have yet demonstrated decreased mortality due to supplemental screening for any high-risk populations.136

A case control study published in 2017, from within the Nijmegen (Dutch) screening programme (1975- 2008) looked at screening outcomes, including cancer mortality in women aged 50-74 years with dense breasts compared to women with non-dense breasts. These women received biennial, screen-film 2D mammography, with density measured using a 4 scale category based on the Wolfe breast density pattern (similar to BI-RADS). Analyses of mortality odds ratios were based on 333 breast cancer deaths occurring between 1977 and 2008, demonstrating an overall 33% lower risk of breast cancer death for women who participated in screening in the 4 years prior to diagnosis compared with women who did not participate. However, the estimated mortality reduction from participating in the screening programme was less for women with dense breasts compared to those with non-dense breasts (13% for dense compared to 41% for non-dense breasts).58 Furthermore, results from the Kopparberg randomised controlled trial in Sweden published in 2010 also confirmed that women with dense breasts have a higher incidence of cancer, increased breast cancer related mortality but no difference in survival once diagnosed. This trial measured baseline breast density with the Tabar classification from screen-film 2D mammography. It prospectively followed 15,658 women aged 45-59 randomised to invitation to screening or no invitation between 1977 and 1981. Enrolled women who were offered screening every 2-3 years (depending on age) were prospectively followed up until 2004, with an average follow-up of 25 years 59 An American study of over 9,000 women with primary invasive breast cancer, with a mean follow-up of 5 years, concluded that high breast density was not associated with risk of death from breast cancer or death from any cause after accounting for other patient and tumour characteristics.61 Therefore, for women with dense breasts there is an increased incidence of cancer, decreased mammographic sensitivity and in some studies, increased mortality from these factors. However, a difference in survival after diagnosis has not been consistently shown. However, the findings from these studies suggest that providing a supplemental screening approach to women with dense breasts could result in improved cancer detection and improved outcomes for these women.

#### Morbidity

In the absence of survival comparisons for women with dense breasts treated with or without supplemental screening the next best outcome measures are cancer detection rates, stage at diagnosis and interval cancer rates. Increased cancer detection may lead to earlier diagnosis of breast cancer with the possibility of treatment at an earlier stage, thus potentially decreasing morbidity and mortality.

Numerous studies, including randomised control trials comparing mammography alone with mammography combined with a supplemental screening test in high-risk women have illustrated statistically significant increases in cancer detection rates. 123,150,182–184 and earlier detection of cancer, reducing incidence of late stage cancers, which could decrease the need for adjuvant therapy and reduce mortality.185

A 2018 meta-analysis of twenty-nine studies published after the year 2000 and including over 100,000 screen results concluded that women with dense breasts who underwent supplemental ultrasound screening reported an average 40% increase in the detection of cancers compared to mammography alone. This equates to an additional 3.8 screen-detected cancers per 1000 mammography-negative women. There was heterogeneity in the studies included with respect to screening types and regimes, study populations, age range and importantly density classification. The inclusion of women with lesser breast density (scattered) slightly diluted the benefit of additional cancer detection by US. Addition of ultrasound was of slightly more benefit after film screen mammography compared to digital mammography.186

The Japanese J-START randomised controlled trial primary analysis published in 2016 reported on over 72,000 women aged 40-49 years randomised to receive either mammography and supplemental ultrasound, or mammography alone. With the addition of ultrasound the cancer detection rate increased from 0.32% to 0.5%, detection of earlier stage cancers (0 and 1) increased from 52% to 71% and there was a decrease in the interval cancer rate from 0.1% to 0.05%.124 A subsequent secondary analysis of 19,000 records with corresponding breast density measures published in 2021, confirmed increased sensitivity and improved detection of early-stage and invasive cancers in women with dense breasts who receive supplemental ultrasound.187 The 2019 DENSE clinical trial investigated the incidence of interval cancer in over 40,000 women with dense breasts, aged 50-75 years old, whom were participating in the Dutch population-based, biennial, digital mammography screening programme. Approximately 4,700 women with extremely dense breasts and a negative mammogram result underwent supplemental MRI screening. A reduction in interval cancers from 5.0 per 1000 to 2.5 per 1000 screenings was observed with the first round of MRI screening compared to the mammography only group.159

Breast cancers detected by screening in general have more favourable characteristics, they are smaller, of lower grade, are less likely to metastasise, and require less extensive treatments, although the debate about the magnitude of overdiagnosis in this context is noted.176–178 Women who participate in breast screening programmes have been shown to have lower rates of mastectomy, lower rates of radiotherapy post mastectomy, fewer axillary dissections and fewer recommendations for chemotherapy compared to women who do not participate in breast screening programmes.179 This has implications for short and long term quality of life. Breast cancer survivors have reported significant long term adverse effects that vary depending on the type of treatment received.188 Breast conservation is associated with a better quality of life compared to mastectomy189. Sentinel node biopsies are preferable over axillary dissections due to less perceived pain, stiffness and lymphedema190,191, whilst chemotherapy and radiotherapy have well recognised acute and long term side effects.192–195 Therefore, early detection and tumour characterisation at diagnosis should help to tailor treatments effectively and minimise harms.

In addition to the morbidity benefits of early cancer detection, treatment costs for early stage breast cancers are reduced compared to late stage breast cancers. A 2024 systemic review including 53 studies estimating the economic burden of breast cancer in the USA, Canada, Australia and Western Europe found that despite heterogeneity in study design and cost estimation, metastatic breast cancer was associated with higher costs than earlier-stage cancer.196 An earlier systemic review from 2018 including 20 studies from 10 different countries concluded that cost data by stage was limited and hard to compare, however, in general treatment costs by stage at diagnosis increased with advancement of stage.197 A 5-year follow-up study, published in 2022, of public healthcare costs associated with breast cancer treatment in Aotearoa New Zealand confirmed that treating patients with early stage breast cancer was less costly than treating those with metastatic disease.198

* 1. Breast screening harms and the potential additional harms of Breast Density reporting

In Aotearoa New Zealand the national breast screening programme is estimated to reduce breast cancer mortality by 30% in regularly screened women (screened ≥3 times and mean screening interval ≤30 months).13 There are inequities in access to the programme by ethnicity with only 63% of eligible wāhine Māori screened in the last two years (as at January 2025) compared to 73% of Other (non-Māori, non-Pacific, non-Asian) women.199 Wāhine Māori also have a higher prevalence of breast cancer, and an increased mortality rate relative to European women.200–203 Given that wāhine Māori may have higher breast density37, this is a potentially compounding risk factor to the access inequities which already exist for Wāhine Māori. Further to this, measuring breast density and provision of supplemental screening would come with a cost. Screening services in Aotearoa New Zealand share limited resources, often with symptomatic breast care services. Therefore, any extra demands placed on screening services could have unintended consequences for access to diagnostic and screening tests for symptomatic patients and current screening participants.204

Given that 50% of the population potentially have dense breasts (10% extremely and 40% heterogeneously), supplemental screening could possibly impact many women. As the prevalence of density, including any ethnic variability in Aotearoa New Zealand is unclear, this has major implications for informing recommendations on breast density reporting in the Aotearoa New Zealand context. An American study calculating a 5 year breast cancer risk using the Breast Cancer Surveillance Consortium (BCSC) model demonstrated that not all women with dense breasts have a high-risk of interval cancer. Therefore in the absence of consideration of risk factors other than dense breasts, half of women could undergo supplemental screening unnecessarily. Conversely, using the combination of breast cancer risk and breast density improves identification of women at high-risk compared with age and breast density alone.205 The addition of breast density measures to standard risk prediction tools also improves identification of high-risk women.206 Therefore a combination of breast density and other risk factors may be required to target women with dense breasts who are at the greatest risk of developing cancer.

The main harm of breast screening is overdiagnosis, which is characterised by the detection of cancers that may have never advanced to hazardous disease.207 Unnecessary treatment is harmful for the patient and reduces the cost effectiveness of screening, however, there is currently no way to avoid some level of overdiagnosis and it is difficult to estimate the magnitude of the problem. Overdiagnosis can be estimated, although rates vary depending on the methodology used.208 Randomised clinical trial estimates range from 10-30% overdiagnosis of breast cancer.209–212 A study of breast cancer incidence rate trends in Aotearoa New Zealand following the 2004 age range extension to the BSA programme concluded that there was no evidence of screening related overdiagnosis.213 There needs to be a balance between increased sensitivity to identify cancerous tissue and decreased specificity of the imaging modality.

As discussed earlier, false positive findings that lead to a recall for assessment are an expected outcome of mammographic screening. Most recalls result in additional imaging (10% of all screens214), with approximately 6% of women regularly screened (over a 10 year period) receiving a biopsy that does not reveal cancer215. The 2019 DENSE clinical trial demonstrating reduced interval cancers with supplemental MRI for women with dense breasts had an overall recall rate of 9.5% and a biopsy rate of 6.3%. The false positive rate[[1]](#footnote-1) was 8%, and 74% of women who underwent biopsy on the basis of MRI did not have cancer. 159 False positive rates for BreastScreen Aotearoa were 7.3% for initial and 2.6% for subsequent screens of all women screened aged 50-69 years between July 2020 and June 2022.17

The anxiety associated with additional testing is generally deemed acceptable by women surveyed in return for the benefit of early diagnosis.216 False negatives occur when a mammogram is reported as normal, but a cancer is present and interval cancers are cancers that are found in the interval between a negative screen and the time a next screen would have occurred. While these can be cancers that develop between screening rounds, they may be due to screening modality limitations, technical or clinical interpretation errors and represent underdiagnosis. 10

If supplemental screening was not funded in Aotearoa New Zealand, women with dense breasts would have to cover the additional cost of supplemental screening which could create stress, fear and anxiety if women cannot afford this and could introduce further inequities in screening access and outcomes. Supplemental screening tests are generally only covered under health insurance for women who, based on risk calculators, have a high lifetime cancer risk (25% in Aotearoa New Zealand), a threshold that most women with dense breasts will not meet in the absence of other risk factors. Women in Aotearoa New Zealand aged 40-50 years considered ‘moderate’ risk (12-25% lifetime risk) should be offered annual mammography (see Appendices: Management of BRCA in Aotearoa New Zealand). This is the scenario that many women with dense breasts would fall within.109,217

Comparative modelling of supplemental ultrasound screening for women with dense breasts suggested that the addition of ultrasound screening after a negative mammogram would substantially increase costs while producing relatively small benefits in breast cancer deaths averted and QALYs gained. 218

1. Breast density reporting
   1. Internationally

Breast density reporting within screening programmes is becoming more widespread. In December 2023 the Royal Australian and New Zealand College of Radiologists (RANZCR) recommended ‘mandating the reporting of breast density in both screening and diagnostic settings in Australia and New Zealand’.219 BreastScreen Australia does not require providers to report breast density although it is voluntarily reported by New South Wales, Western and South Australia screening programmes. A National Policy and Funding Review of BreastScreen Australia is in progress to develop recommendations for evidence-based best practice in breast cancer screening220 with a trial being run in Queensland to investigate various psychosocial outcomes and health service use related to reporting breast density.221

The National Health Service (NHS) Breast Screening Programme in England does not currently include assessment or reporting of breast density on screening mammograms.222 Though the recently published study discussed earlier of a consecutive English screening cohort has concluded that mammographic sensitivity and specificity decreases whilst interval cancers increase with increasing breast density and consideration should be given to offer supplemental imaging to women with extremely dense breasts.54

In Canada, 12 of 13 provinces/territories have independent breast cancer screening programmes that vary in participation criteria, however, breast density is reported in 11 of these. 223 In 2022, the European Society of Breast Imaging (EUOSBI) recommended that women should be appropriately informed about their breast density, and on the diagnostic and prognostic implications of having dense breasts.224 An analysis of national breast screening guidelines in Europe found that as of 25 April 2023 the following countries reported breast density: Austria, Bulgaria, Croatia, Cyprus (for BI-RADS categories C and D), France, Greece, Hungary, Serbia and Switzerland.

From 10 September 2024 in the United States of America (USA) all mammogram result letters to women must report whether the breasts are “dense” or “not dense” and the report to providers must report the BI-RADS density category. 100,225

Breast density reporting internationally needs to be considered in the context of different health care systems. Comparisons between these systems can be complex. Most of the countries discussed above have universal or near-universal health coverage. However, health system funding is varied. Similar to Aotearoa New Zealand, countries such as England, Canada, Italy, and Norway have largely publicly funded and operated health systems. Some, including Australia, France, Croatia, and Germany have mandatory publicly funded insurance whereas others, such as the Netherlands, have a mix of private (non-profit and profit) and public insurance. The United States has a voluntary private insurance system more recently supplemented by public insurance programmes. With this funding, each country provides different levels of service provision. These system differences will influence breast density reporting practices.226,227

Table 5: Breast Density reporting status in International screening programmes

|  |  |  |
| --- | --- | --- |
| Country | Breast density reporting in the national screening programme | Comments |
| Australia | Partial | Reported in New South Wales, Western Australia and South Australia24,228,229 |
| Canada | Yes | In all provinces with an organised screening programme223 |
| United States of America\* | Yes | Mandated from 10th September 2024225 |
| United Kingdom and Ireland | None |  |
| Europe:  Austria,  Bulgaria,  Croatia,  Cyprus,  France,  Greece,  Hungary,  Lithuania,  Serbia,  Switzerland | Yes | Known European countries that report density as at April 2023222 |
| Europe:  Germany,  Iceland,  Italy,  The Netherlands, Norway | None | Known European countries that do not report density as at April 2023222 |

**\*** does not have a national organised screening programme, considered opportunistic

* 1. Supplemental Screening Guidelines

Currently, there is no consensus guideline uniformly recommending supplementary screening based on dense breasts alone. However, women with dense breasts and other risk factors often have an estimated lifetime risk ≥20% and can meet high-risk screening criteria. Current recommendations from professional organisations and guideline development groups on supplemental screening for women with dense breasts are summarised below with further detail in the appendices.230 The European Society of Breast Imaging (EUSOBI) recommends adding screening MRI every two to four years in women aged 50 to 70 years who have extremely dense breasts. The American College of Radiology (ACR) recommendation for women with dense breasts is annual mammography, annual MRI, and to consider CEM or ultrasound as an alternative to MRI (at 40 years or earlier if other risk factors present).231 The German Gynaecological Oncology Working Group (AGO) recommend breast ultrasound for heterogeneously or extremely dense breasts and MRI if a screening mammogram is negative and breast composition is extremely dense for women aged 50-75. The American based National Comprehensive Cancer Network (NCCN), The American Cancer Society (ACS), the ACR, and EUSOBI all recommend annual MRI when dense breast is present in combination with other risk factors that result in a lifetime risk of ≥20%.100 The German Guideline Program in Oncology, The Brazilian College of Radiology and Diagnostic Imaging (CBR), Brazilian Breast Disease Society (SBM), The Brazilian Federation of Gynaecological and Obstetrical Associations (Febrasgo) and the China Anti-Cancer Association all recommend or advise considering supplemental screening with ultrasound.230

Some professional organisations and guideline development groups have concluded that there is insufficient or limited evidence to make a recommendation on supplemental screening for women with dense breasts. This includes The European Commission Initiative on Breast Cancer Guideline Development Group, The United Kingdom National Screening Committee, The Royal College of Radiologists (United Kingdom), The Japanese Breast Cancer Society, The American College of Obstetricians and Gynaecologists, the American Cancer Society, The United States Preventive Services Task Force and The American Academy of Family Physicians.230 The Royal Australian and New Zealand College of Radiologists position statement updated in 2023 suggests that the EUSOBI screening statement is an aspirational goal and that breast density reporting should be mandated whilst a future risk-based model for breast cancer screening is developed. 219

Table 6: Summary of breast density related screening guidelines/recommendations/position statements

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Professional Organisation | Year | Measure Breast Density | Supplemental Screening | Recommendation and relevant comments |
| European Commission Initiative on Breast Cancer Guideline Development Group (GDG)232 | 2020 |  | No | Tailored screening for mammographic breast density |
| European Society of Breast Imaging (EUSOBI)224 | 2022 | Yes | Yes | SS with MRI\* at least every 4 years, preferably every 2–3 years for women with extremely dense breasts aged 50–70. US in combination with DM\* may be used |
| The German Guideline Program in Oncology (German Cancer Society, German Cancer Aid, Association of Scientific Medical Societies (AWMF))233 | 2021 |  | Yes | SS with US, consider tomosynthesis |
| The German Gynaecological Oncology Working Group (AGO)234 | 2020 |  | Yes | Breast US\* for heterogeneously dense, extremely dense mammograms. MRI if screening mammogram is negative and breast composition extremely dense 50–75 years old |
| The Royal College of Radiologists (United Kingdom)235 | 2019 | High-risk | No |  |
| The Royal Australian and New Zealand College of Radiologists219 | 2023 | Yes | No | Aspirational goal to follow EUSOBI guidance |
| The Brazilian College of Radiology and Diagnostic Imaging (CBR), Brazilian Breast Disease Society (SBM), and Brazilian Federation of Gynecological and Obstetrical Associations (Febrasgo)236 | 2017 |  | Yes | Complementary US should be considered |
| Alberta Breast Cancer Screening  Clinical Practice Guideline237 | 2022 |  | Yes | Annual mammography and consider annual breast ultrasound and consider annual clinical breast exam |
| China Anti-Cancer Association238 | 2019 |  | Yes | Breast US |
| The Japanese Breast Cancer Society239 | 2018 | Yes | No |  |
| American College of Radiology240 | 2023 |  | Yes | DBT\* screening usually appropriate  Annual mammography and annual MRI  Consider CEM or ultrasound as alternative to MRI (Age 40 or earlier if other risk factors) |
| American College of Obstetricians and Gynecologists241 | 2020 | Yes | No |  |
| American Cancer Society137 | 2007 |  | No |  |
| The National Comprehensive Cancer Network242 (American) | 2024 |  | Yes | For individuals ≥40 years of age with heterogeneous or extremely dense breasts, consideration should be made for supplemental screening |
| The Society of Breast Imaging243 | 2010 |  | Yes | US |
| The United States Preventive Services Task Force (USPTSF)244 | 2016 |  | No |  |
| The American Academy of Family Physicians245 | 2021 |  | No |  |

\*Abbreviations: SS = Supplemental screening, IV= Intravenous, DM = Digital Mammography, US = Ultrasound, DBT = Digital Breast Tomosynthesis, MRI = Magnetic Resonance Imaging, CEM= Contrast Enhanced Mammography

Source: Adapted from: O'Driscoll et al. 2023230

* 1. Ethical and legal considerations

The framework for ethics analysis of public health programmes proposed by Kass (2001) states that “public health interventions should reduce morbidity or mortality; data must substantiate that a program (or the series of programs of which a program is a part) will reduce morbidity or mortality; burdens of the program must be identified and minimized; the program must be implemented fairly and must, at times, minimize preexisting social injustices; and fair procedures must be used to determine which burdens are acceptable to a community”.246 Considering these factors with regards to notification of breast density within a breast screening programme raises a number of ethical perspectives, some of which have been mentioned in preceding sections, and some are discussed below.

There is uncertainty in the measurement and management of breast density. Mammographic visual assessment of breast density is subjective, though this could be partially addressed with the use of validated automated measurement. The appropriate clinical pathway is also unclear with survival data not yet available from clinical trials evaluating supplemental screening in women with dense breasts.247 Enhanced and earlier cancer detection has been reported with the addition of supplemental screening, however, this can be associated with increased false positives. 124,159,186 This raises concern that any benefits gained from supplemental screening could result in harms to some from overdiagnosis. There would also be additional costs to the programme that would be dependent on the screening modality used and would need to be considered. This uncertainty makes it difficult to evaluate outcomes, fairness and acceptability for participants of the programme and to evaluate potential opportunity costs.

Known inequities already exist in breast cancer outcomes overall, particularly the symptomatic pathway201,248, and also in access to the BreastScreen Aotearoa programme by ethnicity, deprivation level and place of residence.199 It is likely that socio-economic deprivation, income levels, urban/rural residence, and comorbidities also influence interactions with the breast cancer screening programme in Aotearoa New Zealand.249 Women with dense breasts are at a greater risk of developing cancer, have higher rates of interval cancers that are more advanced at the time of diagnosis and do not have the same mortality benefit from population-based mammographic breast screening as women with non-dense breasts. This all suggests that there is also inequality for women with dense breasts in the opportunity to benefit from early diagnosis of breast cancer associated with screening. If supplemental screening is not available to women with dense breasts through the public health system, it will not be accessible to many due to cost. There is already inequity in the current system, as breast density is measured and reported by most private providers of breast screening in Aotearoa New Zealand. These parameters of inequity are unfair, potentially compounding and are likely to further disadvantage some groups of women already facing inequities, for example, wāhine Māori with dense breasts. The code of expectations for health entities’ engagement with consumers and whānau, published by the Health Quality and Safety Commission and required by the Pae Ora Healthy Futures Act 2022 sets the expectations for health entities, including to promote equity and to engage with those with greater health needs, particularly Māori, Pacific peoples and disabled peoples.250,251

Providing adequate and effective breast density information supports women’s autonomy to make informed decisions about their care.247 There are two issues to consider, firstly, the act of providing information on personal breast density and secondly what to do once presented with that information. It has been established that breast density is associated with risk of cancer development and reduced detection on mammography, and that some modalities of imaging are more sensitive at detecting breast cancer in dense breasts. In Aotearoa New Zealand the Code of Health and Disability Services Consumers' Rights establishes the rights of patients, and the obligations and duties of healthcare providers. Right 6 specifically outlines the right to be fully informed, including (but not limited to) the results of tests and an explanation of the options available, an assessment of expected risks, side effects, benefits and cost options, with Right 7 detailing the right to make an informed choice and give informed consent.252 Therefore, if breast density was measured but not disclosed to women this would be depriving women of their right to be fully informed and make an informed decision. The lack of guidance and consensus on how best to clinically manage women with dense breasts may be perceived as unhelpful, and concerning for women, however, it highlights the importance of providing clear information on the harms and benefits of participation. A well-considered and thorough consent process will help to alleviate the issue of uncertainty. What information and how best to provide it could be extrapolated from international evidence, however, ideally this needs to be explored in the Aotearoa New Zealand setting to allow Aotearoa New Zealand women to make the best decisions. Furthermore, to facilitate consent for a complex issue is time consuming and cognitively stressful for healthcare professionals already under significant pressures. Where this responsibility would sit needs to be considered within a health care system already affected by significant capacity issues including the current rollout of breast cancer screening age extension to 70-74 years.

