



UK Interdisciplinary  
Breast Cancer  
Symposium

## Abstract Book

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*Last updated 09/01/2026*

## Plenary Presentations

### Plenary 1 - Does anyone still need a mastectomy?

Anna Weiss - University of Rochester Medical Center, New York, USA

Anna Weiss will explore the ongoing and future clinical trials examining the omission of surgery. She will delve into observation for patients with DCIS, omission of surgery for exceptional responders, and the current data supporting the omission of axillary surgery.

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### Plenary 2 - Cridlan Lecture: Genetics update

Judy Garber - Dana-Farber Cancer Institute & Harvard Medical School, Massachusetts, USA

*More information to follow*

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### Plenary 3 - The NHS now and in the future

Richard Meddings CBE - Immediate past-Chair of NHS England and Chair-Elect of Breast Cancer Now

A presentation to reflect on the current state and position of the NHS, the reality of its challenges and also its record of innovation. The presentation will reflect on how best the future of the NHS could be secured and what the enabling priorities should be.

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### Plenary 4 - Implementation of AI in screening

Fredrik Strand - Karolinska Institute, Solna, Sweden

Artificial intelligence has rapidly advanced from retrospective validation studies to prospective clinical trials, and we are now entering the phase of implementation. This talk will focus on how AI can be integrated into population-based breast cancer screening programs, using evidence from large-scale trials such as ScreenTrustCAD and MASAI, as well as real-world deployment experiences. The central question is no longer whether AI can detect cancers, but how it should be integrated into radiology workflows, how it can be trusted and monitored. Key challenges include defining optimal use cases: triage, independent reading, or double reading replacement. Important are radiologist trust, patient acceptability and robust health economic evaluation. This presentation will highlight landmark study findings, practical lessons learned in workflow integration, and the importance of calibration and monitoring. Ultimately, successful implementation requires moving beyond diagnostic performance studies to a system-level perspective where AI is continuously validated, adapted, and evaluated for real-world impact.

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### Plenary 5 - Dormancy decoded: Strategies to eradicate minimal residual disease

Angela DeMichele - University of Pennsylvania, Philadelphia, USA

This presentation will review the latest data on biology, detection, and treatment of dormant and reactivated minimal residual disease after breast cancer treatment, with a focus on novel trial designs and new therapeutic approaches targeting dormancy to prevent recurrent disease.

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## 1.1 Personalising breast cancer surgery

Personalising risk-reducing surgery for women at high risk of breast cancer  
Marjanka Schmidt - Netherlands Cancer Institute, Amsterdam, Netherlands

In my talk, I will define high-risk breast cancer and review the emerging evidence supporting increasingly stratified approaches to risk classification, including currently available tools for risk prediction. I will also examine the evidence base for risk-reducing surgery in both unaffected women and those with a prior diagnosis of unilateral breast cancer.

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Personalising breast and axillary surgery in 2026  
Henry Cain - Newcastle Upon Tyne Hospitals NHS Foundation Trust, UK

*More information to follow*

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Do all patients with ER+ disease need radiotherapy and endocrine therapy?  
Icro Meattini - University of Florence, Italy

Professor Meattini will contribute to two sessions at the UK Interdisciplinary Breast Cancer Symposium 2026. His first lecture, "How do we combine radiotherapy and targeted therapies optimally?", will address the current evidence and strategies for integrating radiotherapy with targeted agents, focusing on biological rationale, sequencing, safety considerations, and the implications of ongoing clinical trials for daily practice.

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## 1.2 ER-Low: What is it and what are the therapeutic implications?

ER low invasive breast cancer – what it is?

Sarah Pinder - Kings College London, UK

*More information to follow*

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ER-low biology and endocrine sensitivity

Mitch Dowsett - Royal Marsden NHS Foundation Trust/Institute of Cancer Research, London, UK

The PeriOperative Endocrine Therapy - individualised Care trial provide the opportunity to evaluate the biological behaviour of breast cancer samples treated with 2 weeks of aromatase inhibitor treatment both overall and according to intrinsic subtype. ER levels were measured by IHC and ESR1 levels by rtPCR. With VERY FEW exceptions ER IHC Low (1-10%) show poor antiproliferative response to estrogen deprivation with aromatase inhibitors. ESR1 "Low" but ER IHC>10% overlap entirely with ER IHC Low re endocrine responsiveness and intrinsic subtyping. In HER2+ and/or PgR- cases ER IHC 10-c.30% appear to be equally non-endocrine responsive as ER Low in HER2- PgR+. ER Low tumours are a biologically distinct sub-group (with fuzzy edges).

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Should we treat ER-low as triple negative or as ER+ve?

Andrew Tutt - Guy's Hospital & Institute of Cancer Research, London, UK

*More information to follow*

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### 1.3 Tumour immunology and Immunotherapy

Modelling the inflammatory microenvironment associated with obesity  
Stephen Beers - University of Southampton, UK

*More information to follow*

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Unveiling Myeloid Cell Plasticity in Early Breast Cancer Metastasis  
Luigi Ombrato - Queen Mary University of London, UK

The early stages of metastatic colonization remain poorly understood, with many questions surrounding the initial interactions between disseminating cancer cells and the host tissue. Disseminating breast cancer cells ensure their survival in the host tissue by priming stromal, parenchymal and immune cells to support metastatic outgrowth. We have previously observed an unexpected level of developmental plasticity in lung resident epithelial cells within the metastatic niche of breast cancer metastasis and wondered if this phenomenon could also be reflected in the plasticity of immune-recruited cells.

We have found that myeloid immune cells in the lung, notably neutrophils, undergo significant lineage plasticity in the metastatic microenvironment. Using a combination of scRNAseq and high-dimensional flow cytometry, we identified a population of neutrophils, termed moNeu, primarily located near early metastatic lesions. These neutrophils possess a transcriptional program and surface marker expression resembling that of monocytes. Despite the systemic increase in granulopoiesis accompanying metastatic seeding, the presence of moNeu is intrinsic to the lung metastatic niche.

As a proof of concept, we demonstrated that metastatic cancer cells can distinctively convert conventional lung neutrophils into moNeu *ex vivo*, while cancer cells lacking metastatic potential fail to do so. Our results suggest that alongside the "horizontal plasticity" of N1-to-N2-like, which involves shifting between anti-tumor and pro-tumor features, neutrophils also possess a "vertical plasticity" with the unexpected potential to influence their differentiation lineage. To what extent these two types of plasticity are intertwined and functional in the process of metastasis formation remains an open and intriguing question.

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Optimising breast cancer immunotherapy whilst limiting treatment-driven adverse events  
Awen Gallimore - Cardiff University, UK

Despite the promise of immunotherapy, many current regimens fail due to inadequate T-cell activation or the development of immune-related adverse events (irAEs) that necessitate treatment discontinuation. Combination strategies, though potentially more effective, often exacerbate toxicity. Our research focuses on refining dual targeting of regulatory T cells (Tregs) using a PI3K $\delta$  inhibitor in combination with LAG-3 blockade. This approach, while highly effective in preclinical triple-negative breast cancer (TNBC) models, has been limited by poor tolerability. We evaluated several strategies combining the PI3K $\delta$  inhibitor PI-3065 with LAG-3-directed therapies in a murine TNBC model. The goal was to achieve optimal tumour control while reducing the severity of irAEs. Systemic inhibition of the LAG-3 ligand FGL1 failed to enhance tumour suppression and significantly worsened irAEs. Conversely, targeted delivery of anti-LAG-3 antibodies directly to the tumour microenvironment maintained anti-tumour efficacy while mitigating systemic toxicity. Notably, intermittent dosing of the PI3K $\delta$  inhibitor in combination with anti-LAG-3 therapy prevented the onset of irAEs altogether, achieving robust tumour control with excellent tolerability. Our findings highlight the importance of therapeutic precision in combination immunotherapy. By optimising both delivery and dosing strategies, it is possible to sustain anti-tumour immunity while avoiding immune-mediated toxicity. This work underscores the potential of refined immunotherapy regimens to improve patient outcomes and expand the clinical applicability of combination treatments in breast cancer and beyond.

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## 1.4 Managing the gaps in care with healthcare professional and organisational collaborations

Last year of life, unscheduled care. Acute oncology and supportive care: a multi provider perspective

Declan Cawley - East Kent Hospitals, UK

Looking at the considerable uncertainty in prognosticating in itself, but also the advent of newer oncology interventions and more personalised cancer care, estimating the last year of life can present its own challenges. Opportunities for supportive care throughout the cancer pathway, are facilitating better symptom control and overall palliation throughout, rather than seen as a transition to palliative care.

Planned and unscheduled care provision within health care systems varies greatly, dependent on geography, resource and competing priority of needs for the locality. Coupled with the changing cancer pathway prognoses, where metastatic patients are living for years, hospice care can be a further challenge as it is synonymous with terminal / end of life care. Hospice care is usually associated with community-based specialist palliative care services so positioned theoretically, best to meet the changing needs of individuals, especially as they enter that 'last year of life'. However, with reductions in their funding from their ICBs, hospices are struggling to meet the increasing demand for their services with a fiscally tightening noose.

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"Like falling off the edge of a cliff": How to manage the gaps after adjuvant treatment in primary breast cancer

Juanita Caseley - Maidstone & Tunbridge Wells NHS Trust, UK

*More information to follow*

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Myths and misinformation in social media

Dan Papworth-Smyth - Breast Cancer Now

How people access and search for information is undergoing a massive change. Half of adults in the UK are struggling to access trusted health information, and the huge rise in misinformation and creator-led health content has only made it harder to know what to trust. Dan will share the trends we're seeing as well as the work Breast Cancer Now, and other organisations, are doing to address this.

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## 2.1 Genomic testing in breast cancer: germline panels, incidental findings and the PARTNER trial

Germline testing in breast cancer patients: which genes and why?

Helen Hanson - Royal Devon University NHS Foundation Trust/University of Exeter Medical School, Exeter, UK

Increased options for targeted treatments in breast cancer (BC) patients with underlying germline predisposition have resulted in expansion of genetic testing to BC patients via mainstream oncology services. Internationally, the gene panel offered to BC patients varies widely from just BRCA1/BRCA2 through to 'pan-cancer' panels of near 100 genes. If a germline pathogenic variant is detected, the BC proband and other family members also found to have the variant are typically offered interventions such as risk-reducing surgery and enhanced surveillance for the cancers linked to that gene.

The upscale in genetic testing and resultant increase in family members identified through cascade testing has highlighted a need to evaluate the overall clinical-public health utility of genes tested. This talk will discuss our current understanding of breast cancer predisposition and the outcomes of an international expert group (ESMO Precision Oncology Working Group). A framework of criteria was established by which to evaluate a number of breast cancer susceptibility genes for inclusion on a breast cancer multigene panel test for universal mainstream testing for BC cases, considering the evidence of association with breast cancer and clinical utility regarding (i) BC risk estimation, (ii) clinical actionability (iii) evidence of impact on cancer specific mortality (and/or morbidity). Judged as of high or moderate utility via this framework were seven genes: BRCA1, BRCA2, PALB2, RAD51C, RAD51D and TP53.

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ctDNA testing in breast cancer: interpretation of results and managing the unexpected findings

Terri McVeigh - Royal Marsden NHS Foundation Trust, London, UK

*More information to follow*

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The PARTNER Trial - Strategies to identify the optimal treatments in early-stage triple negative breast cancer

Jean Abraham - University of Cambridge, UK

The goal of her research is to identify better ways to personalise breast cancer treatments, avoiding over-treatment and unnecessary toxicity and providing better clinical outcomes.

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## 2.2 Breast radiotherapy – challenges and opportunities of complex treatments

How do we combine radiotherapy and targeted therapies optimally  
Icro Meattini - University of Florence, Italy

"Do all patients with ER+ disease need radiotherapy and endocrine therapy?", will explore opportunities for treatment de-escalation in early-stage ER+ breast cancer. Drawing on recent trial evidence and population-based data, he will examine the role of radiotherapy and endocrine therapy as single or combined modalities, with attention to patient-centred outcomes such as adherence, quality of life, and toxicity.

Together, with his earlier talk Icro will highlight how multidisciplinary collaboration can individualise treatment and optimise care.

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Who should have regional radiotherapy and what is benefit?  
Charlotte Coles - University of Cambridge, UK

*More information to follow*

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Proton beam therapy – what have we learnt from the trials so far?  
Anna Kirby - Royal Marsden NHS Foundation Trust, London, UK

*More information to follow*

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## 2.3 Transforming breast cancer research and management with AI

The evolving role of AI in breast pathology  
Anita Grigoriadis - King's College London, UK

*More information to follow*

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Digital health & PROs in breast cancer care  
Ines Vaz Luis - Gustave Roussy, Paris, France

Inês Vaz-Luis outlines how digital health and patient-reported outcomes (PROs) are reshaping breast cancer care and research. She defines PROs as the direct reports from patients on their symptoms, functioning, and quality of life—critical data to complement clinical outcomes. She presents compelling evidence from randomized trials and multi-centre implementations demonstrating that electronic PRO (ePRO)-based remote monitoring can reduce symptom burden, improve quality of life, and even extend survival, while supporting timely interventions and integration into routine clinical pathways.

Beyond ePROs, she highlights the expanding role of digital health tools in supportive care and self-management—ranging from mobile apps and online educational platforms to structured survivorship programs that empower patients to actively manage fatigue, anxiety, and lifestyle factors. Examples from ongoing initiatives illustrate how digital ecosystems can promote continuity of care and generate valuable real-world data for research.

Looking ahead, Dr Vaz-Luis envisions a future of blended models that integrate ePROs with connected devices such as wearables and biosensors, enabling continuous, personalized monitoring. She emphasizes the importance of data analytics and artificial intelligence to guide smarter triage and resource allocation, while ensuring equity-first design so that innovations benefit all patients—across age groups, education levels, and geographic settings.

Her take-home message is that digital health and PROs should become routine, actionable, and interoperable components of breast cancer care and research—tools that bring patient experience to the centre of precision oncology and accelerate progress toward more humane, responsive, and data-driven care.

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Generative AI and LLM in education and training  
Gerald Lip - NHS Grampian, Aberdeen, UK

*More information to follow*

## 2.4 Abstracts from future leaders

### Black Women's Decisions about Breast Cancer Screening in the UK: From Evidence to Community Impact

Anietie Aliu<sup>1</sup>, Robert Kerrison<sup>1</sup>, Afrodita Marcu<sup>1</sup>

<sup>1</sup>University Of Surrey, Guildford, UK

**Background:** Breast cancer is the most common cancer among women in the UK, with survival closely linked to early detection through screening. Yet, uptake of NHS breast screening is lowest among Black African and Black Caribbean women contributing to inequalities in stage at diagnosis and survival. Our recent systematic review (Aliu et al., 2025) identified critical gaps in evidence regarding barriers to screening for Black women and highlighted the urgent need for focused research to understand barriers and facilitators to screening. The present study was designed to fill this gap.

**Methods:** Seven focus groups and one interview were conducted with 47 Black African and Black Caribbean women in the UK, aged 50–71, all eligible for NHS breast screening. Participants included consistent attenders, inconsistent attenders, and non-attenders. Data were analysed using reflexive thematic analysis and mapped onto the COM-B model and Behaviour Change Wheel to identify behavioural drivers and intervention opportunities.

**Results:** Five themes were developed: (1) Knowledge and awareness (with lower awareness among Black African women born outside the UK compared with UK-born Black Caribbean women who were more familiar with screening); (2) Emotional and motivational responses (fear, fatalism, and cultural silence discouraged participation, while peer support motivated attendance); (3) Competing priorities (work and family responsibilities often outweighed preventive health); (4) Healthcare and access barrier (negative experiences, inflexible appointments, and lack of culturally relevant communication reduced trust and opportunity); and (5) Suggestions for improvement (participants advocated for respectful communication, flexible booking, mobile community-based screening, multimedia reminders, and awareness campaigns featuring relatable Black role models). Findings revealed heterogeneity within "Black women," shaped by ethnicity, migration history, religion, and generational status.

**Conclusions:** This qualitative study directly addressed evidence gaps identified in our systematic review by capturing the lived experiences of Black women in relation to screening. COM-B analysis highlighted that screening participation is influenced by capability (knowledge), opportunity (accessible and trusted services), and motivation (beliefs, fears, social norms). Culturally tailored, community-driven interventions are needed to address these domains.

**Impact:** Beyond research, findings were translated into community impact through Rhythm & Light, an initiative I founded to break the silence surrounding cancer in Black communities. Recognising the theme of fear and silence raised by participants, Rhythm & Light provides a platform for those affected by cancer to share stories through poetry, song, and creative expression, fostering dialogue, awareness, and empowerment. A recent community event in London brought together Black cancer survivors who shared their stories; silence was turned into songs to raise awareness. This integration of behavioural science and community engagement offers a pathway to reduce inequalities in breast screening uptake and outcomes.