Healthcare professionals have a duty of care to take reasonable steps to avoid harm to their patients. This includes informing patients of material risk that could alter their decision making. The Health and Disability Services Consumers' Rights code also details the right to services of an appropriate standard, in a manner that minimises the potential harm to and optimises the quality of life of that consumer.252 However, it may be difficult to determine in advance what is appropriate and reasonable, which may be dependent on personal circumstance. These uncertainties around evidence and guidance can result in a loss of trust and be damaging to the relationship between patient and health professional.247

1. Perspectives on Breast Density Reporting
   1. Consumer information

Breast density information has become more widely available for both patients and healthcare professionals with a primary source of this information being online resources. A 2022 review by Nickel et al. of online information about breast density available in five English-speaking countries concluded that information is not generally presented in a manner that is easy to understand or act upon and there is no consistent pattern of content. The majority of information was based on what breast density is, how it is measured and what dense breasts mean. Only a few websites directly stated benefits and harms of measuring and reporting breast density and these were mainly focused on the use of supplemental screening. The most common recommendation was for women to talk with their doctor, including the suggestion to discuss what breast density means for them, their individual risk and supplemental screening options. Furthermore, most websites did not include directly referenced peer reviewed data or articles. 253

* 1. Participants

The perspectives of breast screening programme participants on measuring and reporting breast density have been studied in the USA for over a decade, and more recently in England and Australia There is no published evidence on participants’ perspective on breast density in Aotearoa New Zealand. As discussed earlier there are differences in funding models and population stratification across health systems that could potentially influence participant and professional perspectives, however, the international evidence provides insights and can inform the approach for exploring the perspectives of BreastScreen Aotearoa participants on breast density reporting.

Breast density notifications vary by screening programme. In the USA current regulations stipulate that patients receive the classification of dense or non-dense, (where dense is defined as BI-RADS category C or D) and notification that dense tissue makes it harder to find breast cancer on a mammogram.254 Breast Screen Western Australia notifies women when a mammogram shows marked increased breast density and they are advised in writing to consult their GP to discuss the significance of their breast density, to have a clinical examination and receive further advice about their breast cancer risk.228 Breast Screen South Australia provide the BI-RADS density category A-D in the patient results letter.24 BreastScreen New South Wales provide participants and their nominated GP a density report in their screening result letter, which is accompanied by a breast density factsheet.229

#### Do people want to be told their breast density at screening?

The majority of women involved in studies based in the USA and Australia would like to know their breast density.253,255–257 Women participating in online focus groups in two Australian states that do not have breast density notification had a two-hour facilitated discussion with trained moderators about breast density. Following this, many felt that they had a ‘right to know’ about their breast density and they would like to be informed and educated about it.257 Prior to this, most had not heard of breast density or did not know what it meant. It was noted that the concept of breast density and implications of having dense breasts can be difficult to understand when first learning about it. Some women argued that as breast density impacts the sensitivity of the test, women should be told about density as a routine part of the screening process .257 They viewed provision of health information as intrinsically valuable, irrespective of whether that information can improve outcomes. A similar positive attitude to breast density reporting was found in a survey of 6922 women in Western Australia, in which two thirds of women felt that knowing their breast density made them feel more informed.258

Similarly, women in the USA felt more informed by knowing their breast density.  In a 2017 survey of 1502 women from states with and without breast density notification legislation, 63% of women wanted to know their breast density, which had increased from 60% in 2012.259 Forty-five percent of participants thought that receiving breast density information would create anxiety and 40% thought it would cause confusion but 90% felt they would be better informed.

Studies suggest that although breast density notification increases anxiety, women value having this information. In a survey of 264 women (48% black, 35% Latina, 17% white) in New York City where women with dense breasts were notified, 40% of the respondents said they would feel anxious if they were told they had dense breasts but the majority (77%) also felt they would be in a better position to make decisions about their health .260 When told that doctors and scientists do not agree on the benefit of having additional tests in the context of dense breasts, 82% of participants said that they would still like to know whether they had dense breasts or not. In a study of Hispanic women in New York City attending breast screening when density notification was mandatory, most appreciated learning about their breast density and thought that this would influence future screening and help cope with any future breast cancer diagnosis.261

A study in the USA undertaken prior to a law mandating breast density notification in April 2013 explored attitudes to breast density reporting by women in an affluent and a more deprived area.262 Most women wanted to know their breast density, with a higher proportion in the women attending the facility that was in a more affluent neighbourhood (94%) compared with those attending the hospital that was in a more deprived area (79%).

The majority of women would like to know their breast density, even when they were advised that there was uncertainty about the benefit of additional tests. Knowing their breast density made women feel more informed and better able to make decisions about their health.

#### What is the psychological impact of breast density notification for participants?

A systematic review of the impact of breast density notification on cognitive, psychological and behavioural outcomes found that women experienced anxiety and confusion related to breast density notification.263 Anxiety could be caused by various issues: misinterpretation and misunderstanding of the information, uncertainty about what to do with the information, and from the psychological impact of increased cancer risk.263,264 Additionally, breast density notification increases supplemental screening uptake, with a subsequent rise in false positive findings.265 The additional screening and unnecessary biopsies can cause psychological and physical harms. In a study in Western Australia, anxiety was higher among those informed about breast density for the first time compared with those who had been notified multiple times.258 Confusion was caused by the lack of evidence about what to do if you have dense breasts. 258

A randomised controlled trial set in Australian states without breast density notification illustrated that informing people of their breast density causes more anxiety and confusion than not informing them. Participants receiving mammogram results were randomly assigned to either not receive breast density results, to receive their breast density results with a standard information leaflet or to receive their breast density results with a health literacy sensitive version of the information leaflet.266 Compared with the control group, more women who received density notification via the standard information leaflet and the health literate version reported feeling anxious (14.2% vs 49.4% and 48.5%; P < .001), confused (7.8% vs 24.0% and 23.6%; P < .001), and worried about breast cancer (quite/very worried: 6.9% vs 17.2% and 15.5%; P < .001). There were no statistically significant differences in the above outcomes between the groups that received the standard or the health literacy sensitive information leaflet.

Australian women participating in an online focus group were asked to imagine being told they had dense breasts, and then to state what their level of anxiety would be: 30% said they would not feel anxious at all, 50% would feel a little anxious, 13% moderately anxious and 5% very anxious.264 When asked what they would do if they were told they had dense breasts, (participants could respond with more than one option) 39% said they would talk with their doctor/GP, 23% that they would have supplemental screening, 15% said they would have annual mammograms and 19% that they would do nothing differently. Dench (2020) noted that women who reported anxiety following breast density notification had increased intention to screen in the future.258

In a systematic review of breast density notification in racial and ethnic groups, eight of the studies (all in the USA) examined emotional reactions to breast density notification.267 Seven studies reported increased anxiety among Black, Hispanic and Asian women compared with White women while one study found no difference in anxiety by ethnicity.268 Anxiety was partly attributed to factors other than ethnicity such as reported discrimination, income and education.269 High income women in the USA reported less anxiety about breast density notification and black women reported higher anxiety and confusion.270 Anxiety was created for Hispanic and Spanish speaking women through difficulty understanding breast density notification271 and concerns around the need for further screening and potential barriers.261

In a USA telephone survey of a diverse sample of 1322 women who had received breast density results, the level of anxiety varied by ethnicity and sociodemographics with non-Hispanic Black, Asian, and Hispanic women and women with low literacy being two to three times more likely to report anxiety than non-Hispanic White women.272 Asian women and those with low literacy did not feel as informed and more often felt confused.

Informing women of their breast density at mammographic screening can cause anxiety and confusion. Studies from the USA indicate that this happens to a greater extent in black, Hispanic and Asian women and in those with lower health literacy. Health literacy can be viewed as a quality of the relationship and communication between a patient and their health care provider69, which needs further exploration in the Aotearoa NZ context, particularly given recognition of the underserved population sub-groups. 273

#### What formats of communication are most effective?

Breast density will be a new concept to most women, therefore effective communication of the results is critical. Some Australian women felt that breast density results should be communicated by health professionals so the results could be put in the context of other risk factors for breast cancer and any anxiety or concerns addressed.274 Others were happy with breast density results being given by letter, and stated that this should also include an explanation of the implications of the result. Some wanted the option of having a trusted healthcare professional to discuss the results with.

A USA telephone survey of 2306 women with in-depth interviews of 61 participants concluded that a multimodal approach to density notification (e.g. letter and option to speak with a healthcare professional) was preferable and that a ‘one size fits all’ approach to breast density education will not work.275 The majority (80%) of survey participants said that they would prefer to receive their breast density information from a healthcare provider, 12% said in a letter and 7% from a website or online portal. Preferences varied by ethnicity with a high proportion (85%) of non-Hispanic black women preferring to receive the information from a health care provider. The qualitative part of the survey found that receiving a letter accompanied by some pictures would be helpful, as was having the option to talk with a healthcare provider. Women surveyed in Massachusetts seven months after the implementation of breast density notification agreed with the need for healthcare professional input, and stated that breast density information should be provided in the context of a woman’s overall risk. 276

Nearly all participants in a qualitative study of breast density notification among Hispanic women in the USA stated that healthcare providers are the most appropriate providers of information about breast density and several stressed the importance of an in-person discussion.261 They also wanted an information leaflet alongside written results.

Breast density reporting commenced in Western Australia in 2008 and women with dense breasts are advised to discuss their result with their GP. Women diagnosed with interval cancer in Western Australia between 2011 and 2020 suggested that screening programmes could offer better education in a clearly understandable format about the limitations of mammography.277 The research identified that the role of the breast screening programme in the management of breast density is a major concern, with conflicting views among participants. Some women suggested that if dense breasts are found, there should be more emphasis on the recommendation to see a GP. Others stated that they were grateful for the letter advising about their dense breasts and the potential implications and attributed earlier detection of their cancer to the letter.

A study testing the acceptability of videos that simulate face to face conversations with a computer-generated counsellor to deliver breast density information found that while there is potential for technology-based interactive solutions, there is potential that some concepts will not be understood.278 The study found that breast density is not an intuitive concept for most women, with many participants struggling to understand what breast density is (the amount of fatty tissue relative to connective tissue).

As a minimum, breast density results need to be given alongside information about what they mean, what women should do about them and what services are available to them. Many women also wanted the option to speak to a healthcare provider who could explain the results, contextualise them within the person’s overall risk of breast cancer and explore any concerns.

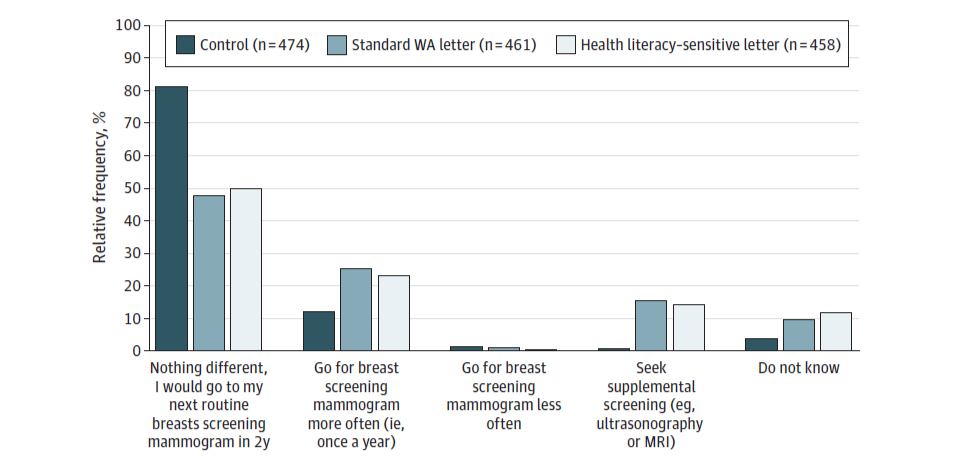
#### Does breast density notification lead to a change in behaviour for those given the results?

Studies in Australia suggest that some women who are told they have dense breasts would seek supplemental screening, while others would prefer to make plans based on their overall breast cancer risk. Women living in Australian states without breast density notification, were asked to consider how they would feel if they were told they had dense breasts.274 Three main perspectives emerged: women would be alert but not alarmed (most common response), women would have supplemental screening for peace of mind, or women would not change anything. Many women felt that they would rather be over-diagnosed than under-diagnosed, with a preference for more frequent mammograms or supplementary screening if they had dense breasts.274 Others were uncertain or felt that they wanted more information about other risk factors before making decisions about further screening. In a scenario about supplemental testing for a woman with dense breasts, participants viewed financial considerations as one of the major determinants of the decision.274

Evidence from Australia suggests that reporting breast density will put additional pressure on health services. Half of the women in Western Australia who were informed they had dense breasts consulted or intended to consult their GP.279 This was higher for women notified for the first time (55%). Of those who consulted their GP, 50% were referred for supplemental screening. Overall, of those women notified of dense breasts, 20% (550 women) had an ultrasound due to breast density.

A randomised controlled trial set in Australian states that did not usually report density sought to assess the effect of provision of breast density results on women’s intentions to seek supplemental screening. Compared with the control group, women who received density notification via the standard information leaflet and the health literate version reported a significantly higher intention to seek supplemental screening (0.8% vs 15.6% and 14.2%; P < .001) or intention to attend breast screening mammography more often (12.4% vs 25.4% and 23.4%; P < 0.01).266 For about half, receiving notification of breast density would not change their course of action (Figure 6), and very few would go for screening less often (<2%).

Figure 6: Screening intentions after receiving mammogram results. The control group did not receive breast density results.



Source: Dolan et al. 2022266

Women’s intention to pursue additional screening in relation to breast density information was studied in a systematic review containing 13 studies (11 from USA, one from Canada and one from Australia).263 Most women intended to have further screening. The knowledge of false positives, overdiagnosis and potential need to pay did not greatly affect this intention. However, another systematic review looking at the impact of breast density notification on psychosocial outcomes for racial and ethnic minorities found a difference in the uptake of supplemental screening for ethnic minority groups.267 Although racial and ethnic minority groups expressed similar or increased motivation as White women to have supplemental screening, studies from before and after breast density notification legislation showed that they were less likely to undergo the supplemental screening. Suggested barriers (extrapolated from known barriers affecting communication with healthcare professionals) were socioeconomic factors, health literacy, language barriers, medical mistrust, and actual or perceived discrimination.280 Further, healthcare professionals in the USA were less likely to order supplemental imaging for Non-Hispanic Black and Hispanic women than non-Hispanic White women (OR 0.38 [95% CI 0.17-0.85] and OR 0.24 [95% CI 0.10-0.61], respectively, p < 0.0001), controlling for patient age, ordering healthcare professional specialty, insurance, BI-RADS score, breast density, and family history of breast cancer. 281

Uptake of supplemental screening in the USA is affected by many factors including ethnicity and socioeconomic status. A systematic review of the impact of mandatory mammographic breast density notification on supplemental screening practice found that patient-level factors such as previous breast biopsy, family history of breast cancer, higher socioeconomic status, ethnicity, age and breast density were associated with supplemental screening uptake.282 In a national survey that included women’s intentions if they were notified about having dense breasts, uptake of supplemental tests was lower for women of lower socioeconomic status and ethnic minority women.270 There was high interest in supplemental screening with ultrasound in a deprived rural area and a more affluent urban setting (73% and 94% of women respectively expressed interest in supplemental screening).262 However, only 22% of women attending the more deprived rural hospital would be willing to pay for this supplemental screening, in contrast to 70% of women attending the more affluent urban centre

A USA telephone survey of women who had received breast density results found that overall 30% would be more likely to have future mammography and 2% less likely.272 The rest had unchanged plans. This varied by ethnicity with 39% of non-Hispanic Black women, 37% of Asian women and 24% non-Hispanic White women indicating they were more likely to have future mammograms. Each women’s breast density was not established, and this could have impacted on people’s intentions. Women with lower levels of anxiety were less likely to change their future screening plans, whereas those with higher levels of anxiety were more likely to report changes to their plans for future mammograms in both directions – some more likely and others less likely to have a future mammogram.

A study in the USA illustrated how the manner of notification impacts the uptake of supplemental screening.283 Less than half (49%) of women who received written notification of breast density attended for follow-up ultrasound scan whereas 87% who also received a phone call had an ultrasound scan.

These studies indicate that there are likely to be significant healthcare resource implications as a consequence of reporting breast density, in terms of reporting and explaining the results and for additional imaging. In Western Australia, half the women with dense breasts consulted or intended to consult their GP and 20% of the women with dense breasts had an ultrasound scan due to breast density. American studies indicate equal intentions but lower uptake of supplemental screening by women of racial and ethnic minorities, as well as by women with low socioeconomic status. Therefore, there is the potential for breast density notification to further disadvantage minority groups and breast density information needs to be carefully considered to ensure understanding by all women.

There is no published evidence of the opinions of breast screening participants in Aotearoa New Zealand on reporting breast density, however, Aotearoa New Zealand breast cancer organisations Breast Cancer Foundation NZ and Breast Cancer Aotearoa Coalition are in favour of breast density being reported by BreastScreen Aotearoa.284 It would be useful to understand if women participating in BreastScreen Aotearoa have a similar perspective to breast density reporting as women in Australia and the USA, and what their intent for supplemental screening may be.

#### Disability Perspectives

Pre-existing disability is associated with a higher likelihood of breast cancer diagnoses.285,286 There is currently no specific literature on the perspectives of disabled people and reporting breast density, however, review studies and meta-analysis have shown that women with disabilities face disparities in receipt of preventative cancer care.287 Disparities in mammography breast screening vary by disability type and severity, and grow over time.287–289 Increasing complexity of disability and other factors such as ethnicity, rurality and socioeconomic status can compound to further lower rates of screening for those with disability.289–291 International studies have identified a number of barriers that contribute to poor breast screening participation. These include physical barriers such as; access, cost/insurance, accommodations, communication, social and professional support, as well as intangible barriers such as being appropriately informed, involved, treated with respect and maintaining control.292–294 Women with a disability are less likely to receive a healthcare professional’s recommendation for mammography screening295 and there are concerns around women with intellectual disability providing informed consent.296 Approaches to reduce disparities in breast cancer screening for women with disabilities should focus on improving accessibility by removing physical barriers like mobility and access to screening centres, equipment, and healthcare facilities. Healthcare professionals require support and education on preventive care for patients with disabilities and regulatory bodies should focus on overcoming socio-economic barriers to equally dispense the national policies across social, ethnic, and economic strata.289

* 1. Perspectives of Healthcare Professionals

Studies from the USA, Australia and England provide evidence on the knowledge, thoughts and concerns of healthcare professionals on breast density reporting. Despite the differing settings (health system structure, presence or not of breast density notification), common themes emerge from the studies: variable knowledge about breast density, a desire for more education, uncertainty over what to advise a woman with dense breasts, the need for national guidelines on breast density including the role of supplemental imaging and putting breast density in the context of other risk factors for breast cancer. The known perspectives of GPs/Primary Care Physicians, Radiologists and Breast Surgeons on breast density measurement and reporting are discussed in greater detail below.

#### General Practitioners / Primary Care Physicians

Two studies in Australia examined General Practitioners (GPs) attitudes to breast density reporting. Interviews of 30 GPs by telephone (including three participants from Western Australia, the only state at the time reporting breast density). Overall, the GPs felt they had a low level of knowledge about breast density and needed training. Many had concerns about how to communicate breast density information to women. Some GPs expressed uncertainty as to how much risk dense breasts confer and were concerned there were no clear guidelines on management. However, they felt that women should be able to make informed decisions and some suggested that knowing about breast density and its implications may make women more vigilant and proactive. They discussed the importance of being open, even in the context of substantial uncertainties.  Some felt there was benefit in women with dense breasts consulting with their GP, who can take into account other risk factors, which could inform discussions about the possible benefits and harms of supplemental screening.263

A survey conducted in 2021 of 60 GPs from various states in Australia, including 11 GPs from Western Australia, found that generally GPs had a positive perspective on breast density reporting.266 Most GPs (87%) had experience with discussing breast density with patients. There was strong support (75%) for breast density to be reported to women and 76% agreed or strongly agreed that notifying women of their breast density would promote informed decision-making. There were varying approaches to offering supplemental screening, with the patient’s overall risk of breast cancer being the most influential factor in decision making. Over three quarters of the respondents (78%) felt that they needed more education on breast density. Most GPs (92%) felt that women have the right to know their breast density, noting that 52% felt that this information may cause undue anxiety. The authors note that their study contained a high proportion of GPs with an interest in women’s health and/or breast health (35%) and that GPs who had taken part in the survey might have a particular interest in this topic and not be representative of all GPs.

Six studies from the USA were included in a systematic review of the impact of breast density notification on GPs.263 Five studies were in states post breast density notification and one in states both pre- and post-legislation. There were mixed views about breast density notification laws. GPs expressed positive attitudes about how the legislation might affect patient engagement. However, they were concerned about the lack of evidence informing next steps for screening patients with dense breasts and about causing stress and anxiety. Similarly to Australian GPs, American GPs wanted to contextualise breast density into a broader conversation about risk factors for breast cancer and were particularly interested in discussions about modifiable risk factors such as exercise and alcohol intake. American based GPs also wanted more education and training around breast density.263,265,297

#### Radiologists

On the whole, radiologists in the USA had a more negative perspective of breast density notification than GPs, with concerns regarding the lack of evidence on supplemental screening and creating additional work for providers and worry for patients.276 In terms of discussing breast density results with participants, some radiologists thought it best done by GPs who were well positioned to assess all the risk factors, others thought a combined approach best and others that it could be done by a non-clinical person such as a health educator.

Breast density knowledge among radiologists in the United Kingdom (UK), where breast density is not reported, was quite variable.298 In a survey of 123 breast radiologists, 16% were not aware that the accuracy of mammograms is affected by breast density and 47% were not aware of the relative risk for breast cancer by degree of breast density. Half the radiologists said they would offer supplementary screening to women with dense breasts, with the most common choice being tomosynthesis, followed by MRI, then ultrasound. Over half (59%) were concerned that routine supplementary imaging could result in overdiagnosis.

#### Breast surgeons

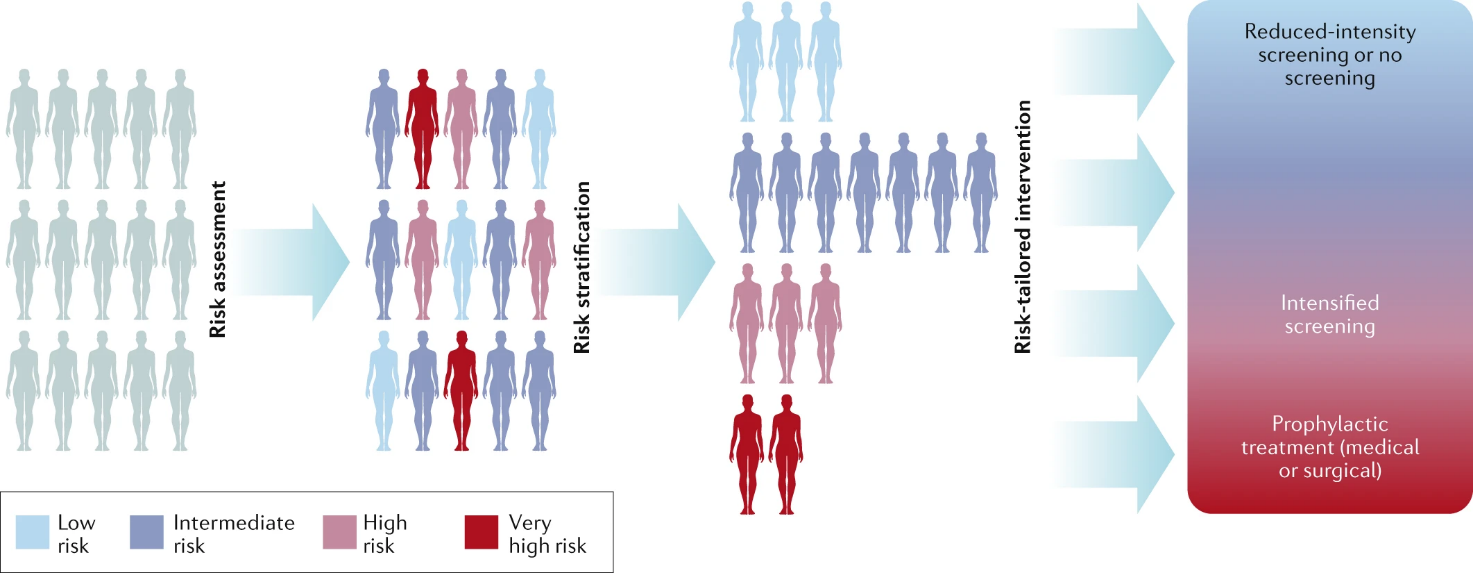
All of the breast surgeons who responded to a survey on breast density (109) in the UK stated that they were aware that mammographic accuracy is affected by breast density.298 Less than half (40%) shared breast density information with their patients, with the most common reason for this being that they do not feel this information should be shared if no alternate imaging is offered, followed by some not having breast density information available, some having time constraints and a few not feeling confident to discuss it. Just over a third (36%) routinely offered further imaging to women with increased breast density, with MRI being the most common, followed by ultrasound. It is not clear from the paper in what context the surgeons were considering mammograms and breast density: it may be at the assessment stage of the screening pathway. Ninety percent agreed that there was need for further guidelines on the management of breast density.

1. Broader Risk Stratification Approaches

There are multiple factors including breast density that are known to increase breast cancer risk for women. However, evidence on how to identify, screen and manage women in high-risk groups within current programmes is still unclear. Risk stratification or risk-based screening protocols use risk assessments and screening technologies to provide personalised screening protocols that vary depending on the overall risk.

As described by Figure 7 below, women entering a personalised screening programme would initially be assessed using a validated tool to calculate their estimated risk of breast cancer. Subsequently, women would be stratified into risk groups such that they can receive tailored interventions. This approach might mean that some women start mammographic screening at a younger age, have different screening intervals or have supplemental screening with another imaging modality, such as MRI. Women deemed to be at higher risk of breast cancer could, in addition, be offered prophylactic treatment. A healthy lifestyle would be recommended to all women, independent of risk level.299 As discussed in section 6. Risk Assessment Tools, there are limitations with using an appropriate tool.

Figure 7: Schematic outlining a personalised approach to early detection and prevention of breast cancer



Source: Pashayan et al.299

* 1. Research on Risk Stratification Approaches

The Roadmap to Optimising Screening in Australia (ROSA) project was established in 2018 to explore risk-based breast cancer screening specifically for Australia. Clinical and economic modelling based on local data indicated that different risk profiles for the current target age range of 50-74 years from 2025 could reduce population level breast cancer mortality by up to 7% (873 lives) in the first 10 years of implementation, with further reductions possible if extended to younger age groups. Risk-based screening could reduce the worse prognosis diagnosis by up to 20% in the higher risk group and consequently reduce treatment intensity. Interval cancer rates in the high-risk group could also be reduced. Conversely, the proportion of invasive screen detected cancers that are overdiagnosed could increase by up to 50%. This model allocated 20% of women to the higher risk group and this was the group expected to benefit most from risk-based screening. Based on this modelling and other key findings the ROSA project recommended a set of activities to guide and support implementation of risk-based screening in the Australian context. Activities include an initial review of policy and guidelines to develop consistent advice with planned co-ordination and data sharing between health services, clinical studies to support the design of a locally based clinical trial, with ongoing enhanced data collection, linkage, monitoring, targeted reviews, consumer and stakeholder engagement as well as engaging in research that addresses evidence gaps.220

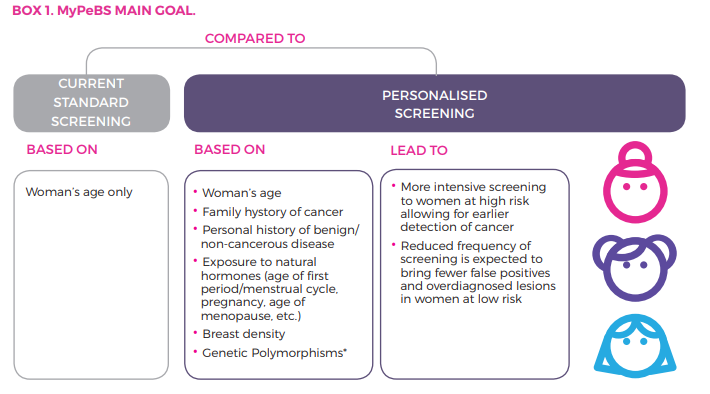
Currently there are six population-based clinical trials underway that have been designed to assess the benefits and harms of various risk-based breast cancer screening protocols. These are summarised in Table 7, with further details in the Appendix.

Table 7: Population level trials of risk–based breast screening

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Trial (age range) | Location | Trial period | Risk groups | Risk Tool | Comparator | Intervention | |
| **Intervals** | Supplemental screening tests |
| MyPeBS – My Personal Breast Screening (40-70) | France, Italy, UK, Belgium and Israel | 2019 -  2025 | BCSC/Tyrer-Cuzick scores  (4 groups) | Algorithm incorporating BCSC score, Tyrer-Cuzick score and genotyping | Various (Annual/biennial/triennial screening, with mammography/ DBT± supplemental US) | 1-4 years | US, MRI |
| WISDOM - Women Informed to Screen Depending on Measures of Risk (40-74) | USA | 2016 -  2020 | BCSC score (4 groups) | BCSC model and genotyping | Annual mammography | 1-2 years  None <50y | MRI |
| TBST - Tailored Screening for Breast Cancer in Premenopausal Women (45-50) | Italy | 2013 -  2022 | BI-RADS 1-2 versus 3-4 | Breast density (BI-RADS classification) | Annual mammography | 2 years for  BI-RADS 1-2 | N/A |
| DENSE - Breast Cancer Screening With MRI in Women With Extremely Dense Breast Tissue (50-75) | Netherlands | 2011 -  2019 | Extremely dense (Volpara D) | Breast density (Volpara grade 4/D) | Biennial mammography | No change | MRI |
| BRAID - Breast Screening – Risk Adaptive Imaging for Density Cluster-RCT (50-70) | UK | 2019 -  2026 | BI-RADS C-D | Breast density (BI-RADS classification C/D), excluding BRACA mutation | Triennial mammography | 18 months | Abbreviated MRI, US,  CEM |
| MISS - What is the Best Interval to Screen Women 45-49 for Breast Cancer (45-49) | Italy | 2020 -  2026 | BI-RADS A-C versus D. | Breast density (BI-RADS classification) | Uncertain (most likely annual tomosynthesis) | 2 years for BI-RADS A-C | N/A |

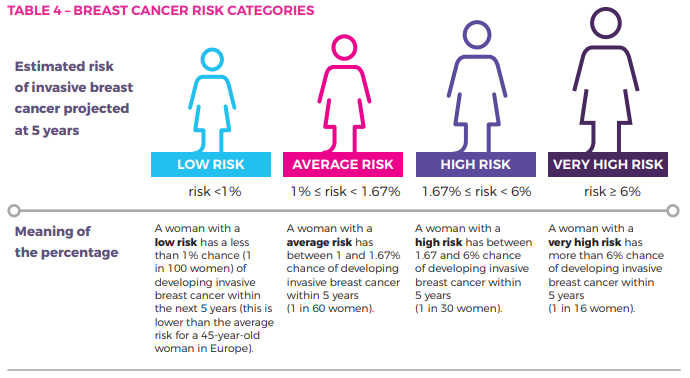
Four of these trials are designed to assess whether risk-based screening, where screening intensity is reduced for some women, is not inferior to standard programmes where women are generally all recommended the same screening protocol. The MyPeBS and WISDOM trials aim to determine if personalised screening based on a 5-year estimated risk of breast cancer (refer figures 8 and 9), is not inferior to standard country-specific age-based screening practices with respect to the rates or proportion of stage 2B or more advanced cancers. The WISDOM trial will also investigate if biopsy rates are lower with personalised screening. The TBST and MISS trials aim to assess the impact of biennial rather than annual screening for premenopausal women with lower breast density, on the incidence of interval cancers (TBST) or more advanced cancers (TBST and MISS).300

Figure 8: MyPeBS Screening options



Source: MyPeBS Questions and Answers301

Figure 9: MyPeBS Risk Categories



Source: MyPeBS Questions and Answers301

The DENSE and BRAID trials are designed to assess if the addition of supplemental screening for women with denser breasts improves outcomes within standard screening programmes. The DENSE trial aims to assess the effectiveness of offering MRI in addition to mammography to women with extremely dense breasts. The interval cancer rate for biennial screening with and without supplemental MRI will be compared for women with extremely dense breasts (>75% mammographic density). The BRAID trial is designed to investigate whether breast cancer detection rates will improve when women with dense breasts (BI-RADS C or D) are offered supplemental imaging in addition to three yearly standard screening. There are three intervention arms where women with dense breasts receive additional mammographic screening at 18 months and supplemental imaging at baseline and at 18 months using one of three imaging modalities; either abbreviated-MRI, automated whole breast ultrasound or contrast-enhanced mammography. The trial aims to assess the different modalities of supplemental screening as well as the effect of providing both supplemental screening and more frequent screening for women with dense breasts compared to standard triennial mammographic screening.300

Clinical trials are the best evidence for protocol development, however, mortality outcomes take time to assess and only a limited range of protocols can be evaluated. Modelling studies have been used to estimate costs, benefits and harms of risk-based screening strategies. Lower breast cancer mortality and improved quality of life was predicted for women at higher risk if screened more frequently and from a younger age.302,303 These benefits however would come at the expense of increased false positives and overdiagnosis303,although, less intensive screening of lower risk women could reduce false positive rates in this group .302 Cost-effectiveness of screening strategies is context specific and hard to compare between studies, with some reporting that risk-based screening would be more cost effective than uniform screening for all women whereas others did not.302–306

* 1. Limitations and considerations of risk stratification

Ideally, risk stratification should use risk factors either strongly negatively or positively associated with the screening condition and should not be highly correlated with one another.307 In reality, this is population dependent and risk factors are often related (for example, diabetes and weight as risk factors for colorectal cancer).307 Any stratification will need internal validation but importantly, it will need external validation in the context for which it is being considered.307,308 Many risk stratification models and approaches are in the research stage. Success in a research setting does not necessarily imply clinical utility or improvement in outcomes.308 Cost effectiveness in different settings is also critical as there will always be associated capacity constraints and considerations (for example, the use of MRI for individuals at high-risk of breast cancer).

Screening programmes must be acceptable to all involved if they are to be successful and it is particularly important that uptake and application do not compound inequities.308 A recent systematic review discussed acceptability of risk stratification in cancer screening from a healthcare providers perspective.309 Only 7 out of 12,039 papers were considered suitable for review, perhaps reflective of a gap in the literature, with 6 focusing on breast cancer screening.309 However, the authors concluded the findings were broadly consistent with evidence on the attitudes of the general public to stratification. They describe risk stratification as acceptable in principle to healthcare providers and the public – with evidence that the public is ‘largely optimistic about risk stratification’. It is seen as a sensible way to address benefits and harms, but successful implementation would need to address a number of concerns.309

Development and use of risk stratification approaches is resource and personnel intensive. Alongside education, awareness and communications, IT, intelligence, and personnel will need to be considered from the outset.310 This includes ensuring perceptions of risk stratification approaches, particularly the interpretation of risk, by patients and healthcare providers is understood and considered.309 Taylor et al., emphasise that “for healthcare providers to find risk-stratified cancer screening acceptable, it is essential to understand whether it is acceptable from the perspective of the general public”.309 Engaging the public throughout development and implementation will be critical to successful use of any risk stratification.307,309

Even though reduced screening for low-risk women presents an opportunity for equivalent outcomes, the potential reduction was highlighted as a concern and would need effective guidance and supportive resources. Similarly, clarity around the management of moderate risk individuals was felt necessary.309 For healthcare providers to use risk stratification appropriately requires a good understanding of the assumptions and rationale behind it.308–310 Without this, there is the risk of incorrect or inappropriate use and to cause harm.308 Training and education would be critical and for change to become embedded and new processes used appropriately, this would need to be repeated and long-term.309

The cognitive load, and time required, on already stretched providers, particularly in primary care, needs to be considered.309 This includes the responsibility for the use and interpretation of any risk stratification, and decisions on risk management where required. Any tools would need to be well integrated with existing electronic patient management systems, require easily available input data, and be simple, quick, and routine.308,309 However, their use would almost certainly require increased time and support for patients. The current breast cancer risk stratification is complex and primary care providers are strongly encouraged to collaborate with specialist breast care providers and geneticists. Managing this and the needs of the individual, who may have significant psychosocial concerns, takes considerable time in a primary care setting that is currently time poor. Capacity and funding requirements would need to be carefully considered during the development and planning for risk stratification amendments to screening programmes. There is risk that the increasing complexity of health information, particularly around the concepts of risk stratification and breast screening compared with investigation of symptoms, in the absence of appropriate guidance / recommendations has the potential to increase inequities. Having clear, accessible communication including explanation of breast cancer risk for the public and for providers would be critical to ensure adequate informed consent and to support equity.309 This would include ensuring uniform guidance with evidence-based clinical guidelines that are consistent with national policy.309 Currently, primary care providers use Community Health Pathways, with district level variation in these including variation in the guidelines for management of individuals at high-risk of breast cancer.

Cost effectiveness in different settings is an important consideration but Taylor et al., emphasised that whilst cost-benefits were seen as important, the health benefits must be seen to be the priority - when communicating the cost-benefits to the public, policymakers should be careful not to undermine these.309

Additional risks include at an individual level with the potential for increased anxiety, or being put off routine screening once ‘labelled’ as either high or low risk. Those considered low risk may be less likely to address modifiable risk factors. Communicating risks in a meaningful way is resource intensive at an individual and population level and it is imperative inequities are not exacerbated.311

Data access, including coded data, for development of algorithms requires large data sets and continued access to this data will be required to evaluate and inform future programmes.310 There may be data collection, sharing and storage implications, and in Aotearoa New Zealand data sovereignty is an important consideration, particularly for Māori. Institutions will need to collaborate and to have clear policies and procedures, including for data sharing and use.310

Genetic data is increasingly used, with particular privacy, storage, and access considerations.310 It is important that genetic data adequately represents the population for whom any risk stratification algorithm is to be used. This is particularly important for ethnicity – with minority ethnicities often under-represented. It is critical that risk stratification models recognise and allow for this to ensure equitable utility.310

It is also important to ensure that the risk stratification models used are adaptable. For example, an individual may change lifestyle behaviours through their life course and their risks may need re-classifying.310,312 Similarly, understanding and interpretation of genetic risks will change as knowledge increases. New treatments will also need to be considered with stratification levels amended where appropriate.310 With this adaptability, there is the need to consider the ethical rights of individuals to be informed of any changes, and the communication required to support this.310

1. Discussion
   1. Key findings in relation to current knowledge

Women with higher breast density have an increased risk of developing breast cancer compared to those with low breast density and are more likely to have a breast cancer missed on mammography. BreastScreen Aotearoa does not currently measure breast density, therefore, the relative distribution in Aotearoa New Zealand women is unknown. Measurement in an appropriate cohort would be required to accurately estimate the number of women in Aotearoa New Zealand with dense breasts, with international studies suggesting up to half of the female population could reach the threshold of moderate to high-risk density. Breast density can be determined by a radiologist through visual assessment of mammography images or through automated breast density reporting tools e.g. AI. These both come at a cost of radiologist time or IT investment respectively.

Internationally, and in Aotearoa New Zealand, supplemental breast screening has been recommended for women deemed to be at high-risk of developing breast cancer. Although evidence for this is growing, particularly in terms of improved cancer detection and reduced interval cancers, mortality benefit has not yet been demonstrated and may be modest.

Supplemental screening options including MRI, ultrasound and CEM have been shown to increase the detection of cancer compared to standard mammography. All methods are associated with varying benefits and risks. MRI has the greatest sensitivity for breast cancer detection but comes with an increased false positive rate and is a costly procedure. Ultrasound is not as sensitive as MRI and has a similar false positive rate, however, it is a less invasive and less costly procedure. CEM is nearly as effective as MRI for cancer detection, with less false positives and is a simpler, lower cost method, however, is not routinely available in New Zealand.

Supplemental screening for women with dense breasts has been shown to increase cancer detection rates, to detect cancers earlier and to decrease the rate of interval cancers. The main harms of supplemental screening are the increase in overdiagnosis and false positives. There are also opportunity costs with potential impacts on both the existing breast cancer screening programme and symptomatic pathway.

Risk-based screening protocols use risk assessments and screening technologies to provide personalised screening protocols that vary depending on the identification of risk. Population-based clinical trials are currently underway designed to assess the benefits and harms of various risk-based breast cancer screening protocols. Some are assessing the effect of supplemental screening for women with dense or extremely dense breasts on screening programme outcomes, and some are assessing risk-based screening that includes reduced screening for some very low risk groups.

In Aotearoa New Zealand there is significant inequity in breast cancer outcomes, particularly related to the symptomatic pathway, but also in access to breast cancer screening. It may be that wāhine Māori have a higher proportion of dense breasts than New Zealand European/Other women, and this may contribute to inequities in breast cancer rates and outcomes. Breast density assessment is currently only available to women who have health insurance or pay for breast screening through private providers. This creates further inequities for women with dense breasts, who already may not receive the same outcome benefits from current breast screening programmes as those with less dense breasts.

* 1. Key Conclusions

Breast density is an important consideration in relation to breast cancer risk including in the breast screening context, given its association with both breast cancer risk and potential reduced accuracy of screening mammograms. As such it should be considered when evaluating a women’s risk of breast cancer.

Women with higher than average risk of breast cancer may benefit from supplemental breast screening, however, currently there is no consensus on how best to manage women with dense breasts. Modelling data supports the use of risk-based screening protocols, including risk assessment tools and screening technologies, to provide personalised screening protocols that improve programme outcomes.

Overseas evidence suggests that women want to know their breast density, although this is associated with anxiety, and does vary across population groups and health care contexts. Failing to address the increased risk of breast cancer in women with dense breasts could be seen as contributing to inequities.

These issues need to be assessed in the context of the current BreastScreen Aotearoa screening programme with an aim to introduce risk-based screening in the future.

Incorporation of breast density notification into an existing screening programme is ethically complex given the lack of consensus for follow-up of women with dense breasts. Issues to consider include equitable care, patient autonomy, physician education, duty of care and uncertainties relating to measurement and clinical management pathways for women with dense breasts.

Consideration needs to be given to the best way to measure breast density within the BSA programme, including the possible use of artificial intelligence (AI) versus visual assessment by a radiologist and what the additional costs for these would be. The prevalence of breast density amongst women in Aotearoa New Zealand needs to be ascertained to understand the potential programme impacts, benefits and costs, including the potential number of women who may be offered supplemental screening.

Further evidence from international trials is required regarding the impact of supplementary screening for women with high breast density on breast cancer outcomes (e.g. mortality) and to provide guidance on risk stratification options, screening modality and interval.

Aotearoa New Zealand specific cost-effectiveness modelling would greatly assist in providing information regarding health system and economic implications of various policy options, including alternate ways to achieve marginal improvements to breast cancer outcomes (e.g. alternate age ranges, modalities (e.g. DBT), intervals, and interventions to improve current programme participation).

The current BSA workforce capacity needs to be assessed with regards to BreastCare nurses and Medical Imaging Technologists (mammographers) potentially needing to explain breast density results and recommendations for supplemental screening with women. As does the funding and workforce enhancements that would be needed to undertake further ultrasound assessments.

The capacity of the wider health system to fulfil supplementary ultrasound or MRI requirements also needs to be assessed. CEM is not routinely available in Aotearoa New Zealand and there is limited availability of DBT. If supplemental screening is not available to women with dense breasts through the public health system, it will not be accessible to many due to cost. This is likely to further disadvantage some groups of women already facing inequities, for example, wāhine Māori with dense breasts and those living in areas of socioeconomic disadvantage.

A more detailed assessment of whole system capacity issues and potential impacts on the BSA programme in the context of current projects and existing coverage inequities for Māori and Pacific women is also required. This knowledge is necessary to produce robust local guidelines and recommendations for women with dense breasts.

1. References

1. Ministry of Health. *Breastscreen Aotearoa National Policy and Quality Standards 2013 (Revised November 2022)*. https://www.tewhatuora.govt.nz/assets/For-the-health-sector/NSU/For-Health-professionals/Breast-screening-/BreastScreen-Aotearoa-National-Policy-and-Quality-Standards-2013-Revised-November-2022-pdf-2.6-MB.pdf (2022).

2. BRCA Gene Changes: Cancer Risk and Genetic Testing Fact Sheet - NCI. https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet (2024).

3. Sogani, J., Mango, V. L., Keating, D., Sung, J. S. & Jochelson, M. S. Contrast-Enhanced Mammography: Past, Present, and Future. *Clin Imaging* **69**, 269–279 (2021).

4. Gordon, P. B. The Impact of Dense Breasts on the Stage of Breast Cancer at Diagnosis: A Review and Options for Supplemental Screening. *Current Oncology* **29**, 3595–3636 (2022).

5. IARC Working Group on the Evaluation of Cancer-Preventive Interventions. Glossary. in *Breast cancer screening* vol. 15 (International Agency for Research on Cancer, Lyon, France, 2016).

6. National Cancer Institute, U. G. NCI Dictionary of Cancer Terms - NCI. *National Cancer Institute at the National Institutes of Health* https://www.cancer.gov/publications/dictionaries/cancer-terms/def/lifetime-risk (2011).