### Needs of people with triple negative breast cancer (TNBC): The Patient's Voice

Hira Yousuf<sup>1</sup>, Susanne Cruickshank<sup>2</sup>, Sarah Adomah<sup>3</sup>, Emma Williams<sup>4</sup>, Robin Woolcock<sup>5</sup>, Chris Twelves<sup>1,6</sup>

<sup>1</sup>St. James's University Hospital, Leeds, UK, <sup>2</sup>Royal Marsden Hospital Institute of Cancer Research, <sup>3</sup>The Royal Marsden Hospital, <sup>4</sup>Cardiff and Vale University Health Board, <sup>5</sup>UK Charity for Triple Negative Breast Cancer, <sup>6</sup>St. James's University Hospital, Leeds, UK

**Background:** About 12% of breast cancers are TNBC, which is more common in younger women, black women and those carrying BRCA 1 or 2 mutations. TNBC has a worse prognosis than other breast cancers, people with early disease having higher (and earlier) relapse rates and survival being shorter in those

with metastatic disease. There is, however, little information specifically on the needs of people with TNBC. This work aims to address this gap, and to improve their care and outcomes.

Methods: Between December 2023 and February 2024, the UK Charity for TNBC and UK Royal College of Nursing information (RCNi) held four, two hour roundtable discussions at cancer centres in England/Wales; patients were invited through posters in clinics and Maggie's Centres. Each roundtable had a facilitator who led discussions with 8 – 12 participants about their TNBC experience using a semi-structured set of questions. Each group was asked additional questions about 1 of 4 topics (early disease, metastatic/advanced disease, diversity and clinical trials). Roundtable outputs were documented and common themes identified.

Results: We recognised as an over-arching concern the lack of visibility of TNBC. Within this we identified 5 related but distinct themes.

1. Excessive negativity, e.g. "If there's a breast cancer type you don't want it's TNBC"; "You go on Google and see the survival rate...and it's quite horrific."
2. The importance of language, e.g. "Triple negative is very aggressive". 'As you know, triple negative is very aggressive.'
3. The need for better information e.g. "He said it's triple negative...there was no information, nothing about what it meant"; "When it's the right information, you can cope."
4. A feeling of isolation, e.g. "I thought I'd be elated I was finishing treatment but I was bereft"; "All I wanted was someone like me."
5. Low awareness of trials, e.g. "I'd have loved to have the option of a trial drug."

The same themes were highlighted in the diversity roundtable but felt even more strongly by the black community.

Conclusions: Our findings underscore the need for information and support specifically developed for those with TNBC. We are exploring this further with the UK Charity for TNBC working with TNBC patient groups and Specialist Breast Care Nurses.

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Does Personalised Stratified Follow-Up (PSFU) meet the needs of people from under-served groups who have completed treatment for breast cancer? (The B-POISED study)

Katie Sutton, Sophie McGrevey, Verna Lavender, Lorraine Marke, Jo Armes

<sup>1</sup>University of Surrey

Background: Personalised Stratified Follow-Up (PSFU) is an approach to follow-up after cancer treatment which involves patients re-accessing care when they think they need to, rather than attending predetermined clinic appointments. The intended benefits of this approach include a more personalised experience for patients and increased capacity in outpatient clinics.

The aim of this study is to find out if PSFU meets the needs of people from under-served groups following treatment for breast cancer and to develop recommendations to improve PSFU experience.

Methods: WS1: A mapping exercise to include:

- A scoping review of the literature relating to PSFU for breast cancer.
- A qualitative interview with the lead for implementation of PSFU at each of the cancer alliances in England.
- A review of Office for National Statistics (ONS) demographic reports to identify three cancer alliances with the highest proportion of under-served groups.

WS2: Qualitative interviews with relevant professionals involved in delivering PSFU in NHS organisations (n=15) as well as up to five people who support those with breast cancer through charities, to explore their experiences of PSFU (total=20) recruited through a 'snowballing' technique.

WS3: Using a sampling frame informed by WS1 findings, we will conduct qualitative interviews with 8-10 patients from each of the three cancer alliances (n=24-30). Following data analysis, we will invite interviewees to three discussion groups, each with 6 participants (total=18) where will discuss our findings and their potential use to inform the development of recommendations and potential interventions.

Results: Preliminary analysis of WS1 data has resulted in the development of themes relating to workforce concerns, remote monitoring systems, and insights into potential issues for people from under-served groups. Our scoping review has identified important findings concerning the key components of PSFU; patient satisfaction and confidence; unmet needs in the form of psychological support and re-accessing clinical teams; the gap in evidence regarding experiences of people from under-served groups. Suggestions to enhance PSFU include the addition of self-management programmes, strategies to improve wellbeing and improved access to psychological assessment and support. Analysis of data from WS2 and WS3 will be completed in early 2026.

Conclusion: This study is the first to explore the ability of PSFU to meet the needs of people with breast cancer from underserved groups, and to propose interventions for future development and feasibility testing that will enhance care. Dissemination of our early findings to NHS organisations has commenced, and our scoping review has been submitted for publication. Following completion of this project, we intend to apply for funding to further develop our interventions and conduct feasibility testing.

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#### Who's Doing What?: Multidisciplinary team perspectives on delivering Self-Directed Aftercare following breast cancer

Anna Isaac<sup>1,2</sup>, Olinda Santin<sup>1</sup>, Gareth Irwin<sup>2</sup>, Stuart McIntosh<sup>1,2</sup>

<sup>1</sup>Queen's University Belfast, Belfast, UK, <sup>2</sup>Belfast City Hospital, Belfast, UK

Background: Self-Directed Aftercare (SDA) is a widely employed but under-researched approach to follow-up, used across the UK and Europe. Staff perspectives on delivering this pathway are not represented in current literature and the extent to which SDA is meeting the holistic needs of patients is unknown. We sought to explore the experiences of staff in a unit which has been delivering SDA for 13 years, and to determine whether the holistic needs of patients are being met.

Methods: Focus group invitations were distributed to the multidisciplinary breast cancer team, with one-to-one interviews offered to staff who could not attend. Focus groups were staff group-specific and facilitated by an academic not known to the team alongside a clinical researcher. These were conducted and analysed according to the CORE-Q checklist for qualitative research. Recordings were transcribed verbatim and initial analysis (according to Braun & Clarke's reflexive thematic analysis framework) was conducted by two researchers independently.

Results: 19 health care professionals (HCPs) participated (5 breast surgeons, 5 breast care nurses, 4 oncology consultants, 1 oncology nurse consultant and 4 medical secretaries). Analysis demonstrated three broad themes: lack of cohesive care, unmet patient needs, and the ongoing evolution of SDA. Staff highlighted that inefficient communication between primary and secondary care results in unnecessary delays to care. HCPs were unclear or had an inaccurate understanding of the roles of other HCP groups, leading to duplication of work and potential gaps in patient care. Staff did not feel equipped to address menopausal symptoms but acknowledged this was an enormous burden on patients which interfered with cancer treatment. Analysis demonstrated ongoing unmet social and psychological patient needs and that patients with unmet needs in one domain frequently have other unmet needs. Discussion highlighted that the constant evolution of systemic treatments makes a uniform approach to SDA challenging.

Conclusions: There is high heterogeneity in how SDA is perceived and delivered by staff even in one well-established team. HCPs recognise that patients continue to have unmet physical, social and psychological needs, but feel ill-equipped to support them. The concept of uniform SDA needs reimagined in light of emerging extended treatments and calls for a more individualised aftercare approach.

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## Digital spatial profiling of male breast cancer

Luca Foley<sup>1</sup>, Elaina Collie-Duguid<sup>1</sup>, Ewan Campbell<sup>1</sup>, Rasha Abu-Eid<sup>2</sup>, Professor Valerie Speirs<sup>1</sup>

<sup>1</sup>University of Aberdeen, Aberdeen, UK, <sup>2</sup>University of Birmingham, Birmingham, UK

**Background:** Male breast cancer (BC) accounts for approximately 1% of all BC cases but the numbers being diagnosed are rising. Despite sharing many histological similarities with female BC, male BC is biologically and clinically different, with over 85% of cases presenting as ER+. Currently, treatment strategies are largely based on those for women. However, outcomes remain poorer for males, indicating the need for sex specific research in BC. Since a detailed transcriptomic spatial analysis of male BC had not been performed before, this study aimed at spatially quantifying the tumour microenvironment in male BC at the transcriptomic level using digital spatial profiling (DSP).

**Methods:** Following ethical approval, a tissue microarray (TMA) comprising 63 cores from 21 male BC patients (all ER+) was prepared. RNA integrity was checked by RNAscope. Samples were profiled using the GeoMx DSP platform, which allowed simultaneous quantification of ~1800 gene targets in spatially defined regions of interest (ROIs) on the TMAs. Tumour (PanCK+) and stromal (SMA+) compartments were identified using DSP for analysis, as well as CD45+ immune cell clusters. The gene expression profiles within and between compartments was quantified. Differential gene expression and pathway enrichment were performed and compared to female BC transcriptomic datasets.

**Results:** Male BC tumour compartments were heavily enriched for well-established breast cancer epithelial markers, with KRT19 identified as the most abundant. GATA3 and CDH1 were highly expressed, consistent with the ER+ phenotype. Stromal compartments were predominantly enriched for collagens with COL1A1 being the most abundant. The most highly expressed genes in the stroma were (in rank order) COL3A1, COL1A2, FN1, COL1A3, MMP11, COL5A1, SFRP2, ACTA2, COMP. This reflected a collagen-rich desmoplastic tumour microenvironment (TME) suggesting carcinoma-associated fibroblast (CAF) involvement. Overall, immune markers including CD74, CD68, HLA-DRA, HLA-DRB were less abundant than typically reported in female BC, indicating a limited immune activity in the TME.

**Conclusion:** This study provides the first spatial transcriptomic characterisation of male BC. Our findings highlight a tumour compartment dominated by cytokeratin 19 and a stroma enriched for collagens, suggesting a strong CAF enrichment of the ECM. These observations align with the recognised low T cell activity in male BC and the growing importance of CAFs. This study identifies features of the TME which appear unique to male BC. This underscores the importance of studying MBC as a separate disease, potentially allowing patient stratification for treatment, providing the foundation for precision-medicine tailored for men with BC.

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## The Clinical and Molecular Landscape of Breast Cancer in Women of African and South Asian Ancestry

Graeme Thorn, Emanuela Gadaleta, AZM Dayem Ullah, Lewis James, Maryam Abdollahyan, Rachel Barrow-McGee, Louise Jones, Claude Chelala

<sup>1</sup>Barts Cancer Institute, Queen Mary University of London, London, UK

Breast cancer is the most commonly diagnosed cancer globally and the leading cause of cancer death in women, with ethnic disparities reported in cancer incidence, prognosis, diagnosis and therapeutic response. Although precision oncology holds the promise of revolutionising healthcare, it could exacerbate the racial disparities it seeks to eradicate unless rigorous efforts are made to address research biases.

We evaluated the molecular and clinical effects of genetic ancestry in African and South Asian women using a combined cohort of 7,136 breast cancer patients available from four data sources – the 100,000 Genomes Project (UK), The Cancer Genome Atlas (US), the Breast Cancer Now Biobank (London, UK) and Genes & Health (UK).

Using patients assigned to the European genetic ancestry as the baseline comparator for all analyses, we find that non-European patients present with breast cancer significantly earlier and die at a younger age. Patients within the African group also have an increased prevalence of higher grade and hormone receptor negative disease. South Asian patients show a small tendency towards lower stage at diagnosis, and a lower tumour mutational burden.

We observed significant differences and similarities in the somatic mutational landscape of the non-European populations. Genes with significant differences in germline mutation rates were identified in African and South Asian populations, including those used in current genetic testing as well as those implicated in breast cancer predisposition in the literature. There is a higher propensity for BRCAness in the African population, with a lower rate in the South Asian population, serving as a potential prognostic indicator into the response to therapies such as PARP inhibitors.

We harness multimodal data to improve our understanding of ancestry-associated differences in breast cancer and highlight opportunities to advance health equity in breast cancer thus taking one step closer to achieving the promise of equitable precision oncology.

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#### Evaluation of staff time and material costs to introduce Trastuzumab Deruxtecan as treatment for metastatic HR+ HER2-low Breast Cancer compared to Paclitaxel

Francesco Abbadessa<sup>1</sup>, Natalia Soe<sup>1</sup>, Catherine Harper-Wynne<sup>2</sup>

<sup>1</sup>Kent And Medway Medical School, Canterbury, UK, <sup>2</sup>Maidstone and Tunbridge Wells NHS Trust, Maidstone, UK

**Background:** Among patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative breast cancer (BC), a significant subset exhibits low HER2 expression. This HER2-low subgroup has recently become a target for a novel therapy Trastuzumab Deruxtecan (T-DXd), an antibody-drug conjugate demonstrating superior clinical outcomes compared to Paclitaxel, a standard chemotherapy used in this setting. Despite its therapeutic advantages, T-DXd carries risks of serious side effects, notably interstitial lung disease (ILD), requiring additional monitoring such as pulmonary function tests (PFTs) and CT imaging. In England, T-DXd is not yet approved by NICE for treating HER2-low BC. While NICE evaluations focus on clinical efficacy and cost-effectiveness, they often overlook the practical and financial aspects of implementing novel therapies locally. This service evaluation aims to address that gap.

**Methods:** A baseline service evaluation was conducted at Maidstone and Tunbridge Wells NHS Trust (MTW). Semi-structured questionnaires were distributed to registered healthcare professionals working in the oncology, radiology, pathology, surgery, pharmacy, and respiratory departments. The evaluation aimed to estimate the staff time and material costs involved in diagnosing HER2-low HR+ metastatic BC and in administering T-DXd and comparing these with Paclitaxel. Data were collected per patient and treatment cycle and scaled up to estimate the annual resource implications.

**Results:** An estimated 9 patients annually at MTW are eligible for HER2-low treatment. Since HER2-low status is only relevant when considering T-DXd, additional diagnostic testing is only undertaken in this context. Analysis of a single tissue sample by pathology takes 5-45 minutes per patient. If a biopsy is required, this takes 10 minutes, while interventional radiology takes 45 minutes. Diagnosing HER2-low using primary tissue incurs a cost of £270; if new tissue is needed, this increases to £400. Re-classification of archived samples older than a year costs £310, compared to £65 for those less than a year old. T-DXd treatment requires 90 minutes of staff time per patient per cycle, compared to 420 minutes for Paclitaxel. This translates to lower per-cycle administration and manufacturing costs: £50.23 for T-DXd versus £145.74 for Paclitaxel. Scaled annually, the administration and manufacturing costs total amount is £452.07 for T-DXd and £1,311.66 for Paclitaxel. T-DXd also requires additional clinical resources: full baseline pulmonary function testing for all eligible patients requires 18 hours of respiratory consultant time, costing £1,800. Paclitaxel requires none. ILD monitoring with T-DXd demands 37.5 hours of radiologist time, plus five additional consultant oncologist follow-up appointments per patient.

Conclusion: While T-DXd offers shorter preparation and administration time with reduced per-cycle costs compared to Paclitaxel, it imposes greater diagnostic and monitoring demands. Performing a comprehensive resource analysis is therefore essential to inform NHS Trusts and facilitate smooth implementation of emerging therapies.



### 3.1 Does the MDT know what it's doing?

Would I receive better care at a different Trust?

Kieran Horgan - Leeds Teaching Hospitals, UK

There are a range of national datasets which document different aspects of care received by breast cancer patients in England and Wales. They are rich in information which is increasingly granular. A notable advance in recent years is the ability to coalesce and analyse this data from separate sources at individual patient level.

Authoritative guidelines exist with advice and recommendations on specific aspects of treatment. Practice in individual trusts can be assessed against these recommendations and performance compared to that seen in other trusts.

It is important that there is a thorough discussion on the wide variation that is apparent. The data is publicly available and in an ever-improving user-friendly format.

How should a patient interpret this data when considering where they might receive best care? How might a clinician explain practice noticeably different to the norm?

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Can good care or poor care be reflected in numbers and rates?

Sarah Downey - James Paget University Hospitals NHS Foundation Trust, Norfolk, UK

*More information to follow*

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Comparing breast cancer outcomes globally: strengths and limitations of existing data

Toral Gathani - Nuffield Department of Population Health, University of Oxford, UK

Global comparisons of breast cancer outcomes are widely used to understand international differences in disease burden, evaluate health system performance, and inform cancer control policies.

Breast cancer is the most commonly diagnosed cancer worldwide, and outcomes vary substantially between countries with higher mortality rates observed in countries with least resources.

Comparing countries is complicated by factors such as differences in demographics, cancer registry coverage, and variable access to and provision of high-quality diagnostic and treatment services.

Understanding the available data and trends can help contextualise breast cancer as a global health challenge.

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### 3.2 Practical issues related to young women and breast cancer

Management of breast cancer during pregnancy  
Anne Armstrong - Christie Hospital, Manchester, UK

*More information to follow*

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Determining menopausal status in women with early breast cancer  
Ephia Yasmin - University College London Hospitals NHS Foundation Trust, UK

Fertility preservation (FP) has become an integral component of supportive care for reproductive-aged women diagnosed with breast cancer, yet multiple practical challenges continue to limit its consistent delivery.