7. National Institute of Biomedical Imaging and Bioengineering. Magnetic Resonance Imaging (MRI). *National Institute of Biomedical Imaging and Bioengineering* https://www.nibib.nih.gov/science-education/science-topics/magnetic-resonance-imaging-mri (2024).

8. Yaffe, M. J. & Mainprize, J. G. Overdetection of Breast Cancer. *Current Oncology* **29**, 3894–3910 (2022).

9. Steele, R. J. Screening and surveillance—principles and practice. *Br J Radiol* **91**, 20180200 (2018).

10. Tsarouchi, M. I., Hoxhaj, A. & Mann, R. M. New Approaches and Recommendations for Risk-Adapted Breast Cancer Screening. *Journal of Magnetic Resonance Imaging* **58**, 987–1010 (2023).

11. Health New Zealand | Te Whatu Ora. National Breast Screening System – Te Puna. *Health New Zealand | Te Whatu Ora* https://www.tewhatuora.govt.nz/health-services-and-programmes/breastscreen-aotearoa/national-breast-screening-system-te-puna (2025).

12. Ministry of Health. *More About Breast Screening and BreastScreen Aotearoa*. https://www.tewhatuora.govt.nz/health-services-and-programmes/breastscreen-aotearoa/information-resources/ (2007).

13. Morrell, S. *et al.* Mammography service screening and breast cancer mortality in New Zealand: a National Cohort Study 1999-2011. *Br J Cancer* **116**, 828–839 (2017).

14. Morrell, S., Taylor, R., Roder, D. & Robson, B. *Cohort and Case Control Analyses of Breast Cancer Mortality: BreastScreen Aotearoa 1999-2011*. https://www.tewhatuora.govt.nz/publications/cohort-and-case-control-analyses-of-breast-cancer-mortality-breastscreen-aotearoa-1999-2011 (2015).

15. Health New Zealand - Te Whatu Ora. BreastScreen Aotearoa Coverage Report. *BreastScreen Aotearoa Coverage Report* https://tewhatuora.shinyapps.io/nsu-bsa-coverage/ (2025).

16. Te Whatu Ora - Health New Zealand. *Te Whatu Ora BSA Quality Improvement Review*. https://www.tewhatuora.govt.nz/assets/Publications/Screening/tewhatuora-bsa-qualityimprovementreview.pdf (2022).

17. Robson, B. *Monitoring Report for Women Screened between 1 July 2020 and 30 June 2022*. (2024).

18. National Screening Unit. BreastSceen Aotearoa Interval Cancer Rates for Women aged 50-69 years screened 2016-17. Preprint at (2024).

19. BreastScreen Aotearoa. BreastScreen Aotearoa Breast Density Position Statement. (2019).

20. Wolfe, J. N. A Study of Breast Parenchyma by Mammography in the Normal Woman and Those with Benign and Malignant Disease. *Radiology* **89**, 201–205 (1967).

21. Freer, P. E. Mammographic Breast Density: Impact on Breast Cancer Risk and Implications for Screening. *RadioGraphics* **35**, 302–315 (2015).

22. Swann, C., Kopans, D., McCarthy, K., White, G. & Hall, D. Mammographic density and physical assessment of the breast. *American Journal of Roentgenology* **148**, 525–526 (1987).

23. American College of Radiology. Breast Imaging Reporting & Data System BI-RADS. *American College of Radiology* https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Bi-Rads (2024).

24. Breast Screen South Australia. Breast density. *BreastScreen SA* https://www.breastscreen.sa.gov.au/breast-cancer-screening/breast-density.

25. Chalfant, J. S. & Hoyt, A. C. Breast Density: Current Knowledge, Assessment Methods, and Clinical Implications. *Journal of Breast Imaging* **4**, 357–370 (2022).

26. Rebolj, M., Blyuss, O., Chia, K. S. & Duffy, S. W. Long-term excess risk of breast cancer after a single breast density measurement. *European Journal of Cancer* **117**, 41–47 (2019).

27. Boyd, N. F. *et al.* Mammographic breast density as an intermediate phenotype for breast cancer. *The Lancet Oncology* **6**, 798–808 (2005).

28. Boyd, N., Martin, L. & Stone, J. A Longitudinal Study of the Effects of Menopause on Mammographic Features. *Cancer Epidemiology Biomarkers & Prevention* **11**, 1048–53 (2002).

29. Huo, C. W. *et al.* Mammographic density—a review on the current understanding of its association with breast cancer. *Breast Cancer Res Treat* **144**, 479–502 (2014).

30. Martin, L. J. & Boyd, N. F. Mammographic density. Potential mechanisms of breast cancer risk associated with mammographic density: hypotheses based on epidemiological evidence. *Breast Cancer Res* **10**, 201 (2008).

31. Checka, C. M., Chun, J. E., Schnabel, F. R., Lee, J. & Toth, H. The Relationship of Mammographic Density and Age: Implications for Breast Cancer Screening. *American Journal of Roentgenology* **198**, W292–W295 (2012).

32. Sprague, B. L. *et al.* Trends in Clinical Breast Density Assessment From the Breast Cancer Surveillance Consortium. *J Natl Cancer Inst* **111**, 629–632 (2019).

33. Kerlikowske, K. *et al.* Association of Screening With Digital Breast Tomosynthesis vs Digital Mammography With Risk of Interval Invasive and Advanced Breast Cancer. *JAMA* **327**, 2220–2230 (2022).

34. Heller, S. L., Hudson, S. & Wilkinson, L. S. Breast density across a regional screening population: effects of age, ethnicity and deprivation. *Br J Radiol* **88**, 20150242 (2015).

35. McCormack, V. A., Perry, N., Vinnicombe, S. J. & Silva, I. dos S. Ethnic variations in mammographic density: a British multiethnic longitudinal study. *Am J Epidemiol* **168**, 412–421 (2008).

36. Ursin, G. *et al.* Mammographic density and breast cancer in three ethnic groups. *Cancer Epidemiol Biomarkers Prev* **12**, 332–338 (2003).

37. Ellison-Loschmann, L. *et al.* Age and ethnic differences in volumetric breast density in New Zealand women: a cross-sectional study. *PLoS One* **8**, e70217 (2013).

38. Aitken, Z. *et al.* Mammographic density and markers of socioeconomic status: a cross-sectional study. *BMC Cancer* **10**, 35 (2010).

39. Viel, J.-F. & Rymzhanova, R. Mammographic density and urbanization: a population-based screening study. *J Med Screen* **19**, 20–25 (2012).

40. Maloney, C. M. *et al.* Breast Density Status Changes: Frequency, Sequence, and Practice Implications. *J Breast Imaging* **6**, 628–635 (2024).

41. Redondo, A. *et al.* Inter- and intraradiologist variability in the BI-RADS assessment and breast density categories for screening mammograms. *British Journal of Radiology* **85**, 1465–1470 (2012).

42. Melnikow, J. *et al.* *Supplemental Screening for Breast Cancer in Women With Dense Breasts: A Systematic Review for the U.S. Preventive Service Task Force*. (Agency for Healthcare Research and Quality (US), Rockville (MD), 2016).

43. Magni, V. *et al.* Development and Validation of an AI-driven Mammographic Breast Density Classification Tool Based on Radiologist Consensus. *Radiol Artif Intell* **4**, e210199 (2022).

44. Matthews, T. P. *et al.* A Multisite Study of a Breast Density Deep Learning Model for Full-Field Digital Mammography and Synthetic Mammography. *Radiology: Artificial Intelligence* **3**, e200015 (2021).

45. Highnam, R., Brady, S. M., Yaffe, M. J., Karssemeijer, N. & Harvey, J. Robust Breast Composition Measurement - VolparaTM. in *Digital Mammography* (eds. Martí, J., Oliver, A., Freixenet, J. & Martí, R.) 342–349 (Springer, Berlin, Heidelberg, 2010). doi:10.1007/978-3-642-13666-5\_46.

46. Kshirsagar, A. QuantraTM 2.2 Software Design Intent and Clinical Performance.

47. Seah, J. C. Y. *et al.* Effect of a comprehensive deep-learning model on the accuracy of chest x-ray interpretation by radiologists: a retrospective, multireader multicase study. *The Lancet Digital Health* **3**, e496–e506 (2021).

48. Dai, L. *et al.* A deep learning system for detecting diabetic retinopathy across the disease spectrum. *Nat Commun* **12**, 3242 (2021).

49. Volpara Health. Breast density assessment and Volpara Scorecard. *Volpara Health* https://www.volparahealth.com/fda-density-notification/breast-density-assessment-and-volpara-scorecard/ (2024).

50. Duffy, S. W. *et al.* Mammographic density and breast cancer risk in breast screening assessment cases and women with a family history of breast cancer. *Eur J Cancer* **88**, 48–56 (2018).

51. Johns, P. C. & Yaffe, M. J. X-ray characterisation of normal and neoplastic breast tissues. *Phys Med Biol* **32**, 675–695 (1987).

52. Boyd Norman F. *et al.* Mammographic Density and the Risk and Detection of Breast Cancer. *New England Journal of Medicine* **356**, 227–236 (2007).

53. Weigel, S., Heindel, W., Heidrich, J., Hense, H.-W. & Heidinger, O. Digital mammography screening: sensitivity of the programme dependent on breast density. *Eur Radiol* **27**, 2744–2751 (2017).

54. Payne, N. R. *et al.* Breast density effect on the sensitivity of digital screening mammography in a UK cohort. *Eur Radiol* **35**, 177–187 (2025).

55. Yaghjyan, L. *et al.* Mammographic Breast Density and Subsequent Risk of Breast Cancer in Postmenopausal Women According to Tumor Characteristics. *J Natl Cancer Inst* **103**, 1179–1189 (2011).

56. Aiello, E. J., Buist, D. S. M., White, E. & Porter, P. L. Association between Mammographic Breast Density and Breast Cancer Tumor Characteristics. *Cancer Epidemiology, Biomarkers & Prevention* **14**, 662–668 (2005).

57. Bodewes, F. T. H., Van Asselt, A. A., Dorrius, M. D., Greuter, M. J. W. & De Bock, G. H. Mammographic breast density and the risk of breast cancer: A systematic review and meta-analysis. *The Breast* **66**, 62–68 (2022).

58. van der Waal, D., Ripping, T. M., Verbeek, A. L. M. & Broeders, M. J. M. Breast cancer screening effect across breast density strata: A case–control study. *International Journal of Cancer* **140**, 41–49 (2017).

59. Chiu, S. Y.-H. *et al.* Effect of Baseline Breast Density on Breast Cancer Incidence, Stage, Mortality, and Screening Parameters: 25-Year Follow-up of a Swedish Mammographic Screening. *Cancer Epidemiology, Biomarkers & Prevention* **19**, 1219–1228 (2010).

60. Sala, M. *et al.* Survival and Disease-Free Survival by Breast Density and Phenotype in Interval Breast Cancers. *Cancer Epidemiology, Biomarkers & Prevention* **27**, 908–916 (2018).

61. Gierach, G. L. *et al.* Relationship between mammographic density and breast cancer death in the Breast Cancer Surveillance Consortium. *J Natl Cancer Inst* **104**, 1218–1227 (2012).

62. Yaghjyan, L., Colditz, G. A., Rosner, B. & Tamimi, R. M. Mammographic Breast Density and Subsequent Risk of Breast Cancer in Postmenopausal Women according to the Time Since the Mammogram. *Cancer Epidemiol Biomarkers Prev* **22**, 1110–1117 (2013).

63. Byrne, C. *et al.* Mammographic features and breast cancer risk: effects with time, age, and menopause status. *J Natl Cancer Inst* **87**, 1622–1629 (1995).

64. Freer, P. E. Mammographic Breast Density: Impact on Breast Cancer Risk and Implications for Screening. *RadioGraphics* **35**, 302–315 (2015).

65. McCormack, V. A. & Dos Santos Silva, I. Breast Density and Parenchymal Patterns as Markers of Breast Cancer Risk: A Meta-analysis. *Cancer Epidemiology, Biomarkers & Prevention* **15**, 1159–1169 (2006).

66. Kim, E. Y. *et al.* Mammographic breast density, its changes, and breast cancer risk in premenopausal and postmenopausal women. *Cancer* **126**, 4687–4696 (2020).

67. Tehranifar, P. *et al.* Longitudinal history of mammographic breast density and breast cancer risk by familial risk, menopausal status, and initial mammographic density level in a high risk cohort: a nested case–control study. *Breast Cancer Research* **26**, 166 (2024).

68. Cuzick, J., Warwick, J., Pinney, E., Warren, R. M. L. & Duffy, S. W. Tamoxifen and Breast Density in Women at Increased Risk of Breast Cancer. *JNCI Journal of the National Cancer Institute* **96**, 621–628 (2004).

69. Cuzick, J. *et al.* Tamoxifen-Induced Reduction in Mammographic Density and Breast Cancer Risk Reduction: A Nested Case-Control Study. *JNCI Journal of the National Cancer Institute* **103**, 744–752 (2011).

70. Eriksson, M. *et al.* Low-Dose Tamoxifen for Mammographic Density Reduction: A Randomized Controlled Trial. *J Clin Oncol* **39**, 1899–1908 (2021).

71. Kerlikowske, K. *et al.* Breast Cancer Risk by Breast Density, Menopause, and Postmenopausal Hormone Therapy Use. *Journal of Clinical Oncology* (2010) doi:10.1200/JCO.2009.26.4770.

72. Picon-Ruiz, M., Morata-Tarifa, C., Valle-Goffin, J. J., Friedman, E. R. & Slingerland, J. M. Obesity and adverse breast cancer risk and outcome: Mechanistic insights and strategies for intervention. *CA Cancer J Clin* **67**, 378–397 (2017).

73. Chu, A. *et al.* Association of body composition fat parameters and breast density in mammography by menopausal status. *Sci Rep* **12**, 22224 (2022).

74. Kerlikowske, K. & Phipps, A. I. Breast Density Influences Tumor Subtypes and Tumor Aggressiveness. *J Natl Cancer Inst* **103**, 1143–1145 (2011).

75. Bertrand, K. A. *et al.* Mammographic density and risk of breast cancer by age and tumor characteristics. *Breast Cancer Res* **15**, R104 (2013).

76. Njiaju, U. O. & Olopade, O. I. Genetic determinants of breast cancer risk: a review of current literature and issues pertaining to clinical application: The breast journal. *Breast J* **18**, 436–442 (2012).

77. Easton Douglas F. *et al.* Gene-Panel Sequencing and the Prediction of Breast-Cancer Risk. *New England Journal of Medicine* **372**, 2243–2257 (2015).

78. Weiss, A., Garber, J. E. & King, T. Breast Cancer Surgical Risk Reduction for Patients With Inherited Mutations in Moderate Penetrance Genes. *JAMA Surgery* **153**, 1145–1146 (2018).

79. Colditz, G. A., Kaphingst, K. A., Hankinson, S. E. & Rosner, B. Family history and risk of breast cancer: Nurses’ Health Study. *Breast Cancer Res Treat* **133**, 1097–1104 (2012).

80. Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. *Lancet* **358**, 1389–1399 (2001).

81. Karavasiloglou, N. *et al.* Risk for Invasive Cancers in Women With Breast Cancer In Situ: Results From a Population Not Covered by Organized Mammographic Screening. *Front Oncol* **11**, 606747 (2021).

82. Langballe, R. *et al.* Systemic therapy for breast cancer and risk of subsequent contralateral breast cancer in the WECARE Study. *Breast Cancer Res* **18**, 65 (2016).

83. Dyrstad, S. W., Yan, Y., Fowler, A. M. & Colditz, G. A. Breast cancer risk associated with benign breast disease: systematic review and meta-analysis. *Breast Cancer Res Treat* **149**, 569–575 (2015).

84. Román, M. *et al.* Long-Term Risk of Breast Cancer after Diagnosis of Benign Breast Disease by Screening Mammography. *IJERPH* **19**, 2625 (2022).

85. Moskowitz, C. S. *et al.* Breast cancer after chest radiation therapy for childhood cancer. *J Clin Oncol* **32**, 2217–2223 (2014).

86. De Bruin, M. L. *et al.* Breast cancer risk in female survivors of Hodgkin’s lymphoma: lower risk after smaller radiation volumes. *J Clin Oncol* **27**, 4239–4246 (2009).

87. Vachon, C. M. *et al.* Mammographic density, breast cancer risk and risk prediction. *Breast Cancer Res* **9**, 217 (2007).

88. Collaborative Group on Hormonal Factors in Breast Cancer. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. *The Lancet* **394**, 1159–1168 (2019).

89. Mørch, L. S. *et al.* Contemporary Hormonal Contraception and the Risk of Breast Cancer. *N Engl J Med* **377**, 2228–2239 (2017).

90. Ma, H. *et al.* Pregnancy-related factors and the risk of breast carcinoma in situand invasive breast cancer among postmenopausal women in the California Teachers Study cohort. *Breast Cancer Research* **12**, R35 (2010).

91. Hamajima, N. *et al.* Alcohol, tobacco and breast cancer--collaborative reanalysis of individual data from 53 epidemiological studies, including 58,515 women with breast cancer and 95,067 women without the disease. *Br J Cancer* **87**, 1234–1245 (2002).

92. Guo, W., Fensom, G. K., Reeves, G. K. & Key, T. J. Physical activity and breast cancer risk: results from the UK Biobank prospective cohort. *Br J Cancer* **122**, 726–732 (2020).

93. Pizot, C. *et al.* Physical activity, hormone replacement therapy and breast cancer risk: A meta-analysis of prospective studies. *Eur J Cancer* **52**, 138–154 (2016).

94. Picon-Ruiz, M., Morata-Tarifa, C., Valle-Goffin, J. J., Friedman, E. R. & Slingerland, J. M. Obesity and adverse breast cancer risk and outcome: Mechanistic insights and strategies for intervention. *CA Cancer J Clin* **67**, 378–397 (2017).

95. Parker, L., Carter, S., Williams, J., Pickles, K. & Barratt, A. Avoiding harm and supporting autonomy are under-prioritised in cancer-screening policies and practices. *European Journal of Cancer* **85**, 1–5 (2017).

96. The Daffodil Centre. *ROSA-Report-2023.-Chapter-4.-Risk-Based-Screening-Protocols-Abridged.Pdf*. https://daffodilcentre.org/wp-content/uploads/2024/05/ROSA-Report-2023.-Chapter-4.-Risk-based-screening-protocols-Abridged.pdf (2024).

97. Clift, A. K. *et al.* The current status of risk-stratified breast screening. *Br J Cancer* **126**, 533–550 (2022).

98. Clift, A. K. *et al.* The current status of risk-stratified breast screening. *Br J Cancer* **126**, 533–550 (2022).

99. Velentzis, L. S. *et al.* Breast Cancer Risk Assessment Tools for Stratifying Women into Risk Groups: A Systematic Review. *Cancers* **15**, 1124 (2023).

100. Berg, W. A., Seitzman, R. L. & Pushkin, J. Implementing the National Dense Breast Reporting Standard, Expanding Supplemental Screening Using Current Guidelines, and the Proposed Find It Early Act. *Journal of Breast Imaging* **5**, 712–723 (2023).

101. Schopf, C. M. *et al.* Artificial Intelligence-Driven Mammography-Based Future Breast Cancer Risk Prediction: A Systematic Review. *Journal of the American College of Radiology* **21**, 319–328 (2024).

102. Yala, A. *et al.* Multi-Institutional Validation of a Mammography-Based Breast Cancer Risk Model. *J Clin Oncol* **40**, 1732–1740 (2022).

103. Yala, A., Lehman, C., Schuster, T., Portnoi, T. & Barzilay, R. A Deep Learning Mammography-based Model for Improved Breast Cancer Risk Prediction. *Radiology* **292**, 60–66 (2019).

104. Vachon, C. M. *et al.* Impact of Artificial Intelligence System and Volumetric Density on Risk Prediction of Interval, Screen-Detected, and Advanced Breast Cancer. *J Clin Oncol* **41**, 3172–3183 (2023).

105. Armstrong, A. C. & Evans, G. D. Management of women at high risk of breast cancer. *BMJ* **348**, g2756–g2756 (2014).

106. Quante, A. S. *et al.* Practical Problems With Clinical Guidelines for Breast Cancer Prevention Based on Remaining Lifetime Risk. *J Natl Cancer Inst* **107**, djv124 (2015).

107. MacInnis, R. J. *et al.* Comparing 5-Year and Lifetime Risks of Breast Cancer using the Prospective Family Study Cohort. *J Natl Cancer Inst* **113**, 785–791 (2020).

108. NICE UK. Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer | Guidance | NICE. *National Institute for Health and Care Excellence* https://www.nice.org.uk/guidance/cg164 (2013).

109. National Breast Cancer Tumour & Standards Working Group. Standards of Service Provision for Breast Cancer Patients in New Zealand – Provisional. (2013).

110. Carle, C., Velentzis, L. S. & Nickson, C. BreastScreen Australia national data by factors of interest for risk-based screening: routinely reported data and opportunities for enhancement. *Aust N Z J Public Health* **46**, 230–236 (2022).

111. BreastScreen Changes in Victoria | RANZCR. https://www.ranzcr.com/whats-on/news-media/breastscreen-changes-in-victoria?searchword=lung%20cancer%20screening.

112. Cancer Insititute New South Wales. BRCA1 or BRCA2 – risk management (female) | eviQ. *Cancer Insititute New South Wales* https://www.eviq.org.au/cancer-genetics/adult/risk-management/3814-brca1-or-brca2-risk-management-female (2023).

113. University of Cambridge. Welcome to CanRisk. *CanRisk* https://www.canrisk.org/ (2024).

114. Paul, C., Skegg, D. C. & Spears, G. F. Depot medroxyprogesterone (Depo-Provera) and risk of breast cancer. *BMJ* **299**, 759–762 (1989).

115. Paul, C., Skegg, D. C., Spears, G. F. & Kaldor, J. M. Oral contraceptives and breast cancer: a national study. *Br Med J (Clin Res Ed)* **293**, 723–726 (1986).

116. Breast Cancer Foundation NZ. Breast Cancer Foundation NZ Risk Calculator. *BreastNet NZ* https://www.breastnet.nz/risk-calculator (2024).

117. Sak, M. A. *et al.* Current and Future Methods for Measuring Breast Density: A Brief Comparative Review. *Breast Cancer Manag* **4**, 209–221 (2015).

118. Warner, E. *et al.* Systematic Review: Using Magnetic Resonance Imaging to Screen Women at High Risk for Breast Cancer. *Ann Intern Med* **148**, 671–679 (2008).

119. Berrington de González, A. & Darby, S. Risk of cancer from diagnostic X-rays: estimates for the UK and 14 other countries. *Lancet* **363**, 345–351 (2004).

120. Sood, R. *et al.* Ultrasound for Breast Cancer Detection Globally: A Systematic Review and Meta-Analysis. *JGO* 1–17 (2019) doi:10.1200/JGO.19.00127.

121. Brem, R. F. *et al.* Assessing improvement in detection of breast cancer with three-dimensional automated breast US in women with dense breast tissue: the SomoInsight Study. *Radiology* **274**, 663–673 (2015).

122. Berg, W. A. Supplemental screening sonography in dense breasts. *Radiologic Clinics of North America* **42**, 845–851 (2004).

123. Berg, W. A. *et al.* Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. *JAMA* **307**, 1394–1404 (2012).

124. Ohuchi, N. *et al.* Sensitivity and specificity of mammography and adjunctive ultrasonography to screen for breast cancer in the Japan Strategic Anti-cancer Randomized Trial (J-START): a randomised controlled trial. *The Lancet* **387**, 341–348 (2016).

125. Neeter, L. M. F. H. *et al.* Comparing the Diagnostic Performance of Contrast-Enhanced Mammography and Breast MRI: a Systematic Review and Meta-Analysis. *J Cancer* **14**, 174–182 (2023).

126. Cheung, Y.-C. *et al.* Diagnostic performance of dual-energy contrast-enhanced subtracted mammography in dense breasts compared to mammography alone: interobserver blind-reading analysis. *Eur Radiol* **24**, 2394–2403 (2014).

127. Pötsch, N., Vatteroni, G., Clauser, P., Helbich, T. H. & Baltzer, P. A. T. Contrast-enhanced Mammography versus Contrast-enhanced Breast MRI: A Systematic Review and Meta-Analysis. *Radiology* **305**, 94–103 (2022).

128. Cheung, Y.-C. *et al.* Diagnostic performance of dual-energy contrast-enhanced subtracted mammography in dense breasts compared to mammography alone: interobserver blind-reading analysis. *Eur Radiol* **24**, 2394–2403 (2014).

129. NCCN Guidelines for Patients: Breast Cancer Screening and Diagnosis. *Breast Cancer Screening and Diagnosis* (2022).

130. Alabousi, M. *et al.* Digital breast tomosynthesis for breast cancer detection: a diagnostic test accuracy systematic review and meta-analysis. *Eur Radiol* **30**, 2058–2071 (2020).

131. Waldherr, C. *et al.* Value of One-View Breast Tomosynthesis Versus Two-View Mammography in Diagnostic Workup of Women With Clinical Signs and Symptoms and in Women Recalled From Screening. *American Journal of Roentgenology* **200**, 226–231 (2013).

132. Gao, Y., Moy, L. & Heller, S. L. Digital Breast Tomosynthesis:Update on Technology, Evidence, and Clinical Practice. *Radiographics* **41**, 321–337 (2021).

133. Grimm, L. J., Mango, V. L., Harvey, J. A., Plecha, D. M. & Conant, E. F. Implementation of Abbreviated Breast MRI for Screening: AJR Expert Panel Narrative Review. *American Journal of Roentgenology* **218**, 202–212 (2022).

134. Mann, R. M., Kuhl, C. K. & Moy, L. Contrast‐enhanced MRI for breast cancer screening. *J Magn Reson Imaging* **50**, 377–390 (2019).

135. Mann, R. M., Kuhl, C. K. & Moy, L. Contrast‐enhanced MRI for breast cancer screening. *J Magn Reson Imaging* **50**, 377–390 (2019).

136. Sardanelli, F. *et al.* The paradox of MRI for breast cancer screening: high-risk and dense breasts—available evidence and current practice. *Insights Imaging* **15**, 96 (2024).

137. Saslow, D. *et al.* American Cancer Society Guidelines for Breast Screening with MRI as an Adjunct to Mammography. *CA: A Cancer Journal for Clinicians* **57**, 75–89 (2007).

138. *Breast MRI for High-Risk Screening*. (Springer International Publishing, Cham, 2020). doi:10.1007/978-3-030-41207-4.

139. Ding, W. *et al.* Magnetic resonance imaging in screening women at high risk of breast cancer: A meta-analysis. *Medicine (Baltimore)* **102**, e33146 (2023).

140. Ghadimi, M. & Sapra, A. Magnetic Resonance Imaging Contraindications. in *StatPearls* (StatPearls Publishing, Treasure Island (FL), 2024).

141. Berg, W. A. *et al.* Reasons Women at Elevated Risk of Breast Cancer Refuse Breast MR Imaging Screening: ACRIN 66661. *Radiology* **254**, 79–87 (2010).

142. Richter, V. *et al.* Contrast-enhanced spectral mammography in patients with MRI contraindications. *Acta Radiol* **59**, 798–805 (2018).

143. Kuhl, C. K. Abbreviated Magnetic Resonance Imaging (MRI) for Breast Cancer Screening: Rationale, Concept, and Transfer to Clinical Practice. *Annu. Rev. Med.* **70**, 501–519 (2019).

144. Seely, J. M. *et al.* Breast Density and Risk of Interval Cancers: The Effect of Annual Versus Biennial Screening Mammography Policies in Canada. *Can Assoc Radiol J* **73**, 90–100 (2022).

145. Klang, E. *et al.* Utility of routine use of breast ultrasound following contrast-enhanced spectral mammography. *Clinical Radiology* **73**, 908.e11-908.e16 (2018).

146. Sorin, V. *et al.* Contrast-Enhanced Spectral Mammography in Women With Intermediate Breast Cancer Risk and Dense Breasts. *American Journal of Roentgenology* **211**, W267–W274 (2018).

147. Diekmann, F. *et al.* Evaluation of contrast-enhanced digital mammography. *European Journal of Radiology* **78**, 112–121 (2011).

148. Fallenberg, E. M. *et al.* Contrast-enhanced spectral mammography versus MRI: Initial results in the detection of breast cancer and assessment of tumour size. *Eur Radiol* **24**, 256–264 (2014).

149. Gordon, P. B. & Goldenberg, S. L. Malignant breast masses detected only by ultrasound. A retrospective review. *Cancer* **76**, 626–630 (1995).

150. Kolb, T. M., Lichy, J. & Newhouse, J. H. Occult cancer in women with dense breasts: detection with screening US--diagnostic yield and tumor characteristics. *Radiology* **207**, 191–199 (1998).

151. Berg, W. A. & Gilbreath, P. L. Multicentric and Multifocal Cancer: Whole-Breast US in Preoperative Evaluation. *Radiology* **214**, 59–66 (2000).

152. Friedewald, S. M. *et al.* Breast cancer screening using tomosynthesis in combination with digital mammography. *JAMA* **311**, 2499–2507 (2014).

153. Partyka, L., Lourenco, A. P. & Mainiero, M. B. Detection of mammographically occult architectural distortion on digital breast tomosynthesis screening: initial clinical experience. *AJR Am J Roentgenol* **203**, 216–222 (2014).

154. Rafferty, E. A. *et al.* Breast Cancer Screening Using Tomosynthesis and Digital Mammography in Dense and Nondense Breasts. *JAMA* **315**, 1784–1786 (2016).

155. Sharpe, R. E. *et al.* Increased Cancer Detection Rate and Variations in the Recall Rate Resulting from Implementation of 3D Digital Breast Tomosynthesis into a Population-based Screening Program. *Radiology* **278**, 698–706 (2016).

156. Conant, E. F. *et al.* Mammographic Screening in Routine Practice: Multisite Study of Digital Breast Tomosynthesis and Digital Mammography Screenings. *Radiology* **307**, e221571 (2023).

157. Yun, S. J., Ryu, C.-W., Rhee, S. J., Ryu, J. K. & Oh, J. Y. Benefit of adding digital breast tomosynthesis to digital mammography for breast cancer screening focused on cancer characteristics: a meta-analysis. *Breast Cancer Res Treat* **164**, 557–569 (2017).

158. Skaane, P. *et al.* Performance of breast cancer screening using digital breast tomosynthesis: results from the prospective population-based Oslo Tomosynthesis Screening Trial. *Breast Cancer Res Treat* **169**, 489–496 (2018).

159. Bakker Marije F. *et al.* Supplemental MRI Screening for Women with Extremely Dense Breast Tissue. *New England Journal of Medicine* **381**, 2091–2102 (2019).

160. Berg, W. A., Rafferty, E. A., Friedewald, S. M., Hruska, C. B. & Rahbar, H. Screening Algorithms in Dense Breasts: AJR Expert Panel Narrative Review. *AJR Am J Roentgenol* **216**, 275–294 (2021).

161. Berg, W. A. & Vourtsis, A. Screening Breast Ultrasound Using Handheld or Automated Technique in Women with Dense Breasts. *J Breast Imaging* **1**, 283–296 (2019).

162. Weigert, J. M. The Connecticut Experiment; The Third Installment: 4 Years of Screening Women with Dense Breasts with Bilateral Ultrasound. *The Breast Journal* **23**, 34–39 (2017).

163. Berg, W. A. *et al.* Prospective Multicenter Diagnostic Performance of Technologist-Performed Screening Breast Ultrasound After Tomosynthesis in Women With Dense Breasts (the DBTUST). *J Clin Oncol* **41**, 2403–2415 (2023).

164. Sung, J. S. *et al.* Performance of Dual-Energy Contrast-enhanced Digital Mammography for Screening Women at Increased Risk of Breast Cancer. *Radiology* **293**, 81–88 (2019).

165. Gluskin, J. *et al.* Contrast-Enhanced Mammography for Screening Women after Breast Conserving Surgery. *Cancers* **12**, 3495 (2020).

166. Hogan, M. P. *et al.* Contrast-Enhanced Digital Mammography Screening for Intermediate-Risk Women With a History of Lobular Neoplasia. *AJR Am J Roentgenol* **216**, 1486–1491 (2021).

167. Comstock, C. E. *et al.* Comparison of Abbreviated Breast MRI vs Digital Breast Tomosynthesis for Breast Cancer Detection Among Women With Dense Breasts Undergoing Screening. *JAMA* **323**, 746–756 (2020).

168. Kuhl, C. K. *et al.* Abbreviated Breast Magnetic Resonance Imaging (MRI): First Postcontrast Subtracted Images and Maximum-Intensity Projection—A Novel Approach to Breast Cancer Screening With MRI. *Journal of Clinical Oncology* (2014) doi:10.1200/JCO.2013.52.5386.

169. Kuhl, C. K. *et al.* Supplemental Breast MR Imaging Screening of Women with Average Risk of Breast Cancer. *Radiology* **283**, 361–370 (2017).

170. Veenhuizen, S. G. A. *et al.* Supplemental Breast MRI for Women with Extremely Dense Breasts: Results of the Second Screening Round of the DENSE Trial. *Radiology* **299**, 278–286 (2021).

171. Marmot, M. G. *et al.* The benefits and harms of breast cancer screening: an independent review. *Br J Cancer* **108**, 2205–2240 (2013).

172. Sardanelli, F. *et al.* Position paper on screening for breast cancer by the European Society of Breast Imaging (EUSOBI) and 30 national breast radiology bodies from Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Israel, Lithuania, Moldova, The Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Spain, Sweden, Switzerland and Turkey. *Eur Radiol* **27**, 2737–2743 (2017).

173. Nelson, H. D. *et al.* Effectiveness of Breast Cancer Screening: Systematic Review and Meta-analysis to Update the 2009 U.S. Preventive Services Task Force Recommendation. *Ann Intern Med* **164**, 244–255 (2016).

174. Bleyer, A., Baines, C. & Miller, A. B. Impact of screening mammography on breast cancer mortality. *Int J Cancer* **138**, 2003–2012 (2016).

175. Løberg, M., Lousdal, M. L., Bretthauer, M. & Kalager, M. Benefits and harms of mammography screening. *Breast Cancer Res* **17**, 63 (2015).

176. Barth, R. J. *et al.* Detection of breast cancer on screening mammography allows patients to be treated with less-toxic therapy. *AJR Am J Roentgenol* **184**, 324–329 (2005).

177. Spillane, A. J. *et al.* Screen-detected breast cancer compared to symptomatic presentation: an analysis of surgical treatment and end-points of effective mammographic screening. *ANZ J Surg* **71**, 398–402 (2001).

178. Malmgren, J., Parikh, J., Atwood, K. & Kaplan, H. Impact of Mammography Detection on the Course of Breast Cancer in Women Aged 40–49 Years. *Radiology* **262**, (2012).

179. Elder, K. *et al.* Treatment Intensity Differences After Early-Stage Breast Cancer (ESBC) Diagnosis Depending on Participation in a Screening Program. *Ann Surg Oncol* **25**, 2563–2572 (2018).

180. World Cancer Research Fund. Cancer survival statistics. *World Cancer Research Fund* https://www.wcrf.org/preventing-cancer/cancer-statistics/cancer-survival-statistics/ (2020).

181. Aye PS, Win SS, Tin Tin S, & Elwood JM. Comparison of Cancer Mortality and Incidence Between New Zealand and Australia and Reflection on Differences in Cancer Care: An Ecological Cross-Sectional Study of 2014-2018. *Cancer Control* **30**, 10732748231152330 (2023).

182. Berg, W. A. *et al.* Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. *JAMA* **299**, 2151–2163 (2008).

183. Kuhl, C. K. *et al.* Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. *J Clin Oncol* **23**, 8469–8476 (2005).

184. Lehman, C. D. *et al.* Cancer yield of mammography, MR, and US in high-risk women: prospective multi-institution breast cancer screening study. *Radiology* **244**, 381–388 (2007).

185. Saadatmand, S. *et al.* MRI versus mammography for breast cancer screening in women with familial risk (FaMRIsc): a multicentre, randomised, controlled trial. *The Lancet Oncology* **20**, 1136–1147 (2019).

186. Rebolj, M., Assi, V., Brentnall, A., Parmar, D. & Duffy, S. W. Addition of ultrasound to mammography in the case of dense breast tissue: systematic review and meta-analysis. *Br J Cancer* **118**, 1559–1570 (2018).

187. Harada-Shoji, N. *et al.* Evaluation of Adjunctive Ultrasonography for Breast Cancer Detection Among Women Aged 40-49 Years With Varying Breast Density Undergoing Screening Mammography: A Secondary Analysis of a Randomized Clinical Trial. *JAMA Netw Open* **4**, e2121505 (2021).

188. Tian, Y., Schofield, P. E., Gough, K. & Mann, G. B. Profile and Predictors of Long-term Morbidity in Breast Cancer Survivors. *Ann Surg Oncol* **20**, 3453–3460 (2013).

189. Arndt, V., Stegmaier, C., Ziegler, H. & Brenner, H. Quality of life over 5 years in women with breast cancer after breast-conserving therapy versus mastectomy: a population-based study. *J Cancer Res Clin Oncol* **134**, 1311–1318 (2008).

190. Sagen, A., Kaaresen, R., Sandvik, L., Thune, I. & Risberg, M. A. Upper limb physical function and adverse effects after breast cancer surgery: a prospective 2.5-year follow-up study and preoperative measures. *Arch Phys Med Rehabil* **95**, 875–881 (2014).

191. Crane-Okada, R., Wascher, R. A., Elashoff, D. & Giuliano, A. E. Long-term morbidity of sentinel node biopsy versus complete axillary dissection for unilateral breast cancer. *Ann Surg Oncol* **15**, 1996–2005 (2008).

192. Park, S. L. *et al.* Association of internal smoking dose with blood DNA methylation in three racial/ethnic populations. *Clin Epigenetics* **10**, 110 (2018).

193. Clark, M. M. *et al.* Physical activity in patients with advanced-stage cancer actively receiving chemotherapy. *J Support Oncol* **5**, 487–493 (2007).

194. Taylor, C. *et al.* Estimating the Risks of Breast Cancer Radiotherapy: Evidence From Modern Radiation Doses to the Lungs and Heart and From Previous Randomized Trials. *J Clin Oncol* **35**, 1641–1649 (2017).

195. Walsh, S. M. *et al.* Postmastectomy radiotherapy: indications and implications. *Surgeon* **12**, 310–315 (2014).

196. Franklin, M. *et al.* Direct and Indirect Costs of Breast Cancer and Associated Implications: A Systematic Review. *Adv Ther* **41**, 2700–2722 (2024).

197. Sun, L., Legood, R., dos-Santos-Silva, I., Gaiha, S. M. & Sadique, Z. Global treatment costs of breast cancer by stage: A systematic review. *PLOS ONE* **13**, e0207993 (2018).

198. Lao, C., Mondal, M., Kuper-Hommel, M., Campbell, I. & Lawrenson, R. Differences in Breast Cancer Costs by Cancer Stage and Biomarker Subtype in New Zealand. *Pharmacoecon Open* **6**, 539–548 (2022).

199. Health New Zealand - Te Whatu Ora. BreastScreen Aotearoa Coverage Report. https://tewhatuora.shinyapps.io/nsu-bsa-coverage/ (2025).

200. Seneviratne, S. Treatment delay for Māori women with breast cancer in New Zealand.pdf. *Ethnicity & Health* **20**, 178–93 (2015).

201. Seneviratne, S. *et al.* Ethnic differences in breast cancer survival in New Zealand: contributions of differences in screening, treatment, tumor biology, demographics and comorbidities. *Cancer Causes Control* **26**, 1813–1824 (2015).

202. Seneviratne, S. *et al.* Breast Cancer Biology and Ethnic Disparities in Breast Cancer Mortality in New Zealand: A Cohort Study. *PLoS ONE* **10**, e0123523 (2015).

203. Seneviratne, S., Campbell, I., Scott, N., Shirley, R. & Lawrenson, R. Impact of mammographic screening on ethnic and socioeconomic inequities in breast cancer stage at diagnosis and survival in New Zealand: a cohort study. *BMC Public Health* **15**, 46 (2015).

204. Meredith, I. & Lawrenson, R. Who does not benefit from our national breast screening programme and who should have oversight? *New Zealand Medical Journal* (2023).

205. Kerlikowske, K. *et al.* Identifying Women With Dense Breasts at High Risk for Interval Cancer: A Cohort Study. *Ann Intern Med* **162**, 673–681 (2015).

206. Brentnall, A. R. *et al.* A Case-Control Study to Add Volumetric or Clinical Mammographic Density into the Tyrer-Cuzick Breast Cancer Risk Model. *J Breast Imaging* **1**, 99–106 (2019).

207. Yaffe, M. J. & Mainprize, J. G. Overdetection of Breast Cancer. *Current Oncology* **29**, 3894–3910 (2022).

208. Puliti, D. *et al.* Overdiagnosis in Mammographic Screening for Breast Cancer in Europe: A Literature Review. *J Med Screen* **19**, 42–56 (2012).

209. Carter, J. L., Coletti, R. J. & Harris, R. P. Quantifying and monitoring overdiagnosis in cancer screening: a systematic review of methods. *BMJ* **350**, g7773 (2015).

210. Miller, A. B. *et al.* Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial. *BMJ* **348**, g366 (2014).

211. Zackrisson, S., Andersson, I., Janzon, L., Manjer, J. & Garne, J. P. Rate of over-diagnosis of breast cancer 15 years after end of Malmö mammographic screening trial: follow-up study. *BMJ* **332**, 689–692 (2006).

212. Voss, T. *et al.* Quantification of overdiagnosis in randomised trials of cancer screening: an overview and re-analysis of systematic reviews. *Cancer Epidemiol* **84**, 102352 (2023).

213. Morrell, S. *et al.* Absence of sustained breast cancer incidence inflation in a national mammography screening programme. *J Med Screen* **26**, 26–34 (2019).

214. Lee, C. S. *et al.* Association of Patient Age With Outcomes of Current-Era, Large-Scale Screening Mammography. *JAMA Oncol* **3**, 1134–1136 (2017).

215. Blanchard, K. *et al.* Long-term Risk of False-Positive Screening Results and Subsequent Biopsy as a Function of Mammography Use. *Radiology* **240**, 335–342 (2006).

216. Mathioudakis, A. G. *et al.* Systematic review on women’s values and preferences concerning breast cancer screening and diagnostic services. *Psychooncology* **28**, 939–947 (2019).

217. Liao, J. M. & Lee, C. I. Strategies for Mitigating Consequences of Federal Breast Density Notifications. *JAMA Health Forum* **4**, e232801 (2023).

218. Sprague, B. L. *et al.* Benefits, Harms, and Cost-Effectiveness of Supplemental Ultrasonography Screening for Women With Dense Breasts. *Ann Intern Med* **162**, 157–166 (2015).

219. The Royal Australian and New Zealand College of Radiologists. RANZCR Breast Density Position Statement. (2023).

220. The Daffodil Centre. The ROSA project summary - Roadmap for Optimising Screening in Australia — Breast Cancer Council Australia. https://daffodilcentre.org/wp-content/uploads/2024/05/ROSA-Report-2023.-Public-facing-summary-28-Sept-2023.pdf (2023).

221. Nickel, B. *et al.* Psychosocial outcomes and health service use after notifying women participating in population breast screening when they have dense breasts: a BreastScreen Queensland randomised controlled trial. *Med. J. Aust.* **Online first**, (2023).

222. Dense Breast-info. Comparative Analysis of National Breast Screening Guidelines in Europe. (2023).

223. Dense Breasts Canada. My Breast Screening Canada. *My Breast Screening* https://mybreastscreening.ca/.

224. Mann, R. M. *et al.* Breast cancer screening in women with extremely dense breasts recommendations of the European Society of Breast Imaging (EUSOBI). *Eur Radiol* **32**, 4036–4045 (2022).

225. Commissioner, O. of the. FDA Updates Mammography Regulations to Require Reporting of Breast Density Information and Enhance Facility Oversight. *FDA* https://www.fda.gov/news-events/press-announcements/fda-updates-mammography-regulations-require-reporting-breast-density-information-and-enhance (2023).

226. The Commonwealth Fund. Country Profiles International Health Care System Profiles. *The Commonwealth Fund* https://www.commonwealthfund.org/international-health-policy-center/countries (2024).

227. The European Observatory on Health Systems and Policies. All countries | Health systems. *The European Observatory on Health Systems and Policies* https://eurohealthobservatory.who.int/overview.

228. Breast Screen Western Australia. BreastScreen WA - Dense breasts. https://www.breastscreen.health.wa.gov.au/Breast-screening/Dense-breasts.

229. BreastScreen New South Wales. BreastScreen NSW uses software to report breast (mammographic) density. *BreastScreen New South Wales* https://www.breastscreen.nsw.gov.au/breast-cancer-and-screening/dense-breast-tissue-and-screening/ (2023).

230. O’Driscoll, J. *et al.* A scoping review of programme specific mammographic breast density related guidelines and practices within breast screening programmes. *European Journal of Radiology Open* **11**, 100510 (2023).

231. Monticciolo, D. L., Newell, M. S., Moy, L., Lee, C. S. & Destounis, S. V. Breast Cancer Screening for Women at Higher-Than-Average Risk: Updated Recommendations From the ACR. *Journal of the American College of Radiology* **20**, 902–914 (2023).