The urgency to commence systemic therapy, particularly regimens with high gonadotoxic potential, often constrains the time available for counselling and completion of FP procedures but streamlined pathways and communication can mitigate risk. Although random-start ovarian stimulation has reduced delays, the required treatment window may be difficult to accommodate during the emotional stress of diagnosis or if response is sub-optimal. Safety concerns are particularly relevant in estrogen receptor-positive disease, where transient increases in estradiol during stimulation raise theoretical risks; however, the use of aromatase inhibitor-based protocols and outcome data on survival have alleviated much of this concern.

Feasibility of FP varies according to age, ovarian reserve, previous reproductive history, and genetic factors such as BRCA mutations, the latter of which may also prompt discussions regarding preimplantation genetic testing. Oocyte and embryo cryopreservation remain the most established FP options. Ovarian tissue cryopreservation provides an alternative for patients requiring immediate treatment but new evidence suggests it should not be used or be limited. Despite growing awareness of FP, access remains uneven.

Decision-making is further complicated by psychosocial distress, ethical considerations surrounding embryo disposition, and communication gaps between oncology and fertility teams. Multidisciplinary coordination, early referral pathways, and comprehensive patient support are essential to improving FP uptake and outcomes for young women with breast cancer.

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HRT after a diagnosis of breast cancer  
Rebecca Bowen - Royal United Hospitals Bath NHS Foundation Trust, Bath, UK

*More information to follow*

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### 3.3 Treating the whole person: Understanding Integrative Oncology

What is Integrative Oncology? Debunking the myths, correcting the narrative  
Penny Kechagioglou - University Hospitals Coventry and Warwickshire NHS Trust, UK

*More information to follow*

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Optimisation of diet and supplements for patients living with and beyond breast cancer  
Nina Fuller-Shavel - National Centre for Integrative Oncology, Reading, UK

ESPEN Clinical Nutrition in Cancer guidelines clearly state that nutrition plays a crucial role in multimodal cancer care. Robust evidence indicates that nutritional issues should be assessed and taken into account since the time of cancer diagnosis and incorporated within a diagnostic and therapeutic pathway. UK NCIO (National Centre for Integrative Oncology) research data based on over 200 participants with breast cancer shows that only 8% of women received useful advice and information about nutrition and diet within standard care, with over 65% reporting dissatisfaction with the lack of guidance provided. Despite WCRF and ASCO guideline availability, both dissemination and implementation of high-quality dietary advice have been a challenge in the UK, particularly amidst online misinformation and hype.

In this session we discuss some of the key data and guidelines pertaining to nutrition and lifestyle in breast cancer, as well as available models of multidisciplinary care that aim to optimise nutritional support. We will also cover common supplementation questions that breast cancer patients may ask their team, important information sources and how to offer safe guidance through a collaborative pathway that integrates input from medical, nutrition and pharmacy teams.

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Science & Synergy: Truths and tools in integrative oncology  
Lauren Watts - NHS England, London, UK

*More information to follow*

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### 3.4 UK Clinical trials

Supporting researcher development in clinical trials

Anna Kirby - Royal Marsden NHS Foundation Trust, London, UK

Focus on current/new UK clinical trials

a. HER2-RADiCAL

Iain MacPherson - University of Glasgow, UK

b. FAST-FORWARD BOOST

Carmel Anandadas - The Christie NHS Foundation Trust, Manchester, UK

c. TADPOLE

Shelley Potter - University of Bristol, UK

d. OPTIMA-YOUNG

Ines Vaz Luis - Gustave Roussy, Paris, France

Enhancing trials using routine data linkage

Lucy Kilburn - The Institute of Cancer Research, UK

Panel discussion

*More information to follow*



#### 4.1 Minimally invasive treatment

Do all small low-risk breast cancers have to be removed?  
Stuart McIntosh - Queen's University Belfast, UK

*More information to follow*

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Tailoring axillary surgery in the upfront setting  
Shelley Potter - University of Bristol, UK

*More information to follow*

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How low should you go – neoadjuvant systemic therapy in small EBCs?  
Iain MacPherson - University of Glasgow, UK

*More information to follow*

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## 4.2 Towards personalisation of screening

### AI in image based risk assessment

Fredrik Strand - Karolinska Institute, Solna, Sweden

Risk-predictive AI has the potential to transform breast cancer screening by moving from a one-size-fits-all strategy to a more individualized approach. Recent advances have produced image-based models that estimate a woman's short-term risk of cancer directly from mammograms. The ScreenTrustMRI trial we conducted showed that an AI model could identify a 7% share of the women with negative screening mammography among which MRI would detect an additional 64 cancers per 1000 MRIs. However, a central challenge is how to integrate AI-based risk models with existing guidelines and policies that define "high risk" and set population-level targets. Moreover, ethical and communication issues must be considered, since risk predictions are probabilistic and may shift over time. This talk will explore the current evidence and the practical hurdles that must be overcome for risk-predictive AI to be responsibly implemented in organized screening programs.

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### Density based screening: MyPeBS and BRAID

Fiona Gilbert - University of Cambridge, UK

Breast density is related to increased risk of developing breast cancer and reduced sensitivity and specificity of screening mammography. Increased breast density has been used in the My Personalised Breast Screening trial together with other risk factors and single nucleotide polymorphisms to test whether or not more frequent screening together with supplemental ultrasound will reduce the incidence of late stage cancer. In the BRAID study (Breast Screening – risk adapted imaging for density) women with increased breast density and a negative mammogram were randomised to either abbreviated MRI, Contrast mammography or whole breast ultrasound or standard of care. There were four times as many cancers found by the two contrast techniques compared to ultrasound and the cancers found were half the size. Predictive AI techniques based on mammographic features are able to give the short-term risk of developing breast cancer over a 3 – 5 year period. If these techniques are combined with supplemental imaging, the predictive AI may be a more reliable way of personalising screening for women at greatest short term risk compared to breast density alone.

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### Digital breast tomosynthesis (DBT) for breast cancer screening

Keshthra Satchithanda - King's College Hospital, London, UK

This presentation will include preliminary results from a national trial to see if screening with 3D mammograms is more effective than the traditional 2D mammograms at screening for breast cancer.

The study began in 2018 and has recruited over 70,000 women to participate in 8 centres in England. The aims were to investigate the accuracy, effectiveness and cost of breast cancer screening using 3D mammograms compared to 2D mammography.

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#### 4.3 Implementation of lifestyle interventions

##### Implementing lifestyle interventions in early breast cancer

Carol Keen - Active Together Cancer Rehabilitation, Sheffield, UK

Dr Carol Keen is a Consultant Physiotherapist and Clinical Lead for the Active Together Cancer Prehabilitation and Rehabilitation service across South Yorkshire. Her clinical and research specialism is in rehabilitation, particularly its impact on patients and delivery in clinical settings.

Active Together is a multi-modal cancer prehabilitation which offers physical activity, dietetic and wellbeing interventions to patients undergoing curative cancer treatment. The service supports patients during prehabilitation i.e. before they start their cancer treatment, during their treatment, and through rehabilitation after treatment has been completed.

Delivered as a collaboration between Sheffield Teaching Hospitals, Sheffield Hallam University and the charity Yorkshire Cancer Research, the service has supported almost 3000 patients since February 2022. The service initially worked with patient having treatment for colorectal, lung and upper GI cancers, and an early evaluation has shown changes in function, quality of life, healthcare resource usage and 1-year survival.

Since November 2024 the service has also been supporting patients undergoing treatment for breast cancer. Carol will speak about the evidence for prehabilitation in patients with breast cancer, experiences of Active Together in extending their service to this patient group, and will share the early findings from this work.

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##### Implementing lifestyle interventions in metastatic breast cancer

Lucy Gossage - Nottingham University Hospitals NHS Trust, UK

*More information to follow*

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##### The NEWDAY study – a bespoke lifestyle intervention after primary treatment for early breast cancer

John Saxton - University of Hull, UK

Weight gain is commonly observed during and after early breast cancer (EBC) treatment and is associated with poorer survival outcomes. International studies have demonstrated the potential effectiveness of supportive lifestyle interventions in EBC patients via emerging signals of efficacy regarding weight loss and improved breast cancer outcomes. However, an important challenge is to design a practically implementable method of developing the skills and confidence for sustainable health behaviour change amongst UK EBC patients via a programme that could be embedded within the NHS breast cancer care pathway. Important barriers to adopting healthy lifestyle behaviours after EBC treatment include cancer-related physical symptoms (e.g., lymphoedema, fatigue, arthralgia, etc.) low self-esteem, family/work schedules and body image concerns. In addition, women commonly experience deficits in the availability of clear and simple information and insufficient support from health professionals. Cultural, social and economic barriers must also be taken into account. NEWDAY-ABC was developed via extensive qualitative research and co-design work with EBC patients and healthcare professionals before the feasibility of implementation was evaluated in an external pilot study. We now aim to evaluate the clinical benefits and cost-effectiveness of NEWDAY-ABC via a multi-centre randomised controlled hybrid intervention-implementation trial. The intervention will comprise group-based motivational workshops involving educational and practical physical activity components and will be delivered by trained lifestyle advisors and registered dietitians either via teleconferencing or in person (face-to-face), according to patient preferences. This presentation will provide a detailed overview of the NEWDAY-ABC clinical trial and report on progress to date.

Integrating physical activity into standard of care after breast cancer  
Sam Orange - Newcastle University, UK

The evidence is compelling — physical activity improves outcomes after breast cancer. Physical activity enhances quality of life, reduces fatigue, and is associated with a lower risk of recurrence and mortality. However, support to be active is not routinely offered as part of standard care. In this session, Sam will explore why this gap exists and present an innovative approach to integrating physical activity into routine care for women after breast cancer.

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#### 4.4 Recent advances in ER+ HER2- metastatic breast cancer

Recent progress with SERDs according to ESR1 genotype; where to next?  
Stephen Johnston - Royal Marsden NHS Foundation Trust, London, UK

*More information to follow*

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Clinical experience with PI3K/AKT inhibitors  
Olga Oikonomidou - University of Edinburgh, UK

This presentation explores the multifaceted issue of breast cancer inequities in the UK, focusing on the disproportionate burden experienced by racial and ethnic minority groups. It digs into the biological underpinnings, including genetic predispositions and epigenetic modifications, and critically examine how structural racism exacerbates these disparities through its influence on social determinants of health and access to care. The talk aims to highlight actionable insights for healthcare professionals to foster a more equitable breast cancer care pathway.

#### Learning Objectives

By the end of the talk, participants will be able to:

1. Recognise the significant racial and ethnic disparities in breast cancer incidence, diagnosis, and outcomes within the UK.
2. Understand the contributing roles of genetic and epigenetic factors in breast cancer risk and progression across diverse populations.
3. Appreciate how structural racism impacts social determinants of health and healthcare access, thereby amplifying breast cancer inequities.
4. Identify practical strategies and interventions to address and mitigate these disparities in clinical practice and broader healthcare systems.

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The role of mutation testing in the treatment and sequencing of the treatment of ER+ HER2- metastatic breast cancer

Richard Baird - Cancer Research UK Cambridge Centre/University of Cambridge, UK

In recent years, the treatment landscape for Oestrogen Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative (ER+ HER2-) metastatic breast cancer (MBC) has incorporated novel therapies which are targeted to specific patient subgroups. Routine molecular profiling, typically via Next-Generation Sequencing (NGS) of tumour tissue or 'liquid biopsy' to test plasma circulating tumor DNA (ctDNA), is now essential to inform treatment sequencing beyond initial endocrine therapy (ET) plus a CDK4/6 inhibitor.

Key actionable mutations now direct which therapies a patient may receive. ESR1 mutations emerge in up to 40% of tumours as a mechanism of resistance to ET (particularly aromatase inhibitors). Detection of an ESR1 mutation can now lead to treatment with a novel oral Selective Estrogen Receptor Degrader (SERD), which is specifically approved for this subgroup (eg. elacestrant).

Similarly, alterations in the PI3K / AKT / PTEN pathway, particularly mutations (found in 30-45% of ER+ HER2- MBC), guide the use of PI3K or AKT inhibitors. Patients with PIK3CA, AKT mutations, or PTEN alterations are eligible for targeted combinations like fulvestrant with alpelisib or capivasertib.

The dynamic nature of cancer evolution and acquired drug resistance means we are moving to a paradigm in which molecular profiling is repeated to more precisely guide treatment at different points. Whilst HER2 status is still generally tested on tissue (including HER2-low status), plasma ctDNA analysis is often the preferred method for detecting acquired mutations due to its non-invasiveness and higher sensitivity in this setting.

## 5.1 Dormancy/late relapse

Relationship of tumour phenotype with time to recurrence

Mitch Dowsett - Royal Marsden NHS Foundation Trust/Institute of Cancer Research, London, UK

There is now a widespread understanding that the pattern of recurrence of breast cancer varies between different subgroups. Detailed knowledge of this can drive monitoring and/or the delivery of therapies to avert recurrence. ER-negative tumours tend to recur within the first five years if recurrence is to occur at all. In contrast ER-positive tumours continue to show a risk of recurrence for decades with more recurring after 5 years than before. In this regard it is of particular note that there is a body of evidence that indicates that while those patients with the highest ER levels show the lowest risk of recurrence during 5 years of adjuvant treatment the same group shows the highest risk after 5 years if treatment ceases at that time. This group may merit special attention from monitoring by ctDNA.

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A gene therapy approach to preventing outgrowth of dormant breast cancer cells in bone

Penny Ottewell - University of Sheffield, UK

Breast cancer recurrence often occurs many years after the patient is thought to be disease free and most commonly occurs in bone. Evidence suggests that tumour cell dissemination to bone is an early event likely to happen before diagnosis of the primary tumour. Therefore, preventing initial seeding of tumours into the bone may not be possible. Once in bone, tumour cells become dormant, and in many patients remain inactive throughout their life. However, in some patients' dormant tumour cells are reawakened to develop into overt metastasis, for which there are no current curative treatments. We have generated substantial evidence that, in bone, the re-awakening of dormant cells is through activation of IL-1 $\beta$  signalling pathways. Importantly, genetic/pharmacological inhibition of the IL-1 receptor (IL-1R1) retains tumour dormancy, likely through modification of the bone metastatic niche. Here we propose a new gene therapy-based approach to retain tumour cells in an indefinite state of dormancy by transducing bone cells to switch off IL-1 $\beta$  signalling only at the point where IL-1 $\beta$  is upregulated in bone.

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The emerging role of ctDNA in early detection and treatment of late metastases

Nick Turner - Royal Marsden NHS Foundation Trust, London, UK

*More information to follow*

## 5.2 Early Breast Cancer Trialists' Collaborative Group (EBCTCG) Update

Introduction to EBCTCG and recent results

Robert Hills - University of Oxford, UK

EBCTCG meta-analyses – what, how, and why?

Richard Berry & Graham Beake -University of Oxford, UK

The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) was conceived in 1983, and based at the University of Oxford's Clinical Trial Service Unit. For forty years it has periodically sought up-to-date data on each individual woman in randomised trials of treatments for early breast cancer for meta-analysis, initially every five years, and more recently on a question-by-question basis. This worldwide collaboration involves over 1000 trialists from about 650 trials, giving a database of some two-thirds of a million women and 6 million woman-years of follow-up. It has demonstrated many moderate but real differences in long-term survival that were not reliably identified in the separate trials. Through a series of step-by-step improvements in local and systemic treatments, each producing only moderate mortality reductions, UK breast cancer mortality rates in middle age have more than halved since the 1980s.

Reliable assessment of the magnitudes of the benefits and risks of the various treatment options for early breast cancer is crucial to informed decision making. Estimates of the effects of treatment based on individual studies or, worse, observational data are often misleading, no matter what precautions are taken. Meta-analyses of individual patient data from all relevant randomised clinical trials provide the most reliable evidence on particular therapeutic questions. By looking at the totality of the randomised evidence, meta-analyses avoid the systematic errors that commonly arise in narrative reviews through selective citation of striking results, and provides the most precise estimates of treatment effects by including larger numbers of patients and events. This talk will provide a background to the methodology of the EBCTCG and discuss recent emerging results, as well as looking forward to ongoing and planned analyses.

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Trying to further progress of personalised breast cancer care in EBCTCG

David Cameron - University of Edinburgh, UK

*More information to follow*

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## 5.3 Introduction of new systemic treatments: Antibody-drug conjugates

### Mode of Action

Neil Masters - Sheffield Teaching Hospitals NHS Foundation Trust, UK

This presentation will cover what an antibody drug conjugate is, then focus on the antibody drug conjugates in current use in breast cancer in the UK (Trastuzumab Emtansine, Trastuzumab Deruxtecan, and Sacituzumab Govitecan). I will discuss the mode of action of each of these treatments, and in relation to Trastuzumab Emtansine and Trastuzumab Deruxtecan the key differences between the two drugs.

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### Clinical applications and toxicity

Andrew Proctor - York and Scarborough Teaching Hospitals NHS Foundation Trust, UK

*More information to follow*

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### Novel forms of drug delivery; ADCs and beyond

Jenny Hiscock - University of Kent, UK

Supramolecular Self-associating Amphiphiles (SSAs) are a novel class of molecules, invented, developed and patented by Jennifer Hiscock at the University of Kent. This library of > 190 compounds produced to date forms the basis of a therapeutic platform technology that has shown clear potential:

- (i) to produce novel drugs;
- (ii) to act as agents to enhance the efficacy of known drugs;
- (iii) to act as drug delivery vehicles.

This molecular technology provides a means to overcome drug resistance and additionally increases opportunities for re-purposing disused therapeutics.

To date a set of reproducible data has been produced which shows that this novel chemistry approach could be used to treat major diseases where current pharmaceutical therapies are failing. It enables re-purposing and/or reactivation of drugs where efficacy or safety is limited by resistance, dose and/or delivery route. Initial opportunities have been identified in cancer and infectious disease. The potential for this class of molecules was further highlighted by the drug-like profiles obtained for 8 lead SSAs in independent *in vitro* and *in vivo* DMPK studies. *In vivo* linear toxicity profiles also support the potential for this class of compounds to be developed into the clinic. Within the scope of this presentation, we hope to provide you an overview of this technology and highlight the application of this innovation towards the treatment of cancer.

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## 5.4 Abstracts from future leaders

Treatment delivery and clinical outcomes from a pilot regional systemic anti-cancer therapy (SACT) clinic for early HER2-positive breast cancer

Santiago Teran<sup>1</sup>, Anne Armstrong<sup>1</sup>, Laura Horsley<sup>1</sup>, Annabel Whitehouse<sup>1</sup>, Tharany Srisatkunam<sup>1</sup>, Suzanne Frank<sup>2</sup>, Barbara Corke<sup>1</sup>, Annie Mckirgan<sup>3</sup>, Dane Bradwell<sup>4</sup>, Abigail Boughton<sup>1</sup>, Dr. Caroline Wilson<sup>1</sup>

<sup>1</sup>Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester, UK, <sup>2</sup>Department of Pharmacy, The Christie NHS Foundation Trust, Manchester, UK, <sup>3</sup>Department of Surgery, Macclesfield District General Hospital, East Cheshire NHS Trust, Macclesfield, UK, <sup>4</sup>Department of Pharmacy, The Christie at Macclesfield, The Christie NHS Foundation Trust, Macclesfield, UK

**Background:** Oncology services face increasing pressure from rising cancer incidence and workforce shortages, particularly in delivering complex but protocol-driven treatments. The current analysis evaluates treatment delivery and outcomes within a regional pilot streamlined model designed to optimize care, follow-up, and treatment in early HER2-positive breast cancer (eHER2+BC).

**Methods:** We retrospectively analyzed 77 patients with eHER2+BC treated under a pilot streamlined systemic therapy model (STR) (September 2024-June 2025). Patients were referred from 4 breast MDTs to a single consultant-led oncology outpatient clinic for a face-to-face new oncology consultation and a pre-cycle 5 telephone consultation before completing (neo)adjuvant therapy, with interim monitoring and support provided by multidisciplinary regional teams. Outcomes were compared with a historical cohort (CTR) managed under a standard model (January 2022-December 2023). Collected data included clinicopathologic features, treatment characteristics, and delivery (regimen, cycle doses, dose reductions, deferrals), radiological and pathology responses, toxicity, and dose intensity metrics (Relative dose intensity-RDI). RDI was calculated for each chemotherapy agent using the Hryniuk method. Average chemotherapy RDI per regimen was also calculated. Associations between RDI and pCR were assessed overall and within cohorts. Continuous variables were summarized as mean/median, and compared using t-test or Mann-Whitney tests. Categorical variables were compared with Pearson's chi<sup>2</sup> or Fisher's exact tests as appropriate. P < 0.05 was considered significant.

**Results:** 77 patients were included in STR and 56 in CTR. Median STR age was 57 (35-81) and 59 (33-83) at CTR. 73 and 46 patients were subject to RDI analysis in each group. 51 (69.9%) and 25 (54.4%) had neoadjuvant treatment (NeoAdj) in STR and CTR (p=0.086). There were 9 (19.6%) vs. 2 (8.3%) CR, 36 (78.3%) vs. 21 (87.5%) PR, and 1 (2.2%) vs 0 PD at mid-cycle MRI. There were 23 (45.1%) pCR in NeoAdj STR vs. 8 (32%) in CTR (p=0.037). Mean/median RDIs were 86.9/91.5 (46-100) and 91.5/96.1 (46.8-100), respectively. Mean/median RDI for NeoAdj and Adj were 84.6/87.6 (46-100) and 93.1/95 (65-100) in STR vs. 94.7/95.7 (46.8-100) and 92.4/100 (50-100) in CTR. 48 (68.6%) and 38 (82.6%) patients had a mean RDI $\geq$ 85%, with 32 (62.8%) vs. 20 (80%) in NeoAdj and 16 (84.2%) vs. 18 (85.7%) in Adj. Mean RDI value did not differ between patients with and without pCR (p=0.963). There was no association between RDI and pCR in STR (p=0.499) and CTR (p=0.664). There were 9 (12.3%) vs. 5 (10.9%) (p=0.810) and 19 (26%) vs. 7 (15.2%) (p=0.165) G3/4 hematologic and non-hematologic toxicities. There were 42 (60%) vs. 13 (28.3%) dose reductions and 31 (44.3%) vs. 17 (37%) dose deferrals (at least 7 days) in STR and CTR.

**Conclusion:** A streamlined treatment model for eHER2+BC appears feasible, maintains treatment intensity, shows similar toxicity, and achieves improved or comparable outcomes with standard care.

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Do brands matter? Insights from the SWITCH study on healthcare professionals' perceptions of oral SACT brand changes

Rebecca Todd<sup>1</sup>, Zoe Moon<sup>1</sup>, Pinkie Chambers<sup>1</sup>, Robert Horne<sup>1</sup>

<sup>1</sup>University College London (UCL), London, UK

**Introduction:** Oral systemic anti-cancer therapy (SACT) is prescribed for many cancers, offering greater convenience and reduced risks compared with intravenous treatment. However, adherence varies widely, and non-adherence, often driven by treatment-related side effects, can increase the risk of disease progression and hospitalisation. Patients have reported that tolerability can differ between medication

brands. Although the mechanism remains unclear, studies suggest switching brands may increase adverse events, reduce adherence, and worsen outcomes. Despite this, patients' reports of brand-related side effects are often met with disbelief by healthcare professionals (HCPs), leaving patients feeling dismissed. Given patient-provider relationships strongly influence adherence and experience, exploring this further is important. This study aimed to examine HCP perceptions and prescribing behaviours regarding oral SACT brand changes.

**Methods:** An online survey was developed, pilot tested, and distributed via UK professional networks such as the British Oncology Pharmacy Association and NHS Cancer Alliances. Respondents were eligible if they had experience working in cancer care. Hosted on Qualtrics, the survey included questions on HCPs' experiences and perceptions of oral SACT brand changes. Quantitative data were summarised as percentages, and qualitative comments analysed thematically.

**Results:** 124 eligible responses were analysed (52% pharmacy, 32% nursing, 15% medical). Drivers of HCP-initiated brand switches were cost and availability, while the predominant issue reported by patients to HCPs following a switch was side effects. When patients requested a brand change, 75% would only accept it half the time or less. Most respondents believed side-effect and safety profiles were consistent between branded and generic medications, and perceived no differences in side-effect profile or efficacy between different generic brands. No significant differences were observed between HCP groups in attributing differences in patient-reported side effects to the medication brand. However, significant variation was found in perceived efficacy of branded versus generic medications (Fisher's exact test,  $p = .005$ ) and in the safety profile of different generics ( $\chi^2 (2, N = 89) = 8.75, p = .011$ , Cramer's  $V = .313$ ), with 39% of doctors reporting potential differences compared with 16% of nurses and 8% of pharmacists.

**Conclusions:** This study provides novel insights into how oral SACT brand switching is managed and highlights opportunities to better support patients. While most HCPs regarded brands as equivalent, many patients report meaningful differences, particularly regarding side effects, which remain a key concern. Despite this, HCPs often do not act on patient requests, potentially leaving patients struggling. Addressing this gap is crucial to strengthen patient-provider trust, improve adherence, and support patients raising concerns. Strengthening clinical guidance on managing brand changes and validating patient experiences will be vital for optimising outcomes and supporting personalised cancer care. Future focus groups will help build on findings to shape best practice and inform oral SACT prescribing policy.

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Using carcinoma-associated fibroblasts as a model to investigate biological differences between male and female breast cancer

Fiona Saunders<sup>1</sup>, Peng Liu<sup>1</sup>, Matthew Everest<sup>1</sup>, Natthaya Eiamamapai<sup>1</sup>, Giulia Conti<sup>2</sup>, Rasha Abu-Eid<sup>1,3</sup>, Valerie Speirs<sup>1</sup>

<sup>1</sup>University of Aberdeen, Aberdeen, UK, <sup>2</sup>Sapienza University of Rome, Rome, Italy, <sup>3</sup>University of Birmingham, Birmingham, UK

Nearly every day a man is diagnosed with breast cancer (BC) in the UK. Male BC is distinct in clinicopathologic features and molecular make-up, and oestrogen receptor is more abundant. Challenges persist in isolating BC epithelial cells from females; this is exacerbated in males. As differences in the tumour microenvironment of male BC are recognised, we took a lateral approach to assess the phenotype of carcinoma-associated fibroblasts (CAFs) derived from male and female BCs.

We isolated CAFs from age, type and grade-matched male (n=4) and female BCs (n=5) and used these to explore biological functions including migration, adhesion and angiogenesis. Progressive changes in CAF motility and migration were analysed using time-lapse data generated by digital holographic microscopy. We generated cell derived matrices (CDMs) and assessed adhesive properties of various cell types, including normal primary mammary epithelial cells from a male donor (hMMEC), using a colorimetric assay. 2-D tube formation was visualised using CD31 immunohistochemical staining from co-cultures of CAFs and HUVEC. Fractal analysis was performed on Picosirius red stained tumour sections from male and female BC to assess collagen fibre complexity.

By scratch assay, male BC-derived CAFs were around 20% faster at closing the wound than those from female BC. This was supported by cell tracking where they showed greater migration. HUVEC cells co-cultured with male CAFs generated shorter tubes (2100  $\mu$ m vs. 3000  $\mu$ m, M vs, F;  $p<0.05$ ) with increased branching (300 vs. 180 branchpoints, M vs F,  $p<0.05$ ). HUVEC exposed to male BC CAF-CM had greater wound closure than those exposed to that of females ( $p<0.01$ ). CDMs derived from male CAFs were thicker and intra-tumoral collagen fibres were denser and more complex in male BC tissue sections. No difference between sexes was seen in peritumour areas. All cell types tested adhered better to the thicker and denser male CAF CDMs and was double that of cells adhering to tissue culture plastic. This was particularly evident with hMMEC which adhered well to all CDMs but was highest on the male CAF CDMs.

Our data demonstrate clear differences in the phenotypic behaviour of CAFs derived from male and female BC, adding to a growing body of evidence that male and female BC are not identical biologically. Since sex differences in matrix remodelling have been reported in other pathologies, adhesion and migration trajectories of CAFs may influence BC cells in a sex-specific manner.

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### Risk of second cancers after hypofractionated radiotherapy among breast cancer survivors in England

Imogen Sawyer<sup>1</sup>, Michael E Jones<sup>1</sup>, Aislinn Macklin-Doherty<sup>1,2</sup>, Montserrat Garcia-Closas<sup>1</sup>, Amy Berrington de Gonzalez<sup>1</sup>

<sup>1</sup>The Institute of Cancer Research, <sup>2</sup>The Royal Marsden NHS Foundation Trust

**Background:** Radiotherapy for breast cancer has undergone major transformation over the past two decades, with hypofractionation (2.7 Gy/fraction) and most recently ultra-hypofractionation (5.2 Gy/fraction) replacing standard fractionation (1.8–2.0 Gy/fraction) in the UK and elsewhere. The impact of hypofractionation on the risk of second cancers is not yet known and difficult to predict given that it typically involves a higher dose per fraction, but lower total dose delivered over a shorter time period. We aim to compare the risk of second cancers after hypofractionation compared to standard fractionation radiotherapy for breast cancer using a national retrospective record linkage study in England.

**Methods:** We will evaluate the long-term second cancer risk in a national cohort of female breast cancer survivors treated with radiotherapy between 1995–2017 in England. Using data from the NHS England Cancer Registry and the National Radiotherapy Dataset (RTDS) we have established a national cohort where we will use causal inference methods, including target trial emulation, to mitigate potential biases that arise in large observational cohort studies using real world data. Standardized incidence ratios (SIRs) will be calculated for second cancers in breast cancer survivors who had moderate hypofractionation compared to standard fractionation. Second cancers will be defined as an invasive primary cancer diagnosed  $\geq 12$  months after the date of first radiotherapy treatment and will exclude ipsilateral second breast cancers.

**Results:** The cohort includes 291,535 invasive breast cancer patients who survived at least 5-years following radiotherapy. Of these 131,622 (45.2%) women were treated with standard fractionation and 159,873 (54.8%) women received moderate hypofractionation. Over the follow-up period (median: 11.2 years, range: 5 to 27 years), 10% ( $n = 30,465$ ) of patients developed a second invasive cancer including: 8,427 contralateral breast cancers, 4,410 lung cancers, 1,179 soft tissue sarcomas and 821 leukaemias. Results will include an evaluation of the risk of second cancers according to dose fractionation considering the effects of age at exposure and time since exposure.

**Conclusion:** As a greater proportion of breast cancer cases are cured, and survivors are living longer, these findings will allow for new insights to be gathered on the risks of second cancers after hypofractionated radiotherapy and other improvements in radiotherapy treatment. Hypofractionation has been introduced more recently, or is being trialled, for other cancers including prostate cancer and these results could also provide insights into second cancer risks for other patient groups.

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## Developing a Rotational Breast CNS Trainee Programme: Building the Future Specialist Nursing Workforce

Esther Kershaw<sup>1</sup>, Dorcas Adjei<sup>1</sup>, Juanita Caseley<sup>1</sup>, Maria Cooper<sup>1</sup>, Emily Sharp<sup>1</sup>, Claire Ryan<sup>1</sup>

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**Background:** Breast care is a complex and evolving specialty requiring highly skilled Clinical Nurse Specialists (CNS) to deliver holistic, patient-centred care across diagnostic, treatment, and survivorship pathways. Recruitment and retention challenges, combined with increasing service demand, highlight the urgent need for innovative training, and workforce strategies to maintain and expand the CNS workforce. The local Trust has faced repeated difficulties filling Band 7 Breast CNS roles, failing to recruit suitable candidates successfully after three interview rounds.

Workforce retention and impending retirements pose a significant challenge for the NHS, particularly within cancer services. While more recent data specifically for specialist cancer nurses is limited, the Macmillan Cancer Support 2021 report highlights the need for nearly 4,000 additional specialist nurses by 2030 to meet rising demand. In 2019, England had 4,020 specialist cancer nurses, with approximately 45% aged 50 or over. Assuming a steady retirement rate, around 181 nurses may retire per year, totalling roughly 1,809 over the next decade. Meanwhile, the UK population is projected to reach 72.5 million by 2032, including 1.7 million more people of pensionable age. The demographic shift will increase demand for cancer services precisely as workforce capacity declines, highlighting the urgent need for strategic workforce planning and sustainability initiatives.

The aim is to design and implement a structured rotational trainee programme that provides nurses with exposure to the full spectrum of breast CNS practice, fostering professional development, role preparedness, and workforce resilience. To offer flex within the breast cancer trajectory and a transferrable model that can be applied to other tumour groups and trusts.

**Methods:** The rotation-based programme is 24 months long incorporating the four pillars of practice and includes supervised placements across key domains (surgical, early oncology, metastatic oncology and research), each being 6 months long. This includes structured teaching, mentorship, and competency-based assessments aligned with national CNS capability frameworks. Evaluation methods include pre/post surveys, reflective practice and professional feedback.

**Results (early findings):** This pilot commenced in September 2024 with four individuals recruited. Initial feedback demonstrates increased trainee confidence, enhanced role clarity, and positive team integration. Service capacity was maintained by embedding rotational roles alongside existing CNS provision. Formal evaluation will capture outcomes on recruitment, retention, and patient experience when the rotation programme completes in September 2026.

**Conclusion:** A rotational CNS trainee programme represents a sustainable approach to developing future breast CNS leaders. Early outcomes suggest it can strengthen workforce resilience, support succession planning, and ensure patients continue to receive expert, holistic care. Therefore, adopting a rotational training model could provide a replicable framework for other cancer CNS specialties, supporting national workforce strategies and addressing the growing demand for specialist nursing expertise.