232. European Commission Initiative on Breast Cancer. European guidelines on breast cancer screening and diagnosis. (2024).

233. German Guideline Program in Oncology. Evidence-based Guideline for the Early Detection, Diagnosis, Treatment and Follow-up of Breast Cancer. Version 4.4 - May 2021. (2021).

234. The German Gynaecologica Oncology Working Group, B. C. Diagnosis and Treatment of Patients with early and advanced Breast Cancer Guidelines of the AGO Breast Committee. (2020).

235. The Royal College of Radiologists. Guidance on screening and symptomatic breast imaging, Fourth edition | The Royal College of Radiologists. (2019).

236. Urban, L. A. B. D. *et al.* Breast cancer screening: updated recommendations of the Brazilian College of Radiology and Diagnostic Imaging, Brazilian Breast Disease Society, and Brazilian Federation of Gynecological and Obstetrical Associations. *Radiol Bras* **50**, 244–249 (2017).

237. Alberta Breast Cancer Screening Program. Alberta Breast Cancer Screening Clinical Practice Guideline 2022 Update. (2022).

238. Association, C. A.-C., Institute, N. C. R. C. for C. (Tianjin M. U. C. & Hospital). Breast cancer screening guideline for Chinese women. *Cancer Biology & Medicine* **16**, 822–824 (2019).

239. Uematsu, T. *et al.* The Japanese Breast Cancer Society Clinical Practice Guidelines for Breast Cancer Screening and Diagnosis, 2018 Edition. *Breast Cancer* **27**, 17–24 (2020).

240. Weinstein, S. P. *et al.* ACR Appropriateness Criteria® Supplemental Breast Cancer Screening Based on Breast Density. *Journal of the American College of Radiology* **18**, S456–S473 (2021).

241. American College of Obstetricians and Gynecologists. Management of Women With Dense Breasts Diagnosed by Mammography Update. (2023).

242. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Breast Cancer Version 2.2024. (2024).

243. Lee, C. H. *et al.* Breast Cancer Screening With Imaging: Recommendations From the Society of Breast Imaging and the ACR on the Use of Mammography, Breast MRI, Breast Ultrasound, and Other Technologies for the Detection of Clinically Occult Breast Cancer. *Journal of the American College of Radiology* **7**, 18–27 (2010).

244. US Preventive Services Task Force. Screening for Breast Cancer US Preventive Services Task Force Recommendation Statement 2024. (2024).

245. Khan, M. & Chollet, A. Breast Cancer Screening: Common Questions and Answers. *afp* **103**, 33–41 (2021).

246. Kass, N. E. An Ethics Framework for Public Health. *Am J Public Health* **91**, 1776–1782 (2001).

247. Ingman, W. V. *et al.* Breast Density Notification: An Australian Perspective. *Journal of Clinical Medicine* **9**, 681 (2020).

248. Tin Tin, S. *et al.* Ethnic disparities in breast cancer survival in New Zealand: which factors contribute? *BMC Cancer* **18**, 58 (2018).

249. Elwood, M. *Epidemiological Aspects of Breast Cancer Screening Relevant to Aotearoa*. https://www.tewhatuora.govt.nz/assets/For-the-health-sector/NSU/Publications/Epidemiological-Aspects-of-Breast-Cancer-Screening-Relevant-to-Aotearoa-pdf-2-MB.pdf (2022).

250. Pae Ora (Healthy Futures) Act 2022 No 30 (as at 27 July 2023), Public Act – New Zealand Legislation. https://www.legislation.govt.nz/act/public/2022/0030/latest/versions.aspx.

251. Health Quality & Safety Commission. HQSC Code of expectations. (2024).

252. Health and Disability Commissioner. Code of Health and Disability Services Consumers’ Rights. *Health and Disability Commissioner* https://www.hdc.org.nz/your-rights/about-the-code/code-of-health-and-disability-services-consumers-rights/ (2024).

253. Nickel, B. *et al.* A systematic assessment of online international breast density information. *The Breast* **65**, 23–31 (2022).

254. Mammography Quality Standards Act. *Federal Register* https://www.federalregister.gov/documents/2023/03/10/2023-04550/mammography-quality-standards-act (2023).

255. Best, R., Wilkinson, L. S., Oliver-Williams, C., Tolani, F. & Yates, J. Should we share breast density information during breast cancer screening in the United Kingdom? an integrative review. *British Journal of Radiology* **96**, 20230122 (2023).

256. Huang, S., Houssami, N., Brennan, M. & Nickel, B. The impact of mandatory mammographic breast density notification on supplemental screening practice in the United States: a systematic review. *Breast Cancer Res Treat* **187**, 11–30 (2021).

257. Nickel, B. *et al.* “It’s about our bodies… we have the right to know this stuff”: A qualitative focus group study on Australian women’s perspectives on breast density. *Patient Education and Counseling* **105**, 632–640 (2022).

258. Dench, E. K. *et al.* Confusion and Anxiety Following Breast Density Notification: Fact or Fiction? *Journal of Clinical Medicine* **9**, 955 (2020).

259. Rhodes, D. J., Jenkins, S. M., Hruska, C. B., Vachon, C. M. & Breitkopf, C. R. Breast Density Awareness, Knowledge, and Attitudes Among US Women: National Survey Results Across 5 Years. *J Am Coll Radiol* **17**, 391–404 (2020).

260. Santiago-Rivas, M., Benjamin, S., Andrews, J. Z. & Jandorf, L. Breast density awareness and knowledge, and intentions for breast cancer screening in a diverse sample of women age eligible for mammography. *J Cancer Educ* **34**, 90–97 (2019).

261. Pacsi-Sepulveda, A. L., Shelton, R. C., Rodriguez, C. B., Coq, A. T. & Tehranifar, P. “You probably can’t feel as safe as normal women”: Hispanic women’s reactions to breast density notification. *Cancer* **125**, 2049–2056 (2019).

262. Trinh, L. *et al.* Patient awareness of breast density and interest in supplemental screening tests: comparison of an academic facility and a county hospital. *J Am Coll Radiol* **12**, 249–255 (2015).

263. Nickel, B. *et al.* Breast Density Notification: A Systematic Review of the Impact on Primary Care Practitioners. *Journal of Women’s Health* **30**, 1457–1468 (2021).

264. Pandya, T. *et al.* Australian Women’s Responses to Breast Density Information: A Content Analysis. *Int J Environ Res Public Health* **20**, 1596 (2023).

265. Houssami, N. & Lee, C. I. The impact of legislation mandating breast density notification - Review of the evidence. *Breast* **42**, 102–112 (2018).

266. Dolan, H. *et al.* Australian Women’s Intentions and Psychological Outcomes Related to Breast Density Notification and Information: A Randomized Clinical Trial. *JAMA Netw Open* **5**, e2216784 (2022).

267. Isautier, J. M. J. *et al.* The impact of breast density notification on psychosocial outcomes in racial and ethnic minorities: A systematic review. *The Breast* **74**, (2024).

268. Moothathu, N. S. *et al.* Knowledge of Density and Screening Ultrasound. *Breast J* **23**, 323–332 (2017).

269. Manning, M. *et al.* Explaining between-race differences in African-American and European-American women’s responses to breast density notification. *Soc Sci Med* **195**, 149–158 (2017).

270. Kressin, N. R., Wormwood, J. B., Battaglia, T. A. & Gunn, C. M. Differences in Breast Density Awareness, Knowledge, and Plans Based on State Legislation Status and Sociodemographic Characteristics. *J Gen Intern Med* **35**, 1923–1925 (2020).

271. Gunn, C. M. *et al.* A Qualitative Study of Spanish-Speakers’ Experience with Dense Breast Notifications in a Massachusetts Safety-Net Hospital. *J GEN INTERN MED* **34**, 198–205 (2019).

272. Kressin, N. R., Wormwood, J. B., Battaglia, T. A., Slanetz, P. J. & Gunn, C. M. Women’s Reactions to Breast Density Information Vary by Sociodemographic Characteristics. *Women’s Health Issues* **33**, 435–442 (2023).

273. Berkman, N. D., Davis ,Terry C. & and McCormack, L. Health Literacy: What Is It? *Journal of Health Communication* **15**, 9–19 (2010).

274. Nickel, B. *et al.* “*It’s about our bodies… we have the right to know this stuff*”: A qualitative focus group study on Australian women’s perspectives on breast density. *Patient Education and Counseling* **105**, 632–640 (2022).

275. Kressin, N. R., Wormwood, J. B., Battaglia, T. A., Slanetz, P. J. & Gunn, C. M. A letter is not enough: Women’s preferences for and experiences of receiving breast density information. *Patient Education and Counseling* **105**, 2450–2456 (2022).

276. Klinger, E. V., Kaplan, C. P., St. Hubert, S., Birdwell, R. L. & Haas, J. S. Patient and Provider Perspectives on Mammographic Breast Density Notification Legislation. *MDM Policy & Practice* **1**, 2381468316680620 (2016).

277. Claringbold, L. *et al.* Reflections from Women with an Interval Breast Cancer Diagnosis: A Qualitative Analysis of Open Disclosure in the BreastScreen Western Australia Program. *Asian Pac J Cancer Prev* **24**, 633–639 (2023).

278. Gunn, C. *et al.* Acceptability of an Interactive Computer-Animated Agent to Promote Patient-Provider Communication About Breast Density: a Mixed Method Pilot Study. *J Gen Intern Med* **35**, 1069–1077 (2020).

279. Darcey, E. *et al.* Post-mammographic screening behaviour: A survey investigating what women do after being told they have dense breasts. *Health Promot J Austr* **32 Suppl 2**, 29–39 (2021).

280. Isautier, J. M. J. *et al.* The impact of breast density notification on psychosocial outcomes in racial and ethnic minorities: A systematic review. *The Breast* **74**, (2024).

281. Ezratty, C. *et al.* Racial/ethnic differences in supplemental imaging for breast cancer screening in women with dense breasts. *Breast Cancer Res Treat* **182**, 181–185 (2020).

282. Huang, S., Houssami, N., Brennan, M. & Nickel, B. The impact of mandatory mammographic breast density notification on supplemental screening practice in the United States: a systematic review. *Breast Cancer Res Treat* **187**, 11–30 (2021).

283. Aripoli, A. *et al.* Supplemental Screening With Automated Breast Ultrasound in Women With Dense Breasts: Comparing Notification Methods and Screening Behaviors. *AJR Am J Roentgenol* **210**, W22–W28 (2018).

284. Milestone to celebrate as College of Radiologists recommends breast density reporting | BCAC Breast Cancer Aotearoa Coalition. https://www.breastcancer.org.nz/content/milestone-celebrate-college-radiologists-recommends-breast-density-reporting.

285. Wilkerson, A. D., Gentle, C. K., Ortega, C. & Al-Hilli, Z. Disparities in Breast Cancer Care—How Factors Related to Prevention, Diagnosis, and Treatment Drive Inequity. *Healthcare* **12**, 462 (2024).

286. Iezzoni, L. I., Rao, S. R., Agaronnik, N. D. & El-Jawahri, A. Associations Between Disability and Breast or Cervical Cancers, Accounting for Screening Disparities. *Medical Care* **59**, 139–147 (2021).

287. Andiwijaya, F. R., Davey, C., Bessame, K., Ndong, A. & Kuper, H. Disability and Participation in Breast and Cervical Cancer Screening: A Systematic Review and Meta-Analysis. *IJERPH* **19**, 9465 (2022).

288. Floud, S. *et al.* Disability and participation in breast and bowel cancer screening in England: a large prospective study. *Br J Cancer* **117**, 1711–1714 (2017).

289. Almohammed, H. I. A Systematic Review to Evaluate the Barriers to Breast Cancer Screening in Women with Disability. *JCM* **13**, 3283 (2024).

290. Parish, S. L., Swaine, J. G., Son, E. & Luken, K. Receipt of mammography among women with intellectual disabilities: Medical record data indicate substantial disparities for African American women. *Disability and Health Journal* **6**, 36–42 (2013).

291. Wei, W., Findley, P. A. & Sambamoorthi, U. Disability and Receipt of Clinical Preventative Services Among Women. *Womens Health Issues* **16**, 286–296 (2006).

292. Llewellyn, G., Balandin, S., Poulos, A. & McCarthy, L. Disability and mammography screening: intangible barriers to participation. *Disability and Rehabilitation* **33**, 1755–1767 (2011).

293. Barr, J. K., Giannotti, T. E., Hoof, T. J. V., Mongoven, J. & Curry, M. Understanding Barriers to Participation in Mammography by Women with Disabilities. *Am J Health Promot* **22**, 381–385 (2008).

294. Ramjan, L., Cotton, A., Algoso, M. & Peters, K. Barriers to breast and cervical cancer screening for women with physical disability: A review. *Women & Health* **56**, 141–156 (2016).

295. Yankaskas, B. C. *et al.* Barriers to Adherence to Screening Mammography Among Women With Disabilities. *American Journal of Public Health* **100**, (2007).

296. Sullivan, S. G., Slack-Smith, L. M. & Hussain, R. Understanding the use of breast cancer screening services by women with intellectual disabilities. *Soz Praventivmed* **49**, 398–405 (2004).

297. Gunn, C. M. *et al.* Primary Care Provider Experience with Breast Density Legislation in Massachusetts. *J Womens Health (Larchmt)* **27**, 615–622 (2018).

298. Varghese, J. *et al.* Breast Density Notification: Current UK National Practice. *Clinical Breast Cancer* **22**, e101–e107 (2022).

299. Pashayan, N. *et al.* Personalized early detection and prevention of breast cancer: ENVISION consensus statement. *Nat Rev Clin Oncol* **17**, 687–705 (2020).

300. The Daffodil Centre. *The ROSA Project: Roadmap for Optimising Screening in Australia – Breast. Chapter 5: Implementation (Abridged)*. https://daffodilcentre.org/wp-content/uploads/2024/05/ROSA-Report-2023.-Chapter-5.-Implementation-Abridged.pdf (2024).

301. Unicancer. MyPeBS Questions and Answers. https://www.mypebs.eu/wp-content/uploads/2020/07/MyPeBS\_QA\_eng\_V2.0\_251119.pdf (2024).

302. Sankatsing, V. D. V., van Ravesteyn, N. T., Heijnsdijk, E. A. M., Broeders, M. J. M. & de Koning, H. J. Risk stratification in breast cancer screening: Cost-effectiveness and harm-benefit ratios for low-risk and high-risk women. *International Journal of Cancer* **147**, 3059–3067 (2020).

303. Shih, Y.-C. T., Dong, W., Xu, Y., Etzioni, R. & Shen, Y. Incorporating Baseline Breast Density When Screening Women at Average Risk for Breast Cancer. *Ann Intern Med* **174**, 602–612 (2021).

304. Wong, J. Z. Y. *et al.* Cost effectiveness analysis of a polygenic risk tailored breast cancer screening programme in Singapore. *BMC Health Services Research* **21**, 379 (2021).

305. Stout, N. K. *et al.* Benefits, harms, and costs for breast cancer screening after US implementation of digital mammography. *J Natl Cancer Inst* **106**, dju092 (2014).

306. Wang, J. *et al.* The cost-effectiveness of digital breast tomosynthesis in a population breast cancer screening program. *Eur Radiol* **30**, 5437–5445 (2020).

307. Hull, M. A., Rees, C. J., Sharp, L. & Koo, S. A risk-stratified approach to colorectal cancer prevention and diagnosis. *Nat Rev Gastroenterol Hepatol* **17**, 773–780 (2020).

308. Kappen, T. H. *et al.* Evaluating the impact of prediction models: lessons learned, challenges, and recommendations. *Diagnostic and Prognostic Research* **2**, 11 (2018).

309. Taylor, L. C. *et al.* Acceptability of risk stratification within population-based cancer screening from the perspective of the general public: A mixed-methods systematic review. *Health Expect* **26**, 989–1008 (2023).

310. Knoppers, B., Bernier, A., Moreno, P. G. & Pashayan, N. Of Screening, Stratification, and Scores. *Journal of Personalized Medicine* **11**, 736 (2021).

311. French, D. P. *et al.* What are the benefits and harms of risk stratified screening as part of the NHS breast screening Programme? Study protocol for a multi-site non-randomised comparison of BC-predict versus usual screening (NCT04359420). *BMC Cancer* **20**, 570 (2020).

312. ten Haaf, K., van der Aalst, C. M., de Koning, H. J., Kaaks, R. & Tammemägi, M. C. Personalising lung cancer screening: An overview of risk‐stratification opportunities and challenges. *Int J Cancer* **149**, 250–263 (2021).

313. Forbes, C., Fayter, D., de Kock, S. & Quek, R. G. A systematic review of international guidelines and recommendations for the genetic screening, diagnosis, genetic counseling, and treatment of BRCA-mutated breast cancer. *Cancer Manag Res* **11**, 2321–2337 (2019).

314. Paluch-Shimon, S. *et al.* Prevention and screening in BRCA mutation carriers and other breast/ovarian hereditary cancer syndromes: ESMO Clinical Practice Guidelines for cancer prevention and screening. *Ann Oncol* **27**, v103–v110 (2016).

315. Foster, A. Management of patients with BRCA gene mutations in New Zealand. (2024).

316. Daly, M. B. *et al.* Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw* **19**, 77–102 (2021).

317. Selamoglu, A. & Gilbert, F. J. Guidelines and Recommendations on High-Risk Breast Cancer Screening All Over the World: Agreements and Differences. in *Breast MRI for High-risk Screening* (eds. Sardanelli, F. & Podo, F.) 251–267 (Springer International Publishing, Cham, 2020). doi:10.1007/978-3-030-41207-4\_16.

318. NICE UK. Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer | Guidance | NICE. *National Institute for Health and Care Excellence* https://www.nice.org.uk/guidance/cg164 (2013).

319. American Cancer Society. ACS Breast Cancer Screening Guidelines. *American Cancer Society* https://www.cancer.org/cancer/types/breast-cancer/screening-tests-and-early-detection/american-cancer-society-recommendations-for-the-early-detection-of-breast-cancer.html.

320. Inturrisi, F. *et al.* Risk of cervical precancer among HPV–negative women in the Netherlands and its association with previous HPV and cytology results: A follow-up analysis of a randomized screening study. *PLOS Medicine* **19**, e1004115 (2022).

321. Hashim, D. *et al.* Real-world data on cervical cancer risk stratification by cytology and HPV genotype to inform the management of HPV-positive women in routine cervical screening. *Br J Cancer* **122**, 1715–1723 (2020).

322. Smith, M. A. *et al.* National experience in the first two years of primary human papillomavirus (HPV) cervical screening in an HPV vaccinated population in Australia: observational study. *BMJ* **376**, e068582 (2022).

323. World Health Organization. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention. (2021).

324. Gage, J. C. *et al.* The Improving Risk Informed HPV Screening (IRIS) Study: Design and Baseline Characteristics. *Cancer Epidemiol Biomarkers Prev* **31**, 486–492 (2022).

325. Lehtinen, M. *et al.* Assessing the risk of cervical neoplasia in the post‐HPV vaccination era. *Int J Cancer* **152**, 1060–1068 (2023).

326. Te Whatu Ora - Health New Zealand. *Clinical Practice Guidelines for Cervical Screening in Aotearoa New Zealand*. https://www.tewhatuora.govt.nz/assets/Our-health-system/Screening/HPV-Primary-Screening/clinical\_practice\_guidelines\_final\_version\_1.1.pdf (2023).

327. Gupta, S. Screening for colorectal cancer. *Hematol Oncol Clin North Am* **36**, 393–414 (2022).

328. Blackmore, T., Lao, C., Chepulis, L., Page, B. & Lawrenson, R. The characteristics and outcomes of patients with colorectal cancer in New Zealand, analysed by Cancer Network. **133**, (2020).

329. Te Aho o Te Kahu - Cancer Control Agency. *Lung Cancer Quality Improvement Monitoring Report 2021*. https://teaho.govt.nz/static/reports/lung-cancer-quality-improvement-monitoring-report-20210225.pdf (2021).

330. Lawrenson, R. *et al.* Characteristics of lung cancers and accuracy and completeness of registration in the New Zealand Cancer Registry. *New Zealand Medical Journal* **131**, (2018).

1. Appendices
   1. Related Considerations

In this section a number of topics related to management of high-risk groups and risk stratification in screening settings are outlined to provide additional context to the consideration of breast density and risk assessment in breast screening.

#### Women with a high-risk of breast cancer: The example of BRCA gene mutation management

As outlined earlier in Section 5, there are a range of factors which impact breast cancer risk. The lifetime risk of breast cancer is significantly increased by the presence of BRCA gene mutations. Whilst BRCA mutations account for around 5 percent of all breast cancers, together they are responsible for over 90 percent of hereditary breast and ovarian cancers.313,314 The estimated prevalence globally is 1:300 to 1:1000 of the general population, but this is population dependent.314 There is no formal BRCA register in Aotearoa New Zealand and its epidemiology in Aotearoa New Zealand is not fully understood; we currently do not know how many women in New Zealand have been assessed, or diagnosed, with a pathogenic BRCA mutation.315 The Australian eviQ guidelines report population carrier frequencies for BRACA1 and BRACA2 of 0.1% and 0.2% respectively, noting that these are approximates and do not account for population specific differences.112

Surveillance is the monitoring of individuals considered at increased risk of a condition and is generally of smaller scale, but increased intensity compared with screening, which effectively identifies high-risk individuals from an average risk population. The differences between surveillance and screening may not be entirely distinct, and screening organisations should work closely with those undertaking surveillance.9

The optimal surveillance approach for those known to be BRCA mutation carriers – including imaging modalities and scheduling – remains uncertain, particularly for younger women.316 Currently, management varies from country to country but generally involves a combination of clinical examination, MRI and mammography, though may involve other imaging modalities such as US, DBT and CEM.313

#### Management of BRCA Internationally

Although many jurisdictions use a combination of surveillance modalities described above, there is a lack of consensus on the details - including modalities used, age of commencement and scheduling. Described below are guidelines from Australia, UK, and USA but recent reviews have described and tabulated recommendations from 19 different countries, highlighting the variance.313,317

#### Australia

eviQ Guidelines112: For individuals known to be BRCA mutation carriers or considered at 50% risk of being a carrier based on a validated risk assessment, surveillance should commence at 25 to 30 years of age with optimal timing determined by shared decision making and use of CanRisk (refer section 6) or equivalent.

* Under 40 years of age: annual MRI (ultrasound if MRI not available or contra-indicated)
* Between 40 and 60 years of age: annual MRI and annual mammogram (mammogram and ultrasound if MRI not possible)
* Over 60 years of age: annual mammogram (consider MRI or ultrasound if high breast density)

Note: eviQ suggests that where MRI is used there is no additional value in using ultrasound or clinical breast examination.