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## Deep Learning Based Breast Lesion Segmentation from Ultrasound in Young Women

Srikanth Keshav Dataram Venkata<sup>1</sup>, Vivek Singh<sup>1</sup>

<sup>1</sup>Barts Cancer Institute, Queen Mary University of London, London, UK

**Background:** Breast cancer is one of the most common cancers worldwide and a leading cause of cancer-related death. In women under 45, it presents additional challenges due to denser breast tissue and more aggressive tumor types, making early detection and treatment more difficult. Accurate and timely diagnosis is therefore critical. Ultrasound is widely used for breast cancer evaluation because it is safe, cost-effective, and particularly useful for dense breast tissue, where mammography has limited

sensitivity. However, manual interpretation of ultrasound images is subjective and relies heavily on clinician expertise, often resulting in variability and inconsistencies in lesion detection. To address these challenges, automated lesion segmentation has received increasing attention in recent years. Deep learning-based methods have shown considerable promise by providing objective and reproducible delineation of tumor boundaries in ultrasound images. These approaches can improve diagnostic accuracy, reduce inter-observer variability, and support more reliable clinical decision-making, which is especially important in younger patients where early intervention is critical.

**Methods:** In this study, we trained and evaluated three state-of-the-art deep learning architectures, namely MobileViT, TransUNet, and Feature Pyramid Network (FPN), for breast lesion segmentation in ultrasound images using multiple publicly available datasets such as BUSI, BUS-BRA and BUS-UCLM that represent patients from diverse ethnic groups and demographic backgrounds. MobileViT combines lightweight convolutional networks with vision transformers, and TransUNet integrates transformer encoders with U-Net, capturing long-range dependencies while preserving fine spatial details for accurate lesion boundaries. The FPN captures multi-scale features to improve segmentation of lesions with varying sizes and shapes. To ensure robust and consistent results, we applied preprocessing and evaluated model performance using standard metrics, including Dice similarity coefficient and Intersection over Union. We also conducted ablation studies on input resolution and performed cross-dataset validation to assess generalizability across different imaging conditions and population subgroups.

**Results:** Our experimental findings show that TransUNet achieved the strongest and most consistent performance, achieving a Dice similarity coefficient of 73% and an Intersection over Union of 64% on the BUSI dataset. We found that an input resolution of  $384 \times 384$  pixels provided the best balance of accuracy and efficiency. Cross-dataset evaluation confirmed the models' robustness, with TransUNet achieving Dice scores of 73% on BUS-UCLM and 88% on BUSBRA. MobileViT showed Dice scores similar to FPN but higher IoU values, indicating more precise lesion boundary delineation.

**Conclusions:** This study shows that deep learning-based segmentation can provide accurate and reliable results for breast ultrasound, with hybrid CNN-Transformer models like TransUNet performing particularly well. These methods can reduce differences between clinicians, make workflows faster, and improve access to quality screening, especially in areas with limited resources. Future work should focus on making the models more robust and integrating them into clinical diagnostic tools.

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#### Expression of VEGF-C in stromal cells in primary breast cancer improves clinical nodal prediction models supporting omission of sentinel node biopsy

Oscar Hernquist<sup>1</sup>, Pauline Jeannot<sup>2</sup>, Pär-Ola Bendahl<sup>1</sup>, Linnea Fischhaber<sup>1</sup>, Emelie Edwardsson<sup>1</sup>, Charlotte Rolny<sup>1</sup>, Lisa Rydén<sup>1</sup>

<sup>1</sup>Lund University, Dept of Clinical Sciences Lund, Lund, Sweden, <sup>2</sup>Lund University, Dept of Translational Cancer Research, Lund, Sweden

**Background:** The sentinel node biopsy is today questioned in low-risk breast cancer patients undergoing breast-conserving surgery. Prediction models for nodal status can aid in supporting abstention of the procedure but merely include clinicopathological data. The biological mechanisms triggering lymphatic spread are largely unknown although cancer cell expression of vascular endothelial growth factor C (VEGF-C) has been implicated to promote lymph angiogenesis and nodal metastasis. Additionally, tumor associated macrophages expressing VEGF-C also drive lymphatic spread.

The aim of the study was to evaluate the nodal predictive information by VEGF-C expression in cancer and stromal cells by manual and script-based scoring. A secondary aim was to relate VEGF-C expression to outcome.

**Methods:** In a prospectively enrolled observational Swedish cohort (n=555), retrospective immunohistochemical staining of VEGF-C on tissue microarrays was evaluated by manual- and script-based QuPath scoring. Two independent assessors performed the semiquantitative manual scoring of cytoplasmatic VEGF-C intensity on cancer cells and the proportion of VEGF-C expressing stromal cells. The correlation between manual and QuPath scoring was assessed both in this cohort and in an

independent cohort. The association between VEGF-C expression in cancer and stromal cells and lymph node metastasis (LNM) was analyzed using multivariable logistic regression models, adjusting for established predictors of LNM. Performance was assessed by calculating the area under the ROC curve (AUC). Survival analysis was performed using Kaplan-Meier estimates, logrank tests and Cox regression models.

Results: Manual VEGF-C scoring was successfully performed in 440 patients and QuPath scoring in 401 of these patients, after exclusion of patients not fulfilling the inclusion criteria and cores not being assessable. The association between manual and QuPath scoring was strong (Spearman's rho=0.67) and confirmed in a separate cohort. In univariable analyses, higher stromal proportion of VEGF-C+ cells was associated with higher odds of LNM irrespective of method of assessment,  $p \leq 0.001$ , whereas VEGF-C expression in cancer cells was not predictive of LNM. Stromal proportion of VEGF-C+ cells was additionally predictive of LNM in the multivariable analysis and improved a predefined clinical prediction model. The AUC:s were 0.765 for the original model, 0.778 for the manual scoring model and 0.783 for the QuPath model. Interestingly, despite association with low risk of LNM, patients expressing a low proportion of VEGF-C+ in stromal cells had the worst survival in this cohort with >25 years of follow-up.

Conclusion: The proportion of VEGF+ stromal cells is an independent predictor of nodal metastasis. Script-based analysis is a replicable method for the assessment suitable for clinical implementation. The assessment should preferably be performed on core needle biopsies to add useful preoperative information for surgical decision making.

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## 6.1 Progress in supporting patients with metastatic breast cancer

Secondary breast cancer summit and patient experience of research

Carlo Palmieri - University of Liverpool, UK & Lesley Stephen - Make 2nds Count, UK

Professor Carlo Palmieri and patient advocate Lesley Stephen will present data and feedback on the UK's first Summits designed specifically for MBC patients. The Summits were designed to educate and empower patients; fill a gap in information covering medical and psychosocial issues; listen to their needs and concerns; and provide a networking opportunity to the community. This will be an annual event for the MBC community.

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Management of oligometastases in 2026

Mark Beresford - Royal United Hospital Bath, UK

*More information to follow*

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Local therapy for brain metastases

Sara Meade - University Hospitals Birmingham NHS Foundation Trust, UK

*More information to follow*

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## 6.2 Communication: harnessing new technology

Managing anger in the breast clinic: a VR training programme  
Val Shilling - University of Sussex, Brighton, UK

*More information to follow*

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You, me and the bot makes 3: influence of AI on consultations  
Richard Simcock - Macmillan Cancer Support, Brighton, UK

*More information to follow*

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Are remote consultations our new normal?  
Lesley Fallowfield - University of Sussex, Brighton, UK

Communicating well with patients is a core clinical skill which when done well has many positive impacts for all concerned; it improves the accuracy of history taking, influences physical and emotional well-being, affects adherence, reduces the risk of litigation and importantly lessens the risk of burnout in HCPs. Studies vary but around 65% of all communication is non-verbal and this can be severely compromised with telephone or video calls. Although some countries were already transitioning to digital solutions for pragmatic, geographical reasons, the COVID-19 pandemic irrevocably changed attitudes and practice with remote consultations becoming the new normal in many hospital and GP settings. Whilst offering some advantages, HCPs may need considerable help adapting to digital technologies that enable them to consult safely and competently with patients. There are genuine concerns about inherent system faults, the inability to examine patients physically as well as anxieties about privacy and other medico-legal liabilities. In this talk I will look at some of the research evidence regarding patient and clinician satisfaction with telemedicine and offer some tips and advice about developing a webside manner that complements a bedside one.

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## 6.3 What to do when a diagnosis of breast cancer collides with existing health disparities

Cancer inequities and unique breast cancer healthcare needs for LGBTIAQ+ community  
Alison Berner - Queen Mary University of London, UK

Both lesbian and bisexual women, and transgender men and non-binary people, are known to experience inequities throughout the breast cancer pathway. While poorer experiences of screening and treatment are well documented, the accurate data on incidence and outcomes are still lacking, so the full scale of the inequalities remain difficult to quantify.

While their cancer risk is lower than for cisgender women, trans men and non-binary people have unique needs with regard to surgical and hormonal management of breast cancer.

This talk will provide an overview of how to provide tailored, evidence-based and culturally humble care to these populations.

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Breast cancer inequities related to race & ethnicity & complex interplay between (epi)genetics & structural racism

Olubukola Ayodele - University Hospitals of Leicester NHS Trust, UK

*More information to follow*

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Challenges of delivering quality, comprehensive breast cancer care in LMICs and solutions  
Miriam Mutebi - Aga Khan University Hospital, Nairobi, Kenya

*More information to follow*

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## Poster Abstracts

*Posters listed alphabetically by presenting author surname*

### Transforming the Breast Cancer Now Biobank Data into the OMOP Common Data Model

**Maryam Abdollahyan<sup>1</sup>, Claude Chelala<sup>1</sup>**

<sup>1</sup>Centre for Cancer Biomarkers & Biotherapeutics, Barts Cancer Institute, Queen Mary University of London, London, UK

**Background:** Standardisation facilitates the governance and management of health data, improves their quality and ensures compliance with the FAIR principles of findability, accessibility, interoperability and reusability. It allows researchers to efficiently integrate health datasets and perform joint analysis on them, which promotes collaboration among various stakeholders and maximises translation of research outputs for patients' benefit. Common data models (CDMs) such as the Observational Medical Outcomes Partnership (OMOP) CDM by the Observational Health Data Sciences and Informatics (OHDSI) network are essential for standardisation. The OMOP CDM aims to harmonise observational health datasets and has been widely adopted by health data initiatives.

**Methods:** We describe the process of transforming the data for over 2,800 patients recruited at the Barts Cancer Institute (BCI) site of the Breast Cancer Now Biobank (BCNB) - the UK's first national breast cancer biobank hosting longitudinal biospecimens and associated data (clinical, genomic and imaging) from breast cancer patients at different stages of their care pathway - into the OMOP CDM. Furthermore, we report several challenges faced during the transformation process and explain how we addressed them.

**Results:** We present the breast cancer characteristics of the resultant patient cohort, i.e., the OMOP-mapped BCNB-BCI dataset. Our transformation pipeline achieved a high coverage, with 83% of source concepts mapped to the OHDSI standard vocabularies. Our OMOP CDM achieved a total pass percentage of 100% in validations using the OHDSI quality assessment tools. Moreover, we discuss the strengths and limitations of adopting the OMOP CDM and their implications for breast cancer research.

**Conclusion:** The OMOP-mapped BCNB-BCI dataset is a valuable resource for breast cancer researchers that can be explored and analysed alongside other breast cancer datasets using emerging methodologies such as federated learning.

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### Mammography AI Breast Cancer Risk Stratification in a UK Population

**Daniel Adams<sup>1,2</sup>, Reuben Frost<sup>1,2</sup>, Penny Coulson<sup>1</sup>, Amy Berrington<sup>1,2</sup>, Elizaveta Semenova<sup>3</sup>, Michael Jones<sup>1,2</sup>, Montserrat Garcia-Closas<sup>1,2</sup>**

<sup>1</sup>Division of Genetics and Epidemiology, The Institute Of Cancer Research, London, UK, <sup>2</sup>Cancer Epidemiology and Prevention Research Unit, The Institute of Cancer Research and Imperial College London, London, UK, <sup>3</sup>School of Public Health, Imperial College London, London, UK

**Background:** Accurate breast cancer risk prediction is essential for guiding personalised counselling and to inform prevention and screening strategies. Clinical risk scores, such as the Gail model, utilise risk factors like age, reproductive factors, medical and family history to estimate an individual's breast cancer risk. Recently, AI-based tools such as Mirai have been developed to estimate risk directly from mammographic images, with the potential for improved predictive performance. Understanding the features driving AI-based predictions and evaluating their performance compared to clinical scores in target populations is critical to assessing their potential value in risk-stratified screening and prevention.

**Methods:** Analyses included 205 breast cancer cases and 406 controls nested within the Generations Study, a prospective cohort in the UK. Digital mammography images were obtained from a screening cycle prior to cancer diagnosis for cases and a similar time for matched controls. Risk factors at the time of the mammogram were determined from recruitment and follow-up study questionnaires. We compared the discriminatory accuracy for 5-year breast cancer risk across Mirai, the Gail model, and Cumulus percent breast density using Harrell's C-index, with bootstrapped 95% confidence intervals. Cumulus density measurements were available on a subset of 83 cases and 153 controls. To evaluate

Mirai performance independent of breast density, we assessed the discriminatory accuracy of Mirai residuals after regression against Cumulus density. Furthermore, we investigated associations between the Mirai risk score with Gail component risk factors and Cumulus density among controls using linear models.

Results: In controls, older age at mammogram and positive family history of breast cancer were associated with higher Mirai scores, but differences were not statistically significant ( $p=0.06$  and  $0.08$ , respectively). Higher Cumulus breast density was significantly associated with higher Mirai risk scores ( $p\leq 0.001$ ). In the full case-control study ( $n=611$ ), Mirai demonstrated higher 5-year discrimination compared to the Gail model (Mirai: C-index 0.70, 95% CI 0.66–0.73; Gail: C-index 0.53, 95% CI 0.49–0.58). Within the subset with Cumulus density measurements ( $n=236$ ), Mirai also outperformed both Cumulus and the Gail model (Mirai: 0.65, 0.59–0.71; Gail: 0.53, 0.47–0.60; Cumulus density: 0.55, 0.49–0.62). Notably, Mirai risk discrimination was only slightly attenuated after adjusting for Cumulus density (Mirai residuals: 0.64, 0.58–0.70).

Conclusion: In this UK population, Mirai, an AI mammographic risk score, demonstrated superior 5-year risk discrimination compared to the Gail model and Cumulus breast density. This demonstrates that Mirai captures relevant mammographic information beyond that provided by traditional risk factors and density measures. These findings contribute to the growing body of evidence indicating that AI-based tools can substantially enhance breast cancer risk stratification. Further studies evaluating risk calibration and clinical utility in target populations are needed to determine the value of mammography AI in personalised screening and prevention.



#### Invasive lobular carcinoma in the breast and its association with residual cancer in re-excisions and locoregional recurrence (ISRCTN12077301)

Anna Allfelt<sup>1</sup>, Pär-Ola Bendahl<sup>1</sup>, Kim Gulis<sup>1</sup>, Lisa Rydén<sup>1</sup>, Julia Ellbrant<sup>1</sup>

<sup>1</sup>Lunds University, Lund, Sweden, <sup>2</sup>Region Skåne/South Swedish Health Care Region, Malmö, Sweden

Introduction: Invasive lobular carcinoma (ILC) is a known risk factor for positive margins after breast conserving surgery (BCS), but its association to residual cancer cells is not yet defined. The main aim of this retrospective observational study was to examine if positive margins and residual cancer cells in the surgical specimen after re-excision are associated with ILC and locoregional recurrence.

Methods: Female patients (>18 years) undergoing BCS for invasive cancer or ductal cancer in situ (DCIS) at site A 2015–2017 and site B 2017 were included in the study. BCS with positive margin was identified and data on residual cancer in re-excised specimens, recurrence, and death was collected from patient medical records and validated through the Swedish quality register for breast cancer 2024. The primary endpoint was the proportion of patients with residual cancer cells in re-excisions and its association with ILC. The secondary endpoints were locoregional recurrence-free interval (LRFi), distant recurrence-free interval (DRFi) and breast cancer specific survival (BCSS).

Results: 770 patients, median age of 63 (interquartile range (IQR) 53–70), undergoing BCS (65% breast cancer of no specific type (NST), 12% ILC, 12% DCIS and 11% other invasive/in situ) were included. 132 patients (17%) had positive margins, 130 accepted re-excision of whom 80 (62%) had residual cancer cells (15% NST, 26% ILC, 54% DCIS and 5% other invasive/other in situ). ILC in comparison to NST was only weakly associated with residual cancer in the re-excision specimen (OR 1.5 (95% CI 0.58–3.92)). In univariable analyses, the strongest predictors of residual cancer were tumor size  $\geq T2$  (OR 3.4 (95% CI 1.25–9.12) and number of positive margins  $>1$  (OR 2.2 (95% CI 1.01–4.88)). Seventeen patients (13%) had positive margin at 1st re-excision and accepted a 2nd re-excision of whom 13 (76%) had residual cancer cells (23% NST and 77% DCIS). None had a positive margin at 2nd re-excision. Of the 130 patients eligible for re-excision, 61 (46%) had mastectomy as a final surgery. Thirty-four patients (4.5%) developed locoregional recurrence with a median follow-up time for recurrence-free survivors of 7.0 years (IQR 6.2–8.0). No evidence for difference in LRFi, DRFi, or BCSS by positive margins or residual cancer cells were observed (all  $P > 0.9$ ).