#### United Kingdom

National Institute for Healthcare and Clinical Excellence (NICE) guidelines.318 Genetic testing should be offered to those considered 10% or more at risk of BRCA mutation or where family history criteria met.

* All individuals considered at increased risk should be encouraged and supported to be ‘breast aware’.

Individuals known to be BRCA mutation carriers or considered greater than 30% risk of being a carrier should be offered:

* 30 to 49 years of age: Annual MRI and
* 40 to 59 years of age and greater than 30% risk of carriage (that is, having a BRCA gene mutation known to increase risk of breast cancer): Annual mammography with a return to routine screening at 60 years of age
* 40 to 69 years of age and known BRCA mutation carriage: Annual mammography with a return to routine screening at 70 years of age.

Consider annual mammography for:

* 30 to 39 years of age: For individuals at high-risk for other reasons but are less than 30% risk of carriage, or assessed as greater than 30% risk of carriage
* 30 to 39 years of age: For known BRCA mutation carriers in addition to MRI

Ultrasound should not be offered unless MRI is not possible, or interpretation is difficult.

#### USA

American Cancer Society screening recommendations for women at high-risk.319 High-risk individuals are considered those known to be BRCA mutation carriers, or with a lifetime risk of 20 to 25% or higher or a strong likelihood of carriage based on family history, or have had chest radiation before 30 years of age:

#### 30 years of age for as long as ‘in good health’: Annual MRI and annual mammogram.

They emphasise that evidence on best age for commencement of surveillance is limited and can be made on a case-by-case basis through shared decision making.

National Comprehensive Cancer Network (NCCN) guidelines.316

Confirmed BRCA mutation carriers:

* Breast awareness from 18 years of age
* Clinical breast examination 6 to 12 monthly from 25 years of age
* 25 to 29 years of age: contrast MRI (mammogram or tomosynthesis if MRI is not possible)
* 30 to 75 years of age: annual mammogram (consider tomosynthesis) and contrast MRI
* After 75 years of age: case-by-case basis.

They note that appropriateness of modalities and scheduling is still under study and that use of MRI depends on capacity and capability.

#### Management of BRCA in Aotearoa New Zealand

In Aotearoa New Zealand, there are three defined categories of risk in breast cancer – average, moderate, and high-risk. Management is guided by the Standards of Service Provision for Breast Cancer Patients in New Zealand 2013 (the Standards NZ) but there may be some regional variations in service provision for publicly funded services.109

Average risk is considered up to 12% lifetime risk and includes over 95 percent of the female population. These individuals are offered routine breast screening through BreastScreen Aotearoa (BSA) between 45 and 69 years of age.

If there are concerns about an increased breast cancer risk, usually based on a family history or a personal history of cancer suggestive of a BRCA mutation, a risk assessment should be undertaken, and this is generally done using eviQ.

The eviQ ‘Breast Cancer referring to genetics’ provides clear guidelines on individuals who should be referred to genetic services and managed by breast care specialists.112 This risk assessment should be undertaken by someone with expertise in interpretation which usually includes the individual’s GP in collaboration with their local breast care service.

For those considered at moderate risk of breast cancer (12-25% lifetime risk) current management recommended by the Standards NZ is that:

* Individuals should be encouraged to be breast aware and to report any concerns promptly to their primary care provider.
* All individuals should have an annual clinical breast examination from 10 years prior to the age of onset for the youngest affected family relative or starting at 25 to 30 years of age.
* An annual mammogram from 40 to 50 years of age. These mammograms are fully funded with funding alternating between BSA and Health New Zealand | Te Whatu Ora. Specialist recommendation may be for a small number of moderate risk women to commence annual mammography prior to 40 years or continue beyond 50 years of age.
* Beyond 50 years of age, if breast cancer had not been identified, the individual should return to routine two yearly mammography through BSA.

Individuals considered high-risk should be referred to Genetic Health Service New Zealand (GHSNZ) for consideration of genetic testing. Referral and testing is publicly funded. GHSNZ geneticists are responsible for determining who should be tested and for what and provide the appropriate genetic counselling. eviQ guidelines recommend referral for testing at a risk of BRCA mutation carriage at 10% or higher.

For surveillance, the Standards NZ consider high-risk a lifetime risk of 25% or higher and includes those known to carry BRCA1 or BRCA2 mutation, or with a strong family history.

All high-risk individuals should be managed through a breast care service with surveillance undertaken outside of BSA but fully funded through Health New Zealand | Te Whatu Ora. Current guidelines recommend surveillance as follows:

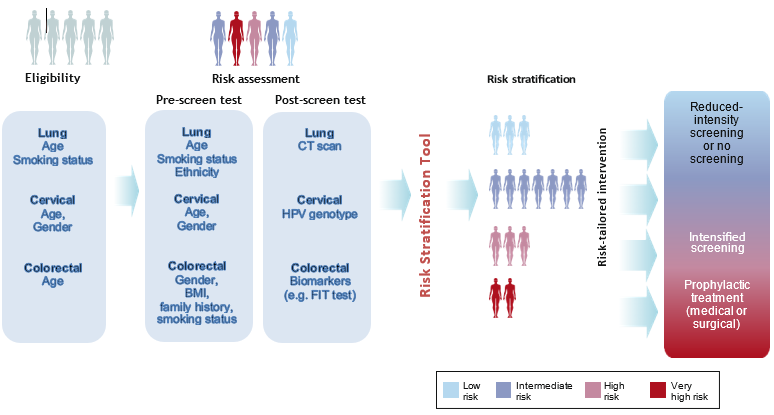
* Individuals should be encouraged to be breast aware and to report any concerns promptly to their primary care provider.
* All individuals should have a clinical breast examination every 6 to 12 months with a breast specialist from 10 years prior to the age of onset for the youngest affected family relative or starting at 25 to 30 years of age.
* Annual MRI and additionally consider annual mammography from 10 years prior to the age of onset for the youngest affected family relative. Before 30 years of age mammography is not recommended as it is less sensitive and carries a risk of radiation-induced cancer.

Although the Standards NZ do not specify an upper age cut off for surveillance, MRI is usually offered and publicly funded until 50 years of age although this may vary on a case-by-case basis or with regional variation. There is no standard in Aotearoa New Zealand for the use of digital breast tomosynthesis, ultrasound or contrast- enhanced imaging.315

* 1. Risk stratification in other cancer screening programmes

Risk stratification aims to modify components of the screening pathway – for example, screening eligibility, tests, and scheduling – in a systematic and reproducible way of translating population risks to individual level risk characteristics to determine personal risk. It has the potential to increase screening and target treatments for those most at risk whilst decreasing screening for those at lower risk, and in doing so deliver individual and population level benefits (see section 10 Broader Risk Stratification Approaches).309 Increasingly, screening programmes are incorporating degrees of risk stratification to inform approaches, some of which are used in Aotearoa New Zealand and discussed further below.

Figure 10: Risk Stratification in screening programmes



Source: Adapted from Pashayan et al.299

#### Cervical cancer screening and Human Papilloma Virus

Human Papilloma Virus (HPV) is strongly associated with cervical cancer, particularly the oncogenic genotypes 16 and 18.320,321 However, there are a number of other genotypes that whilst not as strongly oncogenic, still pose an increased risk.321,322 HPV testing is now well-established as being more sensitive at identifying cervical cancer precursors than liquid-based cytology and has been introduced as the primary cervical cancer screening test in a number of countries, including Aotearoa New Zealand.322–324 However, most identify only HPV 16, 18 or HPV Other (non-16/18 genotypes).

In most HPV-based programmes, a referral for colposcopy is the default for a positive HPV16/18 test given the strong association between these genotypes and cervical cancer. For HPV Other genotypes, infections are often transient and do not result in cervical changes, but distinguishing which will be transient and which may persist and cervical changes/cancer is an area of some uncertainty.321,322,324 It is known that HPV infections persisting for more than one to two years have a higher risk of cervical cancer, and that persistence is more likely in those over 30 years of age.321 With colposcopy services often having limited capacity, there is a need to optimise triage protocols to determine who should be referred.321,324

Using HPV genotyping stratification has the potential to reduce over-referral and increase the effectiveness of HPV-based cervical screening programmes and this is an area of active research.321,324 The use of biomarkers for further triaging is also being studied, particularly in the context of increasing HPV 16/18 vaccination coverage.324,325

Internationally, there is a focus on triaging for referral and screening intervals.322,324 Australia was one of the first countries to adopt a national cervical cancer screening programme using HPV testing as the primary screen and where a proportion of vaccinated women have been included.322 Real-world findings and data following a review of the first two years of the Australian programme have strongly informed adjustments to the programme.322 This has included reviewing triaging and risk stratification, particularly for HPV Other detected tests.322 These findings were considered in the introduction of HPV primary screening into the National Cervical Cancer Screening Programme (NCCSP) in Aotearoa New Zealand, which commenced in September 2023.326

#### Colorectal cancer

Colorectal cancer is one of the most common cancers worldwide.327 Aotearoa New Zealand has one of the highest rates in the world and it is the second highest cause of cancer deaths.328 Late-stage diagnosis contributes to its relatively high mortality rate and early detection including through screening, is critical to improving outcomes.327,328

In many countries including Aotearoa New Zealand, colonoscopy demand is increasing on the background of constrained capacity. The majority of those with a positive screening test referred on for colonoscopy will not have colorectal cancer.307

Variables such as sex, body mass index, family history, smoking status, and biomarkers (of which the currently used faecal immunochemical test, or FIT, is one) could be used to stratify risk and modulate the screening frequency or the positivity threshold of the primary screening test.307 Identifying appropriate risk factors can be difficult when a number associated with colorectal cancer are related – such as diabetes and weight. Different scenarios would need to be considered and understood – for example, how to manage a low risk with a high FIT result and vice versa.307

Currently, there is some evidence that using the FIT with other risk factors may be better at predicting risk than a FIT alone.307 A large number of multivariate screening models have been developed for colorectal cancer, but most are research-based only, and many have not been externally validated.307 Whilst the potential to improve benefits and reduce harms for colorectal cancer through risk stratification is recognised, current evidence remains limited including cost effectiveness and applicability to different settings and populations.307 However, it is an important area for research.

#### Lung cancer

Lung cancer is the leading cause of cancer-related deaths in Aotearoa New Zealand and a significant contributor to the life expectancy gap between Māori and Non-Māori.329 The high mortality is in large part due to late-stage diagnosis.330 However, whilst large randomised controlled trials (RCTs) have demonstrated a reduction in lung cancer mortality using low-dose computed tomography (CT) to screen for lung cancer, associated harms have also been identified, including overdiagnosis, radiation exposure, and false positives.312

Initial trials on screening generally considered age and cumulative lifetime smoking exposure (‘pack year criteria’). These appeared to provide a sufficiently high ‘average’ cancer risk for a population of smokers, but did not consider individual risk. However, even for those meeting pack year criteria, most individuals do not develop lung cancer. Assessment of individual risk has the potential to improve benefits and reduce harms at an individual and a population level.312

Various models have been developed and have shown improved performance at identifying those smokers at higher risk, but optimal methods are still being determined, including how to apply models in practice.312 Of particular importance in the Aotearoa New Zealand context is ensuring models are applicable to the Aotearoa New Zealand population, including for Māori, and to ensure existing inequities are not exacerbated. The carcinogenic effects of smoking vary between ethnicities with evidence that African Americans have a higher risk at any given age and pack history, and Hispanic populations having a lower risk, compared with non-Hispanic white populations.312 The accuracy of risk predictions for different population groups is being assessed in current Aotearoa New Zealand research.

Risk stratification could also be used to determine screening intervals. Current guidelines on the management of nodules identified through low-dose CT screening results in a high proportion of negative CTs.312 The imaging is a substantial proportion of screening costs and there is limited capacity for radiologist and medical imaging technologists in many countries, including Aotearoa New Zealand.312 There are a number of prospective RCTs currently assessing risk stratified approaches to determining screening intervals.312

Biomarkers are a further area of research and have the potential to be included in risk stratification models, although current evidence on their clinical utility and cost-effectiveness is limited.312

Finally, risk prediction developed for lung cancer screening has the potential to be of benefit in smoking cessation.312 Personalised smoking interventions using risk stratification developed for lung cancer screening may be of value in communicating and quantifying effects of cessation on subsequent lung cancer risk and life expectancy for an individual.312 The co-benefits of smoking cessation beyond lung cancer risks are significant.

* 1. Technical Review Process, Questions and Answers

#### Process

The working group developed a project plan to identify and summarise current knowledge of mammographic breast density, how it is measured and distributed in the population and any association with risk of developing breast cancer. Additionally, the plan aimed to investigate current practices in breast density reporting and guidance for supplemental breast screening for women with dense breasts. A number of questions were raised in order to address the areas of interest and were used as a basis for a literature review. Some additional topics were identified during the review process to provide background information. A Te Whatu Ora Waitematā Librarian supported the literature review team with development of the search strategy and execution of the searches, with the working group members undertaking the assessment of results and determination of included studies. A separate search was conducted for each question, using relevant key search terms, including English language. Searches were conducted in Medline, CINAHL Complete, Google and Google Scholar as at June 2024. The results of each search were reviewed for potentially relevant articles, by title and then abstract. Full text review was then undertaken on this shortlist with further relevant articles identified through review articles and reference lists. Additional key references published after this date were included where they were deemed to be of substantial significance to the report.

#### Questions and Answers

*How much risk does breast density confer relative to other known risk factors for breast cancer?*

* Women with higher breast density have an increased risk of developing breast cancer compared to those with low breast density.
* There are two separate risks associated with the measure of dense breasts: a higher incidence of breast cancer development and masking of cancer in mammogram interpretation.
* Studies suggest that the risk can range from 2 to 5-fold, which is comparable to the relative risk of a moderate penetrance genetic mutation. High penetrance breast cancer mutations such as BRCA1/2 have a relative risk of 5 to 12-fold depending on the study.

*How is breast density distributed in the population? That is, for whom does this risk apply and to what degree?*

* Potentially half of the female population are affected by dense breasts, with 6-10% considered to have extremely dense breasts and 40-45% heterogeneously dense in international studies.
* The distribution of breast density in the Aotearoa New Zealand female population is relatively unknown. One Aotearoa New Zealand based study, published in 2013, demonstrated that wāhine Māori have higher absolute breast density compared to the New Zealand European/Other population.

*Can breast density be measured? Are there issues with the measurement itself? What is the current state, with software, with artificial intelligence?*

* Breast density is typically evaluated using two-view mammograms and classified according to the American College of Radiology’s Breast Imaging-Reporting and Data System (BI-RADS). The BI-RADS atlas provides a density scale including four categories, Category A (almost entirely fatty breasts), Category B (scattered areas of fibroglandular density), Category C (heterogeneously dense) to Category D (extremely dense breasts).
* BI-RADS reported distribution in the general female population is A – 10% fatty, B – 40% scattered, C – 40% heterogeneous and D – 10% extremely dense.
* Breast composition is defined by mammographic visually estimated content of fibroglandular-density tissue within the breasts and categorised accordingly. Visual assessment can be highly subjective and varies between observers (inter-observer variability) as well as in the same observer over time (intra-observer variability)
* Artificial intelligence (AI) was developed to provide a more objective and standardised measurement. Algorithms consisting of three broad approaches, physics based, machine learning based or deep learning based have been utilised in tools to measure breast density.
* Volpara, an Aotearoa New Zealand based company provides a well validated physics-based tool (with MedSafe approval) for automated breast density reporting. The output is either through Digital Imaging and Communications in Medicine (DICOM) structured reports or DICOM secondary capture images and integrates into the Picture Archive Communication System (PACS) reading workflow. Density grade, fibroglandular tissue volume, breast volume, and volumetric breast density percentage for left and right breasts are all reported.

*What happens currently with breast screening in Aotearoa New Zealand (BreastScreen Aotearoa and privately)? What is happening in other countries?*

* In Aotearoa New Zealand the publicly funded breast screening programme (BreastScreen Aotearoa (BSA)) does not measure or report on breast density. Approximately 69% of eligible women aged 45 to 69 undergo breast screening every 2 years and there is significant inequity in coverage by ethnicity, with lower coverage rates achieved by BSA for Māori women.
* Breast density reporting is available to women in Aotearoa New Zealand who have health insurance or pay for screening through private providers, with mixed advice being given on supplemental screening for women with dense breasts.
* In Australia, New South Wales, Western and South Australia report breast density in their screening programmes. Western Australia and New South Wales do not offer supplemental screening within their screening programme but direct women to discuss with their GP to receive further advice on their breast cancer risk and supplemental screening options. Breast density reporting has been mandated in the USA, is reported in most Canadian territories and is recommended by the European Society of Breast Imaging (EUOSBI), with at least 9 European countries incorporating reporting. The United Kingdom and Ireland do not report breast density.

*Would routinely returning breast density results lead to benefit (morbidity, mortality, quality of life, choice, information)?*

* The outcome benefits of breast density reporting are yet to be fully evidenced. This is due mainly to a lack of clinical trials having completed mortality follow up.
* Supplemental screening for women with dense breasts has been shown to increase cancer detection rates, to detect cancers earlier and to decrease the rate of interval cancers.
* Providing beast density information supports women’s autonomy to make informed decisions about their care.
* Qualitative studies of breast screening programme participants have reported that women informed about breast density want to know their breast density, agreeing it would make them feel more informed to make decisions about their health. In most cases, this view remained when made aware of uncertainty about what, if any, additional tests should be done for women with dense breasts.
* Many women with dense breasts stated that they had or would intend to have additional surveillance or more frequent mammograms.
* However, without providing equitable access to any additional care (e.g. supplemental screening), advising women of their breast density risks exacerbating existing breast cancer inequities.

*Are there risk stratification/triage approaches based on a high-density result, such as more intensive screening or alternate modalities?*

* Methods for breast cancer risk stratification vary, with a number of tools available utilising different criteria, of which 3 currently include breast density.
* Supplemental breast screening has been recommended for women deemed to be at high risk of developing breast cancer. Screening options including MRI, ultrasound and CEM have been shown to increase the detection of cancer compared to standard mammography but all are associated with varying risks and benefits.
* MRI has the greatest sensitivity for cancer detection but with an increased false positive rate and is a costly procedure.
* Ultrasound is not as sensitive as MRI and has a similar false positive rate, however, it is a less invasive and less costly procedure.
* CEM is nearly as effective as MRI for cancer detection, with less false positives and is a simpler, lower cost method, however, is not routinely available.
* The following organisations recommend supplemental screening for women with dense breasts; The European Society of Breast Imaging (EUSOBI), The American College of Radiology (ACR), The Gynaecological Oncology Working Group (AGO), The National Comprehensive Cancer Network (NCCN), The American Cancer Society (ACS), The German Guideline Program in Oncology, The Gynaecological Oncology Working Group (AGO), The Brazilian College of Radiology and Diagnostic Imaging (CBR), Brazilian Breast Disease Society (SBM), The Brazilian Federation of Gynaecological and Obstetrical Associations (Febrasgo) and the China Anti-Cancer Association.

*What information on breast density is available for women/consumers?*

* Online information is not generally presented in a manner that is easy to understand or act upon and there is no consistent pattern of content.
* The majority of online information is based on what breast density is, how it is measured and what dense breasts means.
* Only a few websites directly address benefits and harms of measuring and reporting breast density and these were mainly focused on the use of supplemental screening.
* The most common recommendation was for women to talk with their doctor to discuss what breast density means for them, their individual risk and supplemental screening options.

*Are there harms or other ethical issues to consider for women such as anxiety or overscreening?*

* There is the potential for anxiety and confusion regarding notification of breast density, understanding breast density advice, exposure to and cost of further investigations.
* Incorporation of supplemental screening for women with dense breasts may increase overdiagnosis and false positive findings.
* Ethical issues to consider include equitable care, patient autonomy, healthcare professional trust, duty of care and uncertainties relating to measurement and clinical management pathways for women with dense breasts.
* Further research is required to determine health benefits, cost effectiveness of supplemental screening options, patient perspectives and maintenance of equity in service provision.

*What are the programme, health professional and consumer perspectives on the measurement of breast density within screening programmes?*

* There are mixed views among healthcare professional on the merits of breast density reporting, with radiologists appearing to be more hesitant about it compared with GPs.
* Healthcare professionals highlight the need for consensus statements and national guidelines on breast density reporting, and clarity on recommendations (or otherwise) regarding supplemental imaging of dense breasts.
* Measuring and reporting breast density in the absence of consistent guidelines for follow-up can lead to inconsistent management as well as anxiety and confusion for the provider and patient.
* Healthcare professionals emphasised the need for education and to contextualise breast density information with other risk factors for breast cancer.
* Most breast screening participants wanted to know their breast density, stating it would make them feel more informed to make decisions about their health. In most cases, this sentiment held when they were informed that there was uncertainty about what, if any, additional tests should be done for women with dense breasts.
* Many women with dense breasts stated that they had or would intend to have additional testing or more frequent mammograms. However, studies found reduced uptake of additional testing for women of ethnic minorities and lower socio-economic status.
* Reporting breast density also created anxiety and confusion for a proportion of women. Women stated the need for clear information about the implications of breast density and many expressed a preference for discussing the result with a healthcare professional who could contextualise the results and address any confusion and anxiety.
* There is no published evidence of the opinions of breast screening participants in Aotearoa New Zealand on reporting breast density, however, Aotearoa New Zealand breast cancer organisations Breast Cancer Foundation New Zealand and Breast Cancer Aotearoa Coalition are in favour of breast density being reported by BreastScreen Aotearoa.
* International evidence suggests significant resource implications for the health system in terms of additional imaging demand and participants’ desire for discussion of results with a healthcare professional.