Conclusions: ILC was only weakly associated with residual cancer in re-excised specimens, whereas DCIS was most common among patients with residual cancer after 1st and 2nd re-excision. The locoregional recurrence rate was 4.5% with a median follow-up time for recurrence free survivors of 7 years, indicating excellent locoregional control despite a high re-excision rate. Positive margin and residual cancer in re-excisions were not found to be associated to LRFi, DRFi and BCSS. Longer follow up is warranted.

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## Incidence and Outcomes of Incidental Breast Lesions Detected on Non-Breast Cross-Sectional Imaging Examinations

Jaya Anand<sup>1</sup>, Khai Wen Ang<sup>1</sup>, Sarah McGarrigle<sup>2</sup>, Dhafir Alazawi<sup>2</sup>, Terry Boyle<sup>2</sup>, Elizabeth Connolly<sup>2</sup>

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The widespread use of cross-sectional imaging techniques such as magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) facilitates the diagnosis and management of various medical conditions. These imaging modalities sometimes detect incidental findings in parts of the body that were not the intended focus of clinical concern, including incidental breast findings.

The aim of this study was to investigate the frequency and outcomes of patients referred to the breast clinic at St. James's Hospital with incidental breast lesions detected on non-breast cross-sectional imaging. A retrospective review of the departmental breast database was performed to identify patients referred with incidental breast lesions detected on cross-sectional imaging. Data were collected on cross-sectional imaging modalities, patient demographics, follow-up and outcomes. Data were analysed using descriptive statistics.

76 patients with a median age of 68.5 years, were referred to the Breast Clinic from external hospitals from January 2022 to December 2023 with incidental breast findings on cross-sectional imaging. The majority (82.9%) of incidental breast findings were identified on CT imaging with 9.2% and 7.9% of incidental breast findings identified on PET and MRI respectively. 63 patients (82.9%) were worked-up with dedicated breast imaging at our institution. Of these, 29 (46%) underwent biopsy and 15 (23.8%) were proven to have a breast malignancy.

Among malignant cases, invasive ductal carcinoma was the most common histological subtype (53.3%), followed by invasive lobular carcinoma (20%), invasive mammary carcinoma (13.3%), and ductal carcinoma in situ (13.3%). Clinical staging at diagnosis demonstrated that 46.7% presented at stage 0 or I, while 20% were stage II and 13.3% were stage III or IV. Tumour grading revealed the majority were grade 2 (66.7%), with smaller proportions of grade 1 (6.7%) and grade 3 (13.3%). The average tumour size was 26.25 mm, and none had lymph node positive disease.

This study highlights the importance of referring patients with incidental breast findings on cross-sectional imaging to the breast clinic for appropriate follow-up with dedicated breast imaging.

Keywords: Incidental breast lesion, cross-sectional imaging, breast cancer

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## Audit of Essential Oil Pessaries (EOPs) for Urogenital Atrophy (UA)

Jacqui Stringer<sup>1,2,3</sup>, Anne Armstrong<sup>1</sup>, Daisy Hopper<sup>1</sup>

<sup>1</sup>The Christie NHS Foundation Trust, Manchester, <sup>2</sup>Division of Cancer Sciences, University of Manchester,

<sup>3</sup>Royal London Hospital for Integrated Medicine / University College London Hospital

Background: Breast cancer is the most common malignancy among women in developed countries. Treatments can lead to Genitourinary Syndrome of Menopause (GSM), which can reduce quality of life and cause treatment discontinuation (1). Endocrine therapies often trigger early menopause by affecting ovarian reserves and vaginal tissue, leading to symptoms such as dryness, burning, bleeding, dyspareunia, and urinary discomfort (2).

Topical oestrogens are standard care for GSM but are under-researched and may pose recurrence risks. The Christie NHS Foundation Trust offers an alternative: a cocoa butter pessary containing essential oils from the Poaceae, Geraniaceae, and Asteraceae families (EOP), known for anti-inflammatory and antimicrobial properties. Previous evaluations suggest effectiveness, and in-vitro testing confirms EOPs do not mimic oestrogen (3). However, this audit is the first time they've been audited since being manufactured to GMP standards.

This audit was approved (Project No. 3693).

**Methods:** Patients with GSM symptoms undergoing breast cancer treatment were referred for EOP therapy. Those deemed suitable provided written informed consent, as EOPs are not a licensed product. Patients received verbal and written instructions, with a standard recommendation to insert one pessary six nights per week for two months. Following that, dosage is adjusted based on clinical need.

Each patient was assessed using a likert-scale, symptom grading system adapted from Lenson et al (4)., 1 (as good as can be) to 10 (as bad as can be):

1. Pain during sex
2. Vulvovaginal dryness
3. Vulvovaginal discomfort or irritation
4. Pain when urinating
5. Distress from symptoms

**Outcomes:** As formal outcome measures are not yet established, patients re-rated their symptoms at the end of months 1 and 2 to monitor changes. They also reported side effects and overall satisfaction with treatment, in line with recommendations (4).

**Results: Demographics:**

Age: 42–71 years (mean: 52)

Endocrine Treatment: Tamoxifen (n=3), Tamoxifen + GnRH agonist (n=1), Aromatase inhibitors (n=4), Aromatase inhibitors + GnRH agonist (n=1), Fulvestrant (n=1)

Previous GSM Treatment: None (n=5), hormone-free moisturiser (n=3), moisturiser + oestrogen cream (n=1), oestrogen cream only (n=1)

Clinic based outcome scores (See table 1).

Table 1 - Clinic based outcome scores

Symptom	Average baseline score	Range of baseline scores	Average 2-month score	Range of 2-month scores	Average improvement score	Excluded Patients: Did Not Report Symptom
Pain with sex	8	6 – 9	4	1 – 9	4	2
Vulvovaginal dryness	6	3 – 10	2	1 – 5	4	0
Vulvovaginal discomfort or irritation	6	2 – 8	2	1 – 4	4	4
Discomfort or pain when urinating	5	2 – 10	3	1 – 5	2	3

\* Small sample size—averages rounded to whole numbers.

Excluding scores for symptoms not experienced, 93.6% of symptom ratings improved by at least one point, 87.1% by two or more points, and 80.7% by three or more. Patient satisfaction was high (average score: 9), with no reported side effects, supporting broader treatment benefit.

Outcome 5 (distress from symptoms) was excluded from analysis due to a high proportion of responses unrelated to GSM-specific symptoms.

Conclusion: The results indicate that EOPs have a positive impact on GSM symptoms, including in the 20% of patients who had previously not responded to oestrogen cream. As the audit remains ongoing, a full evaluation will be conducted upon completion of the final dataset (N=20).

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Personalised Therapy in Triple Negative breast cancer (TNBC), evaluating predictive performance of Bayesian AI Digital Twins

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Background: Despite multiple therapeutic strategies, approximately 40% of women with stage 2-3 Triple Negative breast (TNBC) cancer die. Biomarkers are sparse and treatment related toxicities can be significant, especially when drugs fail.

Objective: Evaluate FarrSight®-Twin, a predictive tool for treatment response in TNBC based on integrating multi-modal clinico-pathological and genomic data, and assess its ability to prospectively identify patients unlikely to achieve a pathological complete response (pCR) and benefit less from neoadjuvant chemotherapy.

Methods: VISION, an observational retrospective clinical study (n=200 RMH, UK) analysed the performance of the predictive algorithm FarrSight®-Twin. Study population included stage 2-3 TNBC, treated with neoadjuvant chemotherapy+/-immunotherapy (IO). Participants were recruited into Arm A (pCR) or Arm B if they had residual disease (non-pCR). Digital or virtual twins of individuals were created using their clinical data, cancer stage and tumour molecular data (WES (n=66), RNA seq n=(43), WES + RNAseq (n=42)) from an FFPE diagnostic biopsy. Treatment response and overall survival were predicted for each individual. Performance and accuracy were assessed by comparing predictions against real outcomes.

Results: In this pre-planned analysis, 34 women were recruited into Arm A and 60 into Arm B with a median age of 51 (24-77yrs). 87% stage 2 (n=82) and 13% stage 3(n=12).

Neoadjuvant treatments administered were: anthracycline-taxane (33%), anthracycline-taxane-platinum (34%) or anthracycline-taxane-platinum-IO (21%) or Other. pCR was used to assess treatment response. pCR rates were highest for anthracycline-taxane-platinum-IO (50%). Similar pCR rates were reported for anthracycline-taxane (35%) and anthracycline-taxane-platinum regimens (31%). "Other" regimens consisting of de-escalated regimens following on treat toxicities and these women had pCR rates of 27%.

Overall, 95% of women were alive at the 1 year time point (1 death; n=4 not reached), which dropped to 73% (7 deaths; n=19 not reached) alive for the study population.

In the first interim analyses we present FarrSight®-Twin accuracy for predicting pCR using the leave one out approach. Following inputs were used: age, tumour type, clinical tumour size (cT), clinical nodal stage (cN) and molecular data from a diagnostic FFPE breast biopsy.

Prediction accuracies for pathological complete response and different chemotherapy drug classes are reported in Table 1.

Predicting pCR for different neoadjuvant chemotherapy regimens.	N	AUC	Accuracy	Positive predictive value	Negative predictive value
			$\frac{TP+TN}{TP+TN+FP+FN}$ Total predictions	$\frac{TP}{TP+FP}$	$\frac{TN}{TN+FN}$
Mutation data (DNA)	66	0.77	71%	60%	74%
Mutation data + RNA seq data	42	0.62	67%	50%	70%
Predicting response for different chemotherapy classes.	N	AUC	Accuracy	Positive predictive value	Negative predictive value
Anthracycline		0.76	66%	49%	89%
Taxane		0.73	65%	49%	83%
Carboplatin		0.69	66%	50%	79%

Table 1

Conclusion: FarrSight®-Twin integrates molecular data from routine diagnostic FFPE samples with limited clinical information, making it both scalable and suitable for incorporation into standard care pathways. In stage II-III TNBC, it accurately predicts an individual patient's probability of non-response or suboptimal response (i.e., non-pCR) to neoadjuvant chemotherapy, an outcome observed in 50-70% of this population.

Does Language act as a Barrier to Early Breast Cancer Diagnosis? The Berkshire Experience

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Introduction: Breast cancer is a leading cause of morbidity and mortality among women worldwide, with early detection critical for improving survival outcomes. De novo metastatic breast cancer accounts for approximately 6% of all new breast cancer diagnoses<sup>1</sup>. In the UK, disparities in diagnosis and prognosis have been reported among women from ethnic minority, particularly those with limited English proficiency<sup>2,3</sup>. Non-English speaking women, especially within South Asian communities, are more likely to experience delayed diagnosis<sup>4</sup>. According to the Office for National Statistics, approximately 90% of residents in the Reading, Wokingham and West Berkshire area speak English as their first language, thus a significant minority may face communication barriers within healthcare<sup>5</sup>.

Objective: To assess whether de novo metastatic breast cancer is more prevalent in non-English speakers in Berkshire and to consider the differences in presentation.

Methods: We retrospectively reviewed the metastatic breast cancer CNS caseload from January, 2023 to December, 2024. Patients diagnosed with Stage IV disease were stratified by whether English was their first language. Demographic characteristics, T-stage at presentation, and proportions of symptomatic presentation were compared.

Results: Thirty-four patients were diagnosed with de novo metastatic breast cancer over a two year period. Fourteen (41%) did not have English as their first language, higher than the 10% reported locally (ONS 2021). The median age of the whole cohort was 65 years (35-96); the median age was 52.2 years in the non-English speaking cohort versus 73.6 years among English speakers. This suggests differences in screening uptake may contribute. Nineteen patients presented with symptoms of metastatic disease; 12 were English speakers, most aged >70, while all symptomatic non-English speakers were <70. T-stage distribution showed 14% T3 and 0% T4 among non-English speakers, versus 25% T3 and 10% T4 in English speakers.

Conclusion: Language barriers may contribute to delayed breast cancer diagnosis in non-English speaking women in Berkshire. Improved access to interpreters, culturally sensitive communication, and targeted awareness campaigns are needed to reduce disparities and improve equity in care.

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## Adherence to WCRF cancer prevention recommendations before and after chemotherapy: results of the Pre-Nutritive feasibility trial

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Chemotherapy is the main systemic treatment for triple-negative breast cancer (TNBC), but not all patients respond equally. Failure of chemotherapy to eradicate disseminated cancer cells can lead to distal metastatic relapse. Predicting which patients will and which will not respond to different chemotherapy agents remains challenging. The World Cancer Research Fund (WCRF) has developed recommendations for cancer prevention; adherence to these recommendations is associated with reduced risk of developing breast cancer and with improved survival. The relationship between adherence to WCRF recommendations and chemotherapy effectiveness in TNBC patients has not been examined. The Pre-Nutritive trial (ISRCTN20130557) was set up to assess the feasibility of collecting and integrating data regarding diet, lifestyle, tumour response to treatment, as well as clinical and anthropometric metrics. Pre-Nutritive is a prospective, non-randomised feasibility study conducted at Leeds Teaching Hospitals NHS Trust (LTHT), UK. Ethical approval was obtained from the West Midlands, Solihull Research Ethics Committee (IRAS Project ID: 311845). Women with newly diagnosed TNBC were recruited between January 2022 and January 2025. Dietary intake was assessed using a Food Frequency Questionnaire (FFQ) and 24-hour dietary recall via Myfood24. Physical activity was measured using the EPAQ2 questionnaire. The WCRF adherence score was determined using a previously operationalised method, and each patient was scored out of a maximum composite score of seven or eight. Blood samples (serum and plasma) were collected for lipidomic analysis, and tumour biopsies were obtained for RNA sequencing. Data were collected pre- and post-chemotherapy. Fifty TNBC patients were identified; 26 were approached, and 15 were recruited. One participant dropped out, blood samples were collected from 14 (93.3%), 13 completed the dietary and physical activity questionnaires (86.7%), and seven provided tumour biopsies (46.7%). The median age was 51 (IQR = 50 – 59) years. Participants had a median BMI of 26.5 (IQR = 23.70 – 32.90) kg/m<sup>2</sup>. WCRF adherence percentage score was unchanged (P = 0.694) between pre- and post-chemotherapy (Pre-chemotherapy median = 4.50, IQR = 3.75 – 5.00; post-chemotherapy median = 3.25, IQR = 2.75 – 3.87). For individual scores, physical activity adherence significantly decreased after chemotherapy (P = 0.038), whereas adherence to alcohol consumption increased significantly after chemotherapy (P = 0.046). Statistically significant reduction was not observed for other WCRF recommendations (P > 0.05).

This study showed that recruiting and data collection in TNBC patients is feasible. However, the low number of biopsies collected is a challenge. A larger study with participants from multiple centres is needed to assess changes in adherence. Adherence to WCRF cancer prevention recommendations may vary during treatment, and support may be needed to help patients maintain PA levels and associated lean muscle mass during treatment.

## Implementation of Mainstream Genetic Testing within a High-Volume breast Unit for Pathogenic Variations Associated with Breast Cancer Using R208 and R444.1 National Test Directory Criterion

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**Introduction:** It is estimated that 5-10% of patients who develop breast cancer have a causative inherited genetic variant. Historically, genetic counselling, testing and delivery of genetic results was undertaken by clinical geneticists. However, in 2018 the UK National Genomic Test Directory published criteria for mainstream genetic testing in patients with a diagnosis of breast cancer - R208. This aimed to streamline access to genetic testing by enabling non-genetic specialists to counsel and test eligible patients. In 2023 further criteria (R444.1) were introduced with a view to identify patients who would benefit from treatment with a PARP inhibitor. By identifying pathogenic variants (PV) during the treatment pathway, we enable patients to make informed decisions about their surgical and oncological treatments. In this study we asked what is the incidence of PV within our cohort, and how did this impact treatment decisions?

**Methods:** Between March 2021 and March 2025 eligibility for testing under the R208/R444.1 criteria was determined for all patients with a new diagnosis of breast cancer. Eligibility for testing under R208 was assessed using clinical parameters and family history data. Eligibility for testing under R444.1 was assessed based on diagnostic and post operative histology. Patients were offered genetic testing alongside targeted counselling. Incidence of PV and the impact test results had on treatment decisions, were examined.

**Results:** 1812 patients were newly diagnosed with breast cancer. 239 of these patients were eligible for testing, of which 190 consented. Of the 190 patients tested 28 (14.7%) were found to have a PV. 27 patients were found to have a PV under R208 testing, of which eight were only eligible under the family history score. Three of 27 were eligible for a PARP inhibitor. Eight patients who were not eligible for genetic testing under R208 were eligible under R444.1. One of these was shown to have a PALB2 mutation. Of the 27 patients found to have a PV under R208 criteria, 20 were eligible for breast conservation surgery, pre-operative genetic results were available for 13 and eight patients opted for bilateral mastectomy rather than breast conservation. Where results were available post-operatively, three of six patients who had breast conservation are planning bilateral risk reducing surgery.