*If there are benefits, what would it take to implement breast density measurement and management in BreastScreen Aoteaora (including costs, programme changes, staffing, cost benefit/effectiveness, research)?*

* Breast density reporting could be facilitated automatically through a software provider at a cost. There would also be wider costs associated with reporting e.g. software licenses, workforce time to support participation.
* Alternatively, breast density could be manually measured by radiologists at the additional cost of extensive auditing of assessment and training to ensure consistency of reporting.
* BreastScreen Aotearoa is rolling out a new information communication infrastructure which offers an opportunity to consider AI in this context.
* BreastScreen Aotearoa workforce is currently operating at capacity and feedback from BreastCare nurses and Medical Imaging Technologists (mammographers) is that there is limited capacity at current staffing levels to talk through breast density results with women.
* BreastScreen Aotearoa does not have the funding or capacity within the programme to undertake further ultrasound assessments.
* Hospital and Specialist Services have reported that capacity to fulfil supplementary ultrasound or MRI within the wider health system is limited.
* A more detailed assessment of whole system capacity issues is required.
  1. National Health Committee (NHC) screening criteria assessment

Table 8: NHC Screening Criteria Assessment

|  |  |  |  |
| --- | --- | --- | --- |
| Screening criteria |  | Assessment | Comment |
| **Breast density reporting** | **Supplemental screening for breast density** |  |
| The condition is suitable for screening | Met | Met | Breast density increases the risk of breast cancer and can also reduce the detection of breast cancers on mammograms (see page **Error! Bookmark not defined.**). |
| There is a suitable test | Met | Met | There are simple, safe, reliable tests for breast density that are validated, sensitive and specific (see page 24). Density grading using currently available software can be correlated with the BI-RADS classification system. |
| There is an effective and accessible treatment or intervention for the condition | Met for breast cancer | Met for breast cancer | Evidence shows that early treatment for breast cancer improves outcomes. |
| There is high-quality evidence that a screening programme is effective in reducing death and illness | Met for the programme, inconclusive for breast density | Met for the programme, inconclusive for supplemental screening | There is high quality evidence that population-based breast cancer screening programmes reduce morbidity and mortality from breast cancer. There is no evidence as yet that measuring breast density or supplemental screening reduces mortality for women with dense breasts (see page 38) |
| The potential benefit of the test should outweigh potential harm | Inconclusive | Inconclusive | The benefit of reporting breast density to women is contingent upon meeting patient needs following receipt of this information e.g. having someone to discuss results with, health literacy needs being met, able to access to additional screening / care / management as appropriate (see page 38). There is evidence that supplemental screening for dense breasts improves cancer detection and outcomes (see page 38). |
| The health sector should be capable of supporting diagnosis, follow-up and programme evaluation | Not met | Not met | Currently BreastScreen Aotearoa does not have the funding or capacity within the programme to implement supplementary screening. Hospital and Specialist Services have informed the NSU that if supplementary screening is recommended to women who have dense breasts, capacity to fulfil this within the wider health system is also limited. There are also significant capacity constraints currently for both MRI and Ultrasound services – with waiting times generally significantly longer than clinically indicated. |
| There is consideration of social and ethical issues | Not met | Not met | Breast density differs by ethnicity, with one study finding Māori have higher absolute volumetric density than New Zealand Europeans. Combined with the higher incidence of breast cancer and higher mortality for wāhine Māori, it is critical that adding breast density reporting and other changes (such as supplementary screening) to the BreastScreen Aotearoa programme does not further entrench or increase inequities in breast cancer outcomes for Māori.  There are also inequities in cancer outcomes by other sociodemographic factors such as rurality and socioeconomic deprivation (NZDep) which need to be considered and addressed.  Consideration should also be given to the opportunity costs of including any breast density-related changes to the programme.  Patient views should also be sought and considered for any proposed changes to the BreastScreen Aotearoa programme. |
| There is consideration of cost-benefit issues | Not met | Not met | Cost to the programme per screen by a provider has been sought and supplied. The full cost will include additional services that could be required e.g. explanation of results and further discussion with a health worker, supplementary screening etc. |

* 1. Mammogram Breast Density Related Screening Recommendations

Table 9: Breast density related screening guidelines/recommendations/position statements

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Professional Organisation | Year | Measure BD | SS | Recommendation and relevant comments |
| European Commission Initiative on Breast Cancer Guideline Development Group GDG232 | 2020 |  | No | Tailored screening for MBD – Yes  DBT for women with high MBD.  Guiding supplemental screening – No |
| European Society of Breast Imaging (EUSOBI)224 | 2022 | Yes | Yes | MBD notification  “Should be informed on the diagnostic and prognostic implications of having dense breasts”.  Guiding supplemental screening – Yes  “SS with MRI at least every 4 years, preferably every 2–3 years for women with extremely dense breasts aged 50–70. If MRI screening is unavailable, US in combination with DM may be used”. |
| The German Guideline Program in Oncology (German Cancer Society, German Cancer Aid, Association of Scientific Medical Societies (AWMF))233 | 2021 |  | Yes | Guiding supplemental screening – Yes  SS with “US appears to be the most suitable method”. Improved sensitivity but lack of long-term evidence that it reduces mortality and “associated with a higher rate of biopsies than the national screening program”.  Use of tomosynthesis can increase sensitivity and “should be considered for testing in a quality assured programme”. |
| The German Gynaecological Oncology Working Group (AGO)234 | 2020 |  | Yes | Guiding supplemental screening – Yes  Breast US for heterogeneously dense, extremely dense mammograms. MRI if screening mammogram is negative and breast composition extremely dense\* 50–75 years old. |
| The Royal College of Radiologists (United Kingdom)235 | 2019 | High-risk | No | Guiding supplemental screening – No  Adjunctive US screening is not routinely recommended. |
| The Royal Australian and New Zealand College of Radiologists219 | 2018 | Yes | No | MBD reporting  Formal report not issued in screening programmes in Australia or Aotearoa New Zealand. |
| The Brazilian College of Radiology and Diagnostic Imaging (CBR), Brazilian Breast Disease Society (SBM), and Brazilian Federation of Gynecological and Obstetrical Associations (Febrasgo)236 | 2017 |  | Yes | Guiding supplemental screening – Yes  Complementary US should be considered |
| Alberta Breast Cancer Screening  Clinical Practice Guideline237 | 2022 |  | Yes | Guiding supplemental screening – Yes  Annual mammography and consider annual breast US and consider annual clinical breast exam |
| China Anti-Cancer Association238 | 2019 |  | Yes | Guiding supplemental screening – Yes  Breast US. |
| The Japanese Breast Cancer Society239 | 2018 | Yes | No | MBD assessment – Yes  MBD notification – No  Guiding supplemental screening – No |
| American College of Radiology240 | 2021 |  | Yes | Guiding supplemental screening – Yes  DBT screening usually appropriate  May be appropriate for average risk females with dense breasts; US breast, Mammography with IV contrast, Abbreviated/MRI breast with and without IV contrast |
| American College of Obstetricians and Gynecologists241 | 2020 | Yes | No | MBD notification  Guiding supplemental screening – No |
| American Cancer Society137 | 2007 |  | No | Guiding supplemental screening  “Insufficient evidence to recommend for or against breast MRI screening for women with heterogeneously or extremely dense breasts.” |
| The National Comprehensive Cancer Network242 | 2024 |  | Yes | Guiding supplemental screening  For individuals ≥40 years of age with heterogeneous or extremely dense breasts, consideration should be made for supplemental screening. |
| The Society of Breast Imaging243 | 2010 |  | Yes | Guiding supplemental screening – Yes  US may be considered for women with dense breasts |
| The United States Preventive Services Task Force (USPTSF)244 | 2016 |  | No | Guiding supplemental screening  Insufficient evidence to assess the balance of benefits and harms of SS using breast US, MRI, DBT, or other methods |
| The American Academy of Family Physicians245 | 2021 |  | No | Supports USPSTF recommendation |

MBD = Mammographic breast density, SS = Supplemental screening, IV= Intravenous DM = Digital Mammography, US = Ultrasound, DBT = Digital Breast Tomosynthesis, MRI = Magnetic Resonance Imaging

Adapted from: O’Driscoll J, et al. A scoping review of programme specific mammographic breast density related guidelines and practices within breast screening programmes. Eur J Radiol Open. 2023 Aug 2;11:100510.

* 1. Current risk–based breast cancer screening randomised control trials

The following tables were sourced from: The ROSA Project: Roadmap for Optimising Screening in Australia – Breast. Chapter 5: Implementation (Abridged). 20 March 2023, abridged 1 May 2024. Produced by the Daffodil Centre on behalf of Cancer Council Australia.

Table 10: Summary of trials comparing risk-based screening with standard non-risk-based screening

|  |  |  |  |
| --- | --- | --- | --- |
| Trial name and ID | MyPeBS – Randomized, Comparison of Risk-Stratified versus Standard Breast Cancer Screening In European Women Aged 40-70  NCT03672331 | | |
| Population | **Intervention** | **Comparator** | **Outcomes** |
| Women aged 40-70 years affiliated to a social security or national healthcare system  With no prior DCIS or breast cancer, atypical breast lesion, lobular carcinoma in situ or chest wall irradiation or known or suspected very high-risk germline mutation  France, Italy, UK, Belgium and Israel | Personalised risk-based screening protocol for 4 years, according to estimated 5-year risk of breast cancer.  Risk determined using algorithm incorporating BCSC score and Tyrer-Cuzick score for women with more than one first degree relative with breast or ovarian cancer. Both scores will be modified to incorporate genotyping results and will be adjusted for country-specific breast cancer incidence.  Risk stratified screening protocols are as follows:  Low risk (<1% 5-year risk): Quadrennial mammogram for all women (i.e at study entry and end)  Average risk (1-<1.67% 5-year risk): Biennial mammogram for all women + ultrasound or ABUS for women with “high” breast density  High-risk (1.67-<6% 5-year risk): Annual mammogram for all women + ultrasound or ABUS for women with “high” breast density  Very high-risk (≥6% 5-year risk): Annual mammogram + MRI for all women  Supplemental tomosynthesis and/or ultrasound will be performed in this arm according to standard screening guidelines in each participating country (i.e. per comparator) | Mammogram with or without supplemental imaging according to guidelines in each participating country for 4 years:  Belgium (Brussels, Leuven): Biennial mammogram +/- tomosynthesis for women aged 50-69 years  Italy (4-6 regions): Biennial mammogram for all women aged 50-69 years, and up to 74 years in some regions. Annual mammogram for women aged 45-49 in some regions  UK (Cambridge, Manchester, Leeds): Triennial mammogram for women aged 50-73 years  Israel (national): Biennial mammogram for women aged 50-74 years +/- tomosynthesis +/- ultrasound per radiologist  France (national): Biennial mammogram for women aged 50-74 years + ultrasound in all women with dense breasts | Primary outcome  4 years follow-up (end of intervention)  Stage 2 or higher breast cancer incidence – non-inferiority  Secondary outcomes  4 years follow-up (end of intervention)  Stage 2 or higher breast cancer incidence – superiority  False positive rate Benign biopsy rate Anxiety  Quality of life  Cost-effectiveness  Stage specific breast cancer and DCIS incidence  Overdiagnosis rate  Interval cancer rate  10 years and 15 years follow-up  Cumulative incidence of all breast cancer and stage 2 or higher breast cancer  Breast cancer-specific survival |
| Women aged 40-74 years  With no prior DCIS or breast cancer  USA | Personalised risk-based screening protocol for 5 years, according to estimated 5-year risk of breast cancer.  Risk determined using the BCSC model, genetic testing for rare high/moderate-penetrance mutations in nine genes and polygenic risk score for 96 lower-risk common genetic variants with known association to breast cancer.  Risk stratified screening protocols are as follows:  Lowest risk (aged 40-49 with <1.3% 5-year risk): No screening until age 50  Average risk (aged 50-74; or aged 40-49 with ≥1.3% 5-year risk): Biennial mammogram (if individual does not meet elevated or highest risk criteria)  Elevated risk (aged 40-49 with BI-RADS 4, or ≥0.75% 5-year risk of ER-breast cancer based on age and ethnicity; or women in top 2.5th percentile of risk by 1-year age category; or ATM, PALB2 or CHEK2 mutation carrier without a positive family history\* of breast cancer): Annual mammogram (if individual does not meet highest risk criteria)  Highest risk (BRCA1/2, TP53, PTEN, STK11, CDH1 mutation carrier; or ATM, PALB2, or CHEK2 mutation carrier with positive family history of breast cancer; or ≥ 6% 5-year risk; or had mantle radiation when aged 10-30): Annual mammogram + MRI  \*Family history: first degree relative with breast cancer, two second-degree relatives with breast cancer, or one second- degree relative diagnosed prior to age 45 | Annual mammogram | Primary outcome  5 years follow-up  Proportion of cancers stage IIB or higher – non-inferiority  Biopsy rate  Secondary outcomes  5 years follow-up  Stage IIB or higher breast cancer rate  Interval cancer rate Systemic therapy rate Mammogram recall rate Breast biopsy rate DCIS rate  Chemoprevention uptake rate  Participant preference – risk- based vs annual screening (in self-assigned cohort)  Participant adherence to assigned screening schedule  Breast cancer anxiety (PROMIS anxiety scale)  Decisional regret (Decision Regret Scale)  Ultra-low risk cancer rate |
| Premenopausal women aged 44-45 years resident in screening centre catchment area invited to attend for mammographic screening  With no prior DCIS or breast cancer, family not at high-risk for breast cancer and no diagnosis of other cancer in last 5 years  Italy | Risk-based screening for women aged 45-50 years according to breast density (BI-RADS classification).  Risk stratified screening protocols are as follows:  Low risk (low breast density; BI-RADS 1-2 on baseline mammogram): Biennial mammogram until aged > 50 years  High-risk (high breast density; BI-RADS 3-4 on baseline mammogram): Annual mammogram  After the age of 50 years, all women will continue to be screened in the usual service screening programme | Annual invitation to mammography for women aged 45-49 years  After the age of 50 years, all women will continue to be screened in the usual service screening programme  (In Italy biennial mammogram for all women aged 50-69 years, and up to 74 years in some regions. Annual mammogram for women aged 45-49 in some regions) | By arm and breast density group:  Primary outcomes  3 years and 6 years follow-up  Cumulative incidence of interval cancer – non-inferiority  Cumulative incidence of T2+/node- positive breast cancer – non-inferiority  Secondary outcomes  3 years and 6 years follow-up  False positive rates  Cumulative incidence of breast cancer  1, 2, 3 ,4, 5 years and 6 years follow-up  Mammography screening attendance |
| Women aged 45-49 years resident in four locations in Italy  With no prior DCIS or breast cancer, no familial risk for breast cancer and no concurrent participation in another clinical trial on breast cancer screening | Biennial tomosynthesis OR  Risk-based screening for women aged 45-49 years according to breast density (BI-RADS classification):  Low risk (breast density; BI-RADS category A-C): Biennial tomosynthesis until aged 50 years  High-risk (breast density; BI-RADS category D): Annual tomosynthesis | Unclear – Annual tomosynthesis? (aim is to compare screening intervals not screening modalities) | Primary outcome  6 years follow-up  Cumulative incidence of cancers stage II or higher – non- inferiority  Secondary outcomes  6 years follow-up  Participation rate within 3 months of invitation  Proportion of women allocated biennial screen who have a screen performed prior to next 2- year screen  Breast cancer detection rate Overall recall rate  Recall rate involving an invasive procedure  Interval breast cancer rate  Cumulative breast cancer incidence  Resource expenditure  Prevalence of dense breast in the target population |

ABUS = automated breast ultrasound; BCSC = Breast Cancer Surveillance Consortium; BI-RADS = Breast Imaging and Reporting Data; DCIS = ductal carcinoma in-situ; HRT = hormone replacement therapy; MRI = magnetic resonance imaging; NA = not applicable; NHS-BSP = National Health Service – Breast Screen Programme

Table 11: Trials comparing different or additional screening modalities with standard screening for higher risk groups

|  |  |  |  |
| --- | --- | --- | --- |
| Trial name and ID | DENSE – Breast Cancer Screening With MRI in Women Aged 50-75 Years With Extremely Dense Breast Tissue  NCT01315015 | | |
| Population | **Intervention** | **Comparator** | **Outcomes** |
| Asymptomatic women aged 50-75 years participating in population-based screening program  With extremely dense breasts (Volpara grade 4/D) and a negative mammogram  Netherlands | Biennial MRI + mammogram for 4 years (3 screening rounds) | Biennial mammogram for 4 years (3 screening rounds) | Primary outcome  6 years follow-up  Incidence of interval cancer  Secondary outcomes  6 years follow-up  Tumour size, stage, grade, histology and molecular subtype  Mortality rate (MISCAN program)  Cost-effectiveness (MISCAN program)  Quality of life (MRI group)  4 years follow-up  MRI screen-detected cancer MRI referral rate  PPV (MRI group)  Number of biopsies per MRI referral |
| Women aged 50-70 years  undergoing triennial population-based screening (NHS-BSP)  With dense breasts (BI-RADS C with high chance of masking or D) on baseline (current) mammogram (negative or positive)  With no known BRCA mutation or < 50% risk of being a BRCA carrier  U.K. | Mammogram + abbreviated-MRI at baseline and 18 months;  mammogram at 3 years or  Mammogram + ABUS at baseline and 18 months; mammogram at 3 years  or  Mammogram + contrast-enhanced spectral mammogram at baseline; contrast-enhanced spectral mammogram only at 18  months; mammogram at 3 years | Triennial mammogram | Primary outcome  3 years follow-up  Cancer detection rates  Secondary outcomes  3.5 years follow-up  Stage II or higher cancer incidence  Cancer detection rate  Interval cancer rate  Recall rate  Sensitivity of supplemental imaging  Specificity of supplemental imaging  0.5 year and 1.75 years follow-up  Cancer detection rate  Recall rate  Sensitivity of supplemental imaging  Specificity of supplemental imaging  1 year follow-up  Cost-effectiveness of each modality |

ABUS = automated breast ultrasound; BCSC = Breast Cancer Surveillance Consortium; BI-RADS = Breast Imaging and Reporting Data; DCIS = ductal carcinoma in-situ; HRT = hormone replacement therapy; MRI = magnetic resonance imaging; NA = not applicable; NHS-BSP = National Health Service – Breast Screen Programme

* 1. Project ROSA

The Australian based ROSA project produced a number of detailed technical reports on risk-based breast cancer screening and published a set of evidence-based recommendations (see below) alongside a roadmap summarised into 5 pillars (see Figure 11) to guide considerations over the subsequent 4-5 years.

#### Project ROSA Recommendations

Policy and guideline reviews – That national BreastScreen Australia guidelines are developed including current policies and practices in relation to women with different risk factors, including women presenting with known high-risk mutations. That current management outside BreastScreen Australia of women assessed at moderately higher breast cancer risk be reviewed, aiming for clear and consistent guidelines and management pathways.

Clinical studies to support trial design - That a well-validated, automated breast density assessment tool is evaluated on a large scale in a BreastScreen Australia setting, reporting on outcomes in the setting such as cancer diagnosis rates, interval cancer rates and false positive screening rates for defined breast density groups. That well-validated breast cancer risk assessment tools are evaluated in BreastScreen Australia settings to continue to build the evidence base towards risk-based breast cancer screening. That technologies for consideration in this context include digital breast tomosynthesis, ultrasound, MRI and contrast-enhanced mammography as primary or supplemental screening tools in some risk-stratified screening group/s.

Trial participation - That evidence on risk-based breast cancer screening is continually reviewed in relation to risk-based screening protocols.

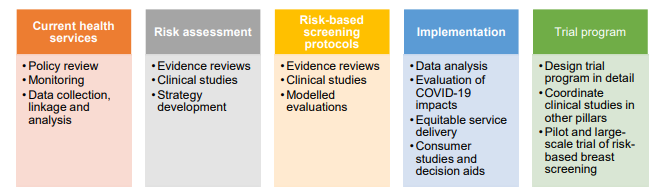
Enhanced data collection and reporting - That BreastScreen Australia develop a framework for data collection and analysis to inform policy and practice for optimal risk-based breast screening.

Data linkage and evaluation of linked data - That BreastScreen data and other health records are linked and analysed to help evaluate ad hoc risk-based breast cancer screening occurring in asymptomatic women outside BreastScreen.

Targeted evidence reviews - That ongoing evidence review includes consideration of factors such as participant/patient history, validation and improvement of risk tools, genetic tests, breast density and evolving technologies. That ongoing evidence review includes estimated group-level benefits and harms of risk-based breast screening technologies. That any implemented approaches to risk-based breast screening technologies be regularly reviewed to ensure optimal approaches to policy and practice are being applied.

Research to address priority evidence gaps - That learnings from the management of COVID-19 and its impact on screening participation, service responses and outcomes are considered in relation to prioritised and stratified approaches to risk-based breast cancer screening.

Figure 11: Project ROSA Roadmap five pillars



#### Recommended actions summarised under the 5 pillars

**Current health services**

* That a framework for data collection and analysis is established to inform potential policy and practice options towards risk-based breast cancer screening.
* That national BreastScreen Australia data on participants aged 40-49 is utilised to inform long term considerations for targeted approaches to risk-based breast cancer screening.
* That BreastScreen data and data on ad hoc breast cancer screening (where feasible) are linked and analysed in relation to hospital admissions, Medicare, PBS and other datasets (including, potentially, through use of deidentified My Health Record data).
* That linked data is used to evaluate ad hoc risk-based breast cancer screening occurring in asymptomatic women outside BreastScreen.
* That BreastScreen Australia guidelines are developed including current policies and practices in relation to women with different risk factors, as work continues towards risk-based breast cancer screening.

**Risk assessment**

* That well-validated breast cancer risk assessment tools are evaluated in BreastScreen Australia settings to continue to build the evidence base towards risk-based breast cancer screening.
* That ongoing evidence review includes a focus on optimal analysis of factors such as participant/patient history, genetic tests, breast density and evolving technologies.
* That a well-validated automated breast density assessment tool is evaluated on a large scale in a BreastScreen Australia setting, reporting on outcomes, the setting such as cancer diagnosis rates, interval cancer rates and false positive screening rates for defined breast density groups.
* That evidence on the effectiveness of breast density tools be continually collected towards developing policy and practice for risk-based breast cancer screening.

**Risk-based screening protocols**

* That priorities for future targeted research include a focus on the expected benefits and risks of potentially important technologies in relation to risk-based breast cancer screening.
* That technologies for consideration in this context include digital breast tomosynthesis, ultrasound, magnetic resonance imaging and contrast-enhanced mammography as primary or supplemental screening tools in some risk-stratified screening group/s.
* That well-validated breast imaging techniques for improved cancer staging at diagnosis are evaluated in a BreastScreen Australia setting.
* That evidence on risk-based breast cancer screening is continually reviewed in relation to risk based screening protocols.
* That any evolving approaches to introducing risk-based breast cancer screening are supported in parallel by coordinated evidence review, including modelling studies and analysis of other trials and pilot studies.
* That modelled evaluations of risk-based breast cancer screening protocols in the Australian setting be used to help identify priority screening protocols to consider for real-world evaluation.

**Evidence-based implementation**

* That BreastScreen Australia reporting for priority populations (e.g., Indigenous, rural/remote, culturally and linguistically diverse) is enhanced to help ensure any moves towards risk-based breast cancer screening do not widen gaps in outcomes between population groups.
* That learnings from the management of COVID-19 and its impact on screening participation, service responses and outcomes are considered in relation to prioritised and stratified approaches to risk-based breast cancer screening.
* That steps towards risk-based breast cancer screening include increased engagement between policy, program and research leads and consumers and other key stakeholder groups, and ongoing exchange of clear, evidence-based information.

**Trial Programme**

* Design and implement of an Australian trial, drawing on clinical studies and other ROSA project recommendations to support it.



1. In this study, the false positive rate was defined as “the percentage of women who had a positive result on screening MRI but who were later found not to have breast cancer”.159 [↑](#footnote-ref-1)