**Conclusion:** 14.7% of patients eligible and tested for a breast cancer-related hereditary genetic variant were positive. This aligns with the expected number predicted by Genomics UK ( $\geq 10\%$  probability). Testing changed surgical decision-making for 55% of patients who tested positive and enabled 3 patients to receive a PARP inhibitor - indicating that genetic testing has an impact on clinical practice. However, this vital part of patient work up is incredibly time consuming, and a decision-making algorithm should be considered to enable a stream-lined and efficient eligibility assessment.

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# The association of house value with stage at diagnosis and survival in breast cancer patients - results from a population-based cohort study in Northern Ireland

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**Background** Socio-economic inequalities in breast cancer survival persist globally, including in the UK.: House value of residence has been shown to be a useful measure of individual-level socio-economic status in the UK. We aimed to examine stage at primary diagnosis and breast cancer-specific mortality in a population-based cohort of breast cancer patients in Northern Ireland (NI).by house value of residence at primary diagnosis and also compared results with traditional area-based deprivation measures (e.g. Multiple Deprivation Measures (MDMs).

**Methods:** Women diagnosed with primary breast cancer between 2011 to 2021 (12 years) were identified using the Northern Ireland Cancer Registry. House value was determined from Valuation and Lands Agency property valuation data, and area-based deprivation was determined from the NI Multiple Deprivation Measure (NI MDM). The primary outcome was breast cancer-specific mortality. Secondary outcomes included stage at diagnosis. Cox regression models calculated adjusted hazard ratios (HR) and (95%CIs) for cancer-specific mortality by house value category and separately for deprivation, adjusting for confounders.

**Results:** The final cohort included 12,766 women with breast cancer. Associations were much more pronounced for house value than area-based deprivation. Women in the lowest house value category (under £75,000), compared to the highest value category (over £200,000), were more likely to be diagnosed with stage 4 disease (7.5% versus 4.1%;  $P<0.001$ ) and had a 60% increase in mortality (adjusted HR=1.60 95%CI 1.34, 1.92). In contrast, when considering traditional area-based deprivation measures (based on Multiple Deprivation Measures) women living in the most versus least deprived areas were not more likely to be diagnosed with stage 4 disease (5.9% vs 5.0%;  $P =0.157$ ) and had only a 26% increase in mortality (adjusted HR=1.26 95%CI 1.08, 1.47).

**Conclusions:** Individual patient-level house value was more strongly associated with breast cancer stage at diagnosis and survival outcomes than traditional area-based socio-economic and deprivation measures (e.g. Multiple Deprivation Measures). House value may serve as a more sensitive indicator for monitoring health inequalities in breast cancer patients, helping inform targeted interventions aimed at reducing these inequalities.

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## The risk of contralateral breast cancer after radiotherapy and hormonal therapy in the NCI-Kaiser Permanente Breast Cancer Survivors Cohort

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**Background:** Incidental radiation exposure to the contralateral breast from radiotherapy increases contralateral breast cancer (CBC) risk. Hormone therapy decreases ER+ CBC risk. The combined effect of these treatments on this risk is not known.

**Methods:** The NCI-Kaiser Breast Cancer Survivors Cohort is a retrospective record linkage study with detailed hormonal therapy prescription data, radiotherapy treatment information (including fields, prescribed dose, wedge placement and angles) and cancer registry linkage for subsequent cancer diagnoses. We included 5-year breast cancer survivors aged 20–84 years who had an incident stage I–III cancer diagnosis between 1990 and 2012, and who had survived for at least five years, followed-up for subsequent cancers and mortality to 2017. Radiation dose was estimated for each quadrant of the contralateral breast for a subset of patients (n=2442, 25%) using a comprehensive set of out-of-field measurements of absorbed dose for a variety of breast radiotherapy beam configurations. Doses were then calculated for the rest of the cohort using a custom deep neural network. The network was trained to predict doses from each radiotherapy field using abstracted treatment parameters and the previously reconstructed doses as the ground truth. We used multivariable Poisson regression to estimate relative risks (RRs) and the radiation dose-response as the excess relative risks per Gray (ERR/Gy), stratified by hormone therapy use and ER-status of the contralateral breast cancer.

**Results:** The cohort included 9,053 five-year breast cancer survivors; 353 developed CBC (73% ER+ CBC) during a mean follow-up of 6 further years. Among women with ER+ first breast cancer, radiotherapy increased the risk of ER+ CBC in non-users of hormonal therapy (RR=2.20, 95% CI:1.20–4.14), but not in hormonal therapy users (RR=0.88, 95% CI:0.61–1.26). The upper inner quadrant of the contralateral breast received the highest radiation dose, which decreased over time from a median dose of 1.8Gy in 1990 to 1.1Gy in 2012 from (mostly) 50Gy tangential fields. There was a dose-response for radiation dose for ER+ CBC among non-users of hormone therapy (ERR/Gy=1.39, 95% CI:0.33–3.66), but not among users (ERR/Gy=−0.13, 95%CI: -0.36–0.23). Radiotherapy was also associated with an elevated risk of ER- CBC (RR=1.85, 95%CI: 0.95–3.59), but there were too few cases for a dose-response analysis.

**Conclusions:** Radiotherapy was associated with increased CBC risk, but hormonal therapy appeared to mitigate the risk of ER+ CBC. Radiation dose to the contralateral breast decreased over time and may have decreased further since the study period with lower prescribed doses. The potential for hormone therapy to prevent radiation-related cancers has potential implications for other breast cancer patients exposed to high-dose chest radiation.

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## Building Confidence in SACT Supportive Care: Pilot Evaluation of the Confirm for SACT Programme

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**Background:** Systemic Anti-Cancer Therapy (SACT) is associated with significant side-effects, requiring timely recognition and management by clinicians across oncology teams. While final prescribing authority rests with senior oncologists, early-career doctors including Foundation doctors, Internal Medicine Trainees (IMTs), and doctors starting oncology registrar training frequently encounter patients undergoing SACT and play an important role in supporting their care. To address this training gap, we developed the

Confirm for SACT programme, a structured e-learning initiative aimed at enhancing knowledge, confidence, and skills in supporting patients (including those with breast cancer) receiving SACT and recognising common side-effects of treatment

Research Question: Does the Confirm for SACT programme improve early-career doctors' (Foundation, IMT, and Oncology Speciality doctors) in postgraduate training confidence and competence in supporting patients undergoing SACT, particularly in recognising and managing complications?

Methods: A pilot run of the Confirm for SACT programme was conducted with 22 participants: 17 Oncology registrars, two IMTs, and three Foundation Doctors. The programme comprised approximately nine hours of interactive video modules, quizzes, and case-based examples. Participants completed structured post-course questionnaires assessing clarity, relevance, coverage of complications, understanding of management, pacing, confidence in supporting patients on SACT, and overall satisfaction. Quantitative data were analysed descriptively, and free-text responses were thematically reviewed.

Results: Participants reported high satisfaction with clarity of content (mean 8.62) and relevance of examples in the content (mean 8.08). The programme improved understanding of complications which have a mean value of 8.23 and confidence in supporting patients undergoing SACT with a mean value of 7.77. Foundation Doctors reported the greatest improvement in confidence (mean 9.7). Strengths included comprehensive content, logical flow, and useful resources. Suggested improvements included: (1) clearer MCQ answer explanations, (2) shorter module duration, (3) expanded coverage of immune-mediated toxicities and practical case examples, and (4) provision of downloadable slides/resources. The likelihood of recommending the course was high with an average value of 8/10.

Conclusion: The Confirm for SACT pilot demonstrates the value of targeted training for Foundation Doctors, IMTs, and Oncology registrars, equipping them with greater confidence to support patients and manage complications of systemic anti-cancer therapy. While the programme does not confer authority to prescribe or sign off SACT, it addresses an important skills gap for early-career clinicians. Constructive feedback will guide refinements, with further development planned to expand content and scope.

Keywords: Systemic Anti-Cancer Therapy (SACT), Oncology Registrars, Internal Medicine Trainees (IMT's), Foundation Doctors

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Audit of Axillary Node Clearance: Evaluating Sentinel Node Ratio as a Predictor of Residual Nodal Disease and Its Impact on Adjuvant Therapy Initiation

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Introduction: The management of the axilla in breast cancer continues to evolve, with an increasing emphasis on surgical de-escalation. Sentinel lymph node biopsy (SNB) has largely replaced routine axillary nodal clearance (ANC) in clinically node-negative patients, minimising morbidity without compromising oncological safety. Nevertheless, ANC is still performed in selected cases, particularly when nodal involvement is confirmed or highly suspected. While SNB provides valuable staging information, there are currently no robust predictive tools to determine the likelihood of residual nodal disease following a positive SNB. Previous studies have suggested that the ratio of positive to total sentinel nodes may help identify patients at low risk of further nodal involvement, potentially sparing them from ANC. In addition to oncological safety, there is growing concern that extensive axillary surgery may delay the initiation of adjuvant therapy due to postoperative complications, thereby influencing long-term outcomes.

This audit aims to evaluate the role of SNB ratios in predicting negative ANC and to assess whether undergoing ANC has an impact on the timeliness of adjuvant therapy initiation.

Methods: A retrospective audit will be conducted of all patients who underwent axillary nodal clearance between January 2022 and December 2024 at Altnagelvin Hospital. Electronic medical records and

operative databases will be reviewed. Inclusion criteria will be women with invasive breast cancer undergoing ANC following an initial SNB.

Data collected will include patient demographics, tumour characteristics (size, grade, receptor status), number of sentinel nodes excised, number of positive sentinel nodes, SNB ratio (positive/total nodes), total nodal yield from ANC, and number of additional positive nodes. Timing of surgery, postoperative recovery, and dates of initiation of adjuvant systemic therapy (chemotherapy and/or endocrine therapy) will also be recorded. Complications such as seroma formation, wound infection, or delayed healing will be documented.

**Results:** As this is an ongoing audit, results are not yet available. It is anticipated that analysis will focus on whether a low SNB ratio ( $\leq 0.33$ ) predicts a negative ANC and whether ANC is associated with a clinically significant delay in initiating adjuvant treatment compared with standard targets (e.g.,  $\leq 6-8$  weeks from surgery).

**Conclusion:** This audit will provide real-world evidence from a contemporary patient cohort on the predictive value of SNB ratio for residual nodal disease and on the potential impact of ANC on the timing of adjuvant therapy. Findings may support refinement of axillary management pathways and highlight opportunities to safely reduce the use of ANC, thereby minimising morbidity and ensuring timely delivery of systemic treatment.



### Physical Activity and Breast Cancer Recurrence and Survival in The Breast Cancer Now Generations Study

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**Background:** Interest is growing in the role of physical activity in improving cancer outcomes. Evidence suggests that higher physical activity before and after diagnosis is associated with reduced risk of all-cause mortality, breast cancer mortality, and breast cancer recurrence. The quality of the existing evidence is limited due to small number of participants, few events, and potential biases. Causal inference methods can be used to obtain higher quality evidence with observational data. The Breast Cancer Now Generations Study (GS) is a longitudinal observational study with long follow up and a rich array of data, including repeat questionnaires and detailed tumour characteristics. We will utilise a survivor cohort embedded in the GS to investigate pre-diagnostic and post-diagnostic physical activity and breast cancer survival and recurrence outcomes with quantitative bias assessment methods.

**Methods:** Physical activity was ascertained from questionnaires immediately before and after breast cancer diagnosis. Women reported frequency of different activity types during a typical week in the past year. Duration and Metabolic Equivalent of Task (MET) values were used to calculate total and leisure-time MET hours per week (MET-h/w). We are implementing causal inference principles to guide the analysis and minimise biases. Survival analysis is underway, with quantitative bias analysis planned to quantify any residual bias.

**Results:** There were 4,891 participants diagnosed with incident breast cancer between 2004–2024; 19% in situ cases; 46% pre-menopausal. Where stage and ER status were known, 73% were stage 1-2 and 85% were ER-positive. Mean age at diagnosis was 60 years. There were 365 breast cancer deaths, 233 deaths from other causes and 529 distant recurrences. About a third of participants were either inactive or did not meet WHO physical activity guidelines (equivalent of 9 MET-h/w) either before or after breast cancer diagnosis. Over a third of participants had pre- and post-diagnostic physical activity levels that exceeded the guidelines at least three times ( $>27$  MET-h/w). The analysis is in progress and results for physical activity and breast cancer outcomes will be presented.

**Conclusions:** High quality evidence on physical activity and breast cancer survival and recurrence is needed to inform clinical decision making. Previous evidence is limited due to quality issues of existing studies. We did not find similar studies in the UK. An advantage of GS is the access to tumour

characteristics, treatment and recurrence data. Furthermore, in GS, pre-diagnostic physical activity was assessed prospectively, whereas in other studies it is usually recalled retrospectively. We are using principles of causal inference to minimise common biases at study design and plan to incorporate quantitative bias analysis. Our findings will strengthen the evidence base for developing physical activity guidance for women living with or beyond breast cancer.

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## Enhancing GP Trainee Competence in Breast Disease Assessment: A Pilot Interdisciplinary Training Programme

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**Background:** General Practitioners (GPs) are the first point of contact for patients presenting with breast symptoms. However, variability in trainee confidence in examination, referral, and patient communication may compromise the quality of referrals to secondary care. To address this, a collaboration between the RCS Surgical Tutor and the GP Training Programme Director (TPD) developed a pilot supervised training initiative, enabling GP trainees to develop competencies by attending consultant-led breast clinics.

**Methods:** GP trainees were invited to attend breast clinics, gaining structured exposure to clinical assessment and patient counselling. A competency-based questionnaire was administered to 9 trainees who attended the breast clinic and 6 who did not. Domains assessed included breast examination, referral decision-making, preparing patients for referral, explaining the breast clinic process, discussing intimate health issues, and promoting breast screening. Confidence was rated on a five-point Likert scale, with "very" and "extremely confident" combined to represent high confidence. Proportions of high confidence were compared between groups using Fisher's exact test.

**Results:** In this ongoing study, fifteen GP trainees participated (9 attenders; 6 non-attenders). Attenders consistently reported greater confidence across all domains. For breast examination, 8/9 attenders (88.9%) reported high confidence compared with 0/6 non-attenders ( $p=0.002$ ). Referral decision-making confidence was 8/9 (88.9%) versus 0/6 ( $p=0.002$ ). Preparing patients for referral was reported by 8/9 (88.9%) attenders compared with 1/6 (16.7%) non-attenders ( $p=0.01$ ). Confidence in explaining the breast clinic process was 9/10 (90.0%) for attenders versus 2/6 (33.3%) for non-attenders ( $p=0.04$ ). Discussing intimate health issues was endorsed by 8/9 (88.9%) attenders versus 0/6 ( $p=0.002$ ). Promoting breast screening was reported by 6/9 (66.7%) attenders compared with 0/6 ( $p=0.03$ ). Across all domains, differences were statistically significant in favour of attenders.

**Conclusion:** Attendance at supervised breast clinics was strongly associated with significantly higher confidence in clinical and communication competencies among GP trainees. These findings highlight the educational value of breast clinic attachments, supporting their integration into GP training curricula to strengthen the role of primary care in the breast cancer diagnostic pathway.

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## Leveraging Telehealth for the Prevention of Breast Cancer: A Systematic Review

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**Background:** Breast cancer stands as one of the most prevalent cancers among women, underscoring the need for robust and evolving strategies in prevention and management. In recent years, telehealth has emerged as a pivotal tool for remote patient engagement, education, and monitoring across various preventive health domains. This is particularly relevant for breast cancer prevention, where consistent engagement, risk factor modification, and screening adherence are crucial for reducing incidence and improving outcomes. This systematic review aims to explore and highlight the synergistic impact of optimized screening protocols and telemedicine in transforming breast cancer prevention.

**Methods:** A systematic review was performed based on a systematic search of literature published from 2014 to 2024, conducted in MEDLINE and PubMed, using keywords "breast cancer", "breast malignancy",

"screening", "teleconsults," "telemedicine," and "telehealth." The search was limited to English-language journals, with the 10-year publication limit applied to ensure relevance to recent advancements in telemedicine. Inclusion criteria focused on studies discussing telemedicine and its application in breast cancer prevention or related care, while studies not discussing telemedicine were excluded. Prior to inclusion, studies were evaluated for relevance and applicability to the research question. Included studies were analyzed for methodology, sample size, data collection methods, and key findings.

**Results:** The literature search yielded 19 studies which met the inclusion criteria for analysis. Telemedicine demonstrates significant potential in enhancing breast cancer prevention by increasing access to preventive services, particularly for rural or underserved populations, through remote education on risk factors, self-exams, and lifestyle modifications. Virtual consultations facilitate early detection by enabling clinicians to identify high-risk individuals and direct them to appropriate screening, such as mammography, which significantly improves prognosis. Telehealth also provides ongoing support and symptom monitoring, allowing for regular follow-up and timely intervention if abnormalities arise. Furthermore, telemedicine interventions, including eHealth and mHealth platforms, promote healthy behaviors (e.g., smoking cessation, weight management) associated with lower breast cancer risk. By reducing travel needs and scheduling barriers, telehealth enhances the reach and equity of preventive care delivery, benefiting those facing logistical or financial obstacles.

**Conclusion:** While telemedicine offers substantial benefits, it is important to acknowledge its limitations: it cannot fully replace physical examinations or diagnostic imaging but serves as a valuable adjunct to in-person care. Adoption barriers include the need for patient and provider training, technology access, and reimbursement challenges.

Despite these limitations, this systematic review underscores telemedicine's crucial role in advancing breast cancer prevention. By improving access to preventive services, facilitating early detection, promoting healthy behaviors, and enhancing patient satisfaction and quality of life, telemedicine offers a powerful tool to complement traditional care. Addressing its limitations will further solidify its position as an indispensable component of a comprehensive, equitable, and patient-centered approach to breast cancer prevention.

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## Telehealth - A Promising Modality in the Management of Breast Cancer

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**Background:** The global prevalence of breast cancer is high, with a projected 1 in 20 women worldwide diagnosed in their lifetime. There were 2.3 million new cases and 670,000 deaths from female breast cancer in just 2022 alone. Annual rates continue to increase by between 1-5%, with many women requiring long-term treatment and follow-up care. The demand for accessible and effective management strategies is growing, and telehealth has emerged as a promising solution to help address these needs.

**Methods:** A systematic review was conducted to evaluate the role of telehealth in breast cancer management. The search was performed on MEDLINE and PubMed databases, limited to English-language literature published from 2014 to 2024. Keywords used in the search included "breast cancer," "breast malignancy," "management," "teleconsults," "telemedicine," and "telehealth." Inclusion criteria focused on studies discussing telemedicine and its application in breast cancer management or survivor care. Studies not discussing telemedicine were excluded, and all included studies were analyzed for their methodology, sample size, data collection methods, and key findings.

**Results:** The literature search yielded 21 studies that met the inclusion criteria. Studies show that telehealth interventions—including telephone, web-based, and smartphone application models—consistently improve access to care, which is particularly impactful for rural and underserved populations experiencing geographic or logistical barriers. These interventions enable ongoing support, symptom monitoring, and timely follow-up, resulting in positive effects on both physical and mental health, as well as overall quality of life. Patient-reported satisfaction with telehealth is notably high, especially for follow-up appointments, with many patients valuing the convenience and reduced need for travel. Additionally,

telemedicine is associated with potential cost savings by decreasing the indirect and non-medical burdens of care. However, some studies also note that the effectiveness of telehealth depends on patient digital literacy, infrastructure readiness, and the capacity for in-person assessments when required, as certain aspects such as physical exams cannot be completely replaced. Overall, the literature supports telemedicine as a complementary and integrative approach that not only enhances care delivery but also reduces treatment burden and improves health-related outcomes for breast cancer patients, provided that contextual challenges are addressed.

Conclusion: While telehealth offers substantial benefits, it is important to acknowledge its inherent limitations, as it cannot fully replace physical examinations or diagnostic imaging crucial for accurate diagnosis and monitoring. Instead, it serves as a valuable adjunct to in-person care. This review highlights key adoption barriers, including the need for adequate patient and provider training on new technologies and persistent challenges with technology access in certain areas. Despite these limitations, this systematic review underscores the crucial and expanding role of telemedicine in advancing breast cancer management and enhancing patient care.

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WRAP53 is differently expressed in triple negative breast cancer – results from a population-based cohort

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Background: The aim of this study was to study the expression of WRAP53 in a triple negative breast cancer cohort and its relation to prognosis. A biphasic expression pattern has been suggested for the DNA repair protein WD40-encoding RNA antisense to p53 (WRAP53). In cancer progression, cellular WRAP53 levels initially rise as the DNA damage load increases and subsequently reduces when the cancer cells learn to evade the damage response. Supporting this, we have previously shown that when breast cancers display low expression of nuclear WRAP53, they are still enriched in DNA repair and proliferation pathways. These tumors were associated with increased incidence of local recurrence and breast cancer death. Low WRAP53 was more common among the triple negative breast cancer subtype (TNBC), a subtype with poor prognosis and less effective treatment options. Thus, new prognostic markers are needed for TNBC.

Methods: The cohort was formed by data from the national Swedish cancer registry and the SCAN-B study (ClinicalTrials.govID NCT02306096). Patients were diagnosed with early-stage TNBC in Region Skåne, Sweden, between 2010 and 2015. A cohort of 232 patients with associated treatment and outcome data was assessed for nuclear levels of WRAP53 using immunohistochemistry in a tissue microarray. RNA sequence data from 194 tumors was used for gene expression analysis.

Results: Out of immunohistochemistry analysis, high levels of the proliferation marker Ki67 were more common among tumors with high WRAP53 ( $p=0.004$ ). Gene set enrichment analysis revealed an enrichment of pathways related to proliferation and DNA repair in tumors with high WRAP53. Tumors expressing high levels of WRAP53 were more likely to be of Basal like 1 subtype ( $p=0.024$ ) and less likely to be of Luminal androgen receptor subtype ( $p=0.020$ ). In the competing risks regression analysis, there was no evidence of WRAP53 being prognostic for breast cancer death (SHR 0.73, 95% CI 0.36-1.5).

Conclusion: In TNBC, high nuclear WRAP53 is associated with proliferation and DNA repair, opposite to previous findings in a large early-stage breast cancer cohort with all breast cancer subtypes. The regulation of WRAP53 may be different in TNBC than in other subtypes as high, rather than low, WRAP53 expression was associated with DNA repair. However, WRAP53 is not prognostic for breast cancer death in TNBC.

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Identification of patients with a genetic predisposition to breast cancer through the Breast Molecular Tumour Board

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**Background:** In 2023 our Breast Unit established a Breast Molecular Tumour Board (B-MTB) to discuss somatic (molecular) test results from patients diagnosed with metastatic disease. The purpose was to inform future treatment options including clinical trials and to familiarise the team with laboratory reports.

Discussion in the B-MTB also provided an opportunity to review whether germline testing had been offered, or should now be offered, either because patients met the eligibility criteria set out in the National Genomic Test Directly (NGTD), or because somatic testing hinted at the possibility of an underlying germline pathogenic or likely pathogenic (P/LP) variant.

In the latter scenario, careful consideration was given to the conversion rate of tumour to germline findings and to potential clinical utility to avoid inappropriate worry to patients and unnecessary referrals to Clinical Genetics. An "intermediate conservative" approach was adopted as outlined by the ESMO Precision Working Group, focusing on genes where germline findings have "most" actionability or on breast cancer predisposition genes (BCPG) with "high" actionability.

Here we detail germline genetic testing in patients discussed in the first 2 years of our B-MTB.

**Methods:** A retrospective, observational service evaluation was undertaken reviewing all patients discussed at the B-MTB between January 2023 and December 2024. Clinical details, somatic and any germline reports, and B-MTB outcomes were obtained through our digital healthcare record (EPIC).

**Results:** A total of 151 individual patients were discussed over 2 years by the B-MTB.

Of the 157 somatic tests reported, 86 were standard of care (PIK3CA) requests, 30 from clinical trials or tissue studies, and 41 were in private care.

97 tests utilised tumour tissue and 60, circulating tumour DNA.

88 patients had already undertaken germline genetic testing. 71 had NHS testing including 22 participants in the BRCA-Direct study or Transformation programme, and 1 predictive test. 17 had private testing. Inherited P/LP variants had been identified in 11 patients.

Somatic variants were identified in a gene of "most" or "high" actionability class in 111 patients of which 104 were in BCPG (BRCA1, BRCA2, PALB2, TP53, PTEN) and 8 were concordant with already known germline LP/P variants.

Of the remainder, only 4 met the "intermediate conservative" approach for onward referral to Clinical Genetics. Subsequent testing identified 2 patients with germline P/LP variants with both patients were able to receive olaparib.

Somatic variants in TP53 and PTEN were the most frequently reported (56 and 26 respectively) but no onward referrals were required after consideration of variant classification, variant allele frequency and age of initial diagnosis of breast cancer (all > 30 years).

**Conclusion:** The B-MTB provides a useful setting for revisiting germline genetics and the "intermediate conservative" approach a helpful framework for determining onwards referrals.



## Upregulation of SFRP2 influences matrix production in carcinoma-associated fibroblasts derived from male breast cancer

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**Background:** Breast cancer (BC) is rare in men and often diagnosed later resulting in increased mortality. There are no laboratory models to study male BC. Recognising that cancer-associated fibroblasts (CAFs) are the most abundant cell type in the tumour microenvironment we hypothesised that these might define biological function in male BC.

**Methods:** We generated and characterised CAFs from male and female ER-positive BC. We applied an unbiased -omic approach using public data (The Cancer Genome Atlas (TCGA); Human Protein Atlas; ESTIMATE) and in house RNAseq analysis of these CAFs. Potential genes that were upregulated in male CAFs were validated using qPCR and then knocked down using shRNA. Cell derived matrices (CDM) were generated through ascorbic acid treatment of the knockout and parental male CAFs. CDM thickness and adhesive properties were determined.

**Results:** Immunofluorescent characterisation showed the presence of ACTA and vimentin and absence of epithelial markers, confirming provenance. Using a combination of data mining and unpublished transcriptomic data to identify genes selectively overexpressed in CAFs derived from male BC, we selected the secreted frizzled-related protein family member 2 (SFRP2) for further study. Validation of its upregulation in male CAFs was confirmed by qPCR and online data mining. Indeed, SFRP2 showed the highest expression in CAFs, but particularly in male BC-derived CAFs over all other cell types tested (CAF derived from female BC, BC epithelial, endothelial and adipose). SFRP2 also correlated strongly with ESTIMATE stromal score in the 12 male BC cases on TCGA. Interestingly when stratified for previously reported CAF-subtypes male BC-derived CAFs aligned more strongly with iCAF and myCAF phenotypes. Male BC-derived CAFs deposited a thicker CDM than equivalent female CAFs. SFRP2 knockout in the male BC-derived CAFs resulted in a thinner CDM compared to controls. SFRP2 knockout was successfully achieved in 2 male BC-derived CAFs, validated by qPCR and Western blot. We also showed that normal male mammary epithelial cells showed a significant increase in adhesion to male CDMs over female which disappeared in the knockout model.

**Conclusion:** We have shown that BC-derived CAFs display sex-specific gene profiles. SFRP2 upregulation in male BC, and particularly CAFs, was confirmed through multiple approaches. We also identified a link between SFRP2 upregulation and matrix deposition, which may be a factor in driving carcinogenesis in male BC. Further studies are required to address this more fully.

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## Impact of COVID19 pandemic on breast cancer patient experiences of healthcare services in Northern Ireland: findings from large-scale cross-sectional survey

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**Background:** The COVID-19 pandemic disrupted many services, including breast cancer screening and management. Some changes introduced during the pandemic have persisted. It is therefore essential to explore and understand users' experiences of these services during and after the pandemic.

**Research Question:** To explore breast cancer patients' experiences of the COVID-19 pandemic on healthcare appointments and preferences for service modality within Northern Ireland.

**Methods:** An anonymous, online, self-completed cross-sectional survey with closed and open-ended questions was accessed between September 2023 and April 2024. The survey was open to international

respondents and promoted online via social media platforms plus through relevant charitable organisations. Descriptive findings from Northern Ireland respondents are presented.

**Results:** 262 of the 3,295 respondents identified themselves as living in Northern Ireland. Over half (59%) reported their general health had worsened during the pandemic. Reported service disruption (cancellation, change in delivery method, delays) ranged from 24% (surgical consultant clinic) to 39% (GP or primary care physician). Scan or procedure disruption varied from 4% (ECHO heart scan) to 20% (mammogram). Disruption to service provision also was reported for location of service delivery with 22% reporting the location of one or more in-person hospital appointment changed during the pandemic. 69% reported difficulties bringing a support person to in-person healthcare appointments, with approximately one-third reporting they were not permitted to bring anyone, and the same number were only allowed for some appointments. 20% of participants reported accessing private care during the pandemic. 68% of patients preferred in-person appointments for their main hospital-based breast cancer care, although 27% indicated their preference for in-person versus remote (telephone or video) appointments varied.

**Conclusion:** Breast cancer patients in Northern Ireland reported disruptions to several services they experienced during the pandemic. This also affected their ability to access support, particularly persons accompanying them to appointments. Although in-person service delivery was generally preferred, some patients valued being offered choice in service modality. Now in the recovery phase, it is essential that future service provision consider patient experiences, including the impact of restricted access to support persons, to help minimise negative interactions with healthcare services in the event of future disruptions.

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#### Risk factors for interval compared to screen-detected breast cancers: a case-only analysis of the UK Generations Cohort

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**Background:** Interval breast cancers (IBC), diagnosed between routine screening rounds, tend to have a worse prognosis than screen-detected breast cancers (SDBC), making it critical to improve detection and identify risk factors to reduce IBCs. We evaluated associations of reproductive, hormonal, lifestyle and medical factors with IBC, accounting for the role of breast density.

**Methods:** Analyses included 1,940 women diagnosed with breast cancer after enrolment in the Generations Study, a prospective cohort of women in the UK, who were linked to national screening programmes. Pre-diagnostic risk factors were assessed at enrolment, and breast density was estimated using mammograms from the screening round preceding diagnosis. Associations between breast density and risk factors were evaluated in a subset of 1,191 cases with density measurements. Screening histories were used to identify 1,185 SDCBs and 755 IBCs. Logistic regression models estimated odds ratios (OR) and 95% confidence intervals (CI) for risk factors with IBC (vs. SDBC), accounting for density and tumour characteristics.

**Results:** Higher breast density was associated with multiple risk factors for breast cancer: later age at menarche, nulliparity, breastfeeding, history of benign breast disease (BBD), alcohol drinking, lower body mass index (BMI) at recruitment and at age 20, and current use of menopausal hormone therapy (MHT). In a mutually adjusted model, IBC was inversely associated with being overweight at recruitment (0.74 (0.58–0.93) vs normal weight), and directly associated with high density (OR (95% CI) = 2.13 (1.44–3.17) for Q4 vs Q1), later age at menopause (1.60 (1.02–2.50) 55+ vs <50), current MHT use (1.41 (1.04–1.91) vs never users), history of BBD (1.36 (1.11–1.68)), being underweight at age 20 (1.65 (1.14–2.38) vs normal weight), family history of breast cancer (1.26 (1.00–1.58) and ever using oral contraceptives (1.25 (0.93–1.69) vs never). These risk factor associations with IBC were independent of tumour characteristics.

Conclusions: Breast density and multiple risk factors appear to independently increase the odds of being diagnosed with IBC risk and thus could help identify women who could benefit from tailored screening strategies to reduce IBCs. Further research is needed to disentangle detection-related versus potential biological mechanisms underlying IBC development.

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## An Integrated Research Environment for Translational Breast Cancer Research within the Breast Cancer Now Biobank

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Translational cancer research relies on access to structured, high-quality specimens linked with rich longitudinal clinical and molecular data. However, integrating and querying such multi-faceted datasets remains a significant barrier to progress. Biobanks address this need for high-quality samples, but the underlying ethos of the bank fundamentally shapes its informatics framework and long-term utility. A biobank with a narrow, transactional focus may implement a simple system for sample access, whereas a biobank that recognises the enduring value of multi-modal data evolves into a dynamic, integrated platform capable of delivering linked clinical, imaging, pathological and molecular data to accelerate discovery.

We developed the Breast Cancer Now Biobank Research Environment, an informatics platform that interconnects diverse data sources within the biobanking ecosystem. Functioning as an informatics niche, the platform extends throughout the ecosystem linking clinical, histopathological, digital and radiological data from electronic health records; and molecular research data generated using biobank samples. These interconnected pathways facilitate seamless access to specimens and their associated clinical and research data, enabling streamlined discovery, data exploration and translational analysis.

The Research Environment comprises three interlinked modules: Analytics Hub, Research Catalogue and Cohort Browser. These enable flexible querying, exploratory analytics and cohort selection, facilitating hypothesis generation, project planning and data-driven collaboration across the full translational research lifecycle, from concept to validation.

The BCNB model serves as a sustainable, model for data integration and user engagement in biobank-based translational cancer research, extending the utility of the biobank beyond its original transactional functions.

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## Implementation of a Screening Pathway for ESR1 Mutation Testing: A Single Centre Experience and Preliminary Results

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Background: Somatic mutations in the ESR1 gene are a principal mechanism of acquired endocrine resistance. These alterations are detected in approximately 4–5% of patients' after-adjuvant AI therapy for early-stage disease, increasing to 20–40% in the metastatic setting, and potentially exceeding 50% in later lines of treatment. The prevalence of PIK3CA detected in circulating tumour ctDNA in mBC is about 35% and the co-occurrence rate of PIK3CA and ESR1 alterations is 10–15%. Both mutations are associated with poorer progression-free and overall survival, underscoring their prognostic and therapeutic significance.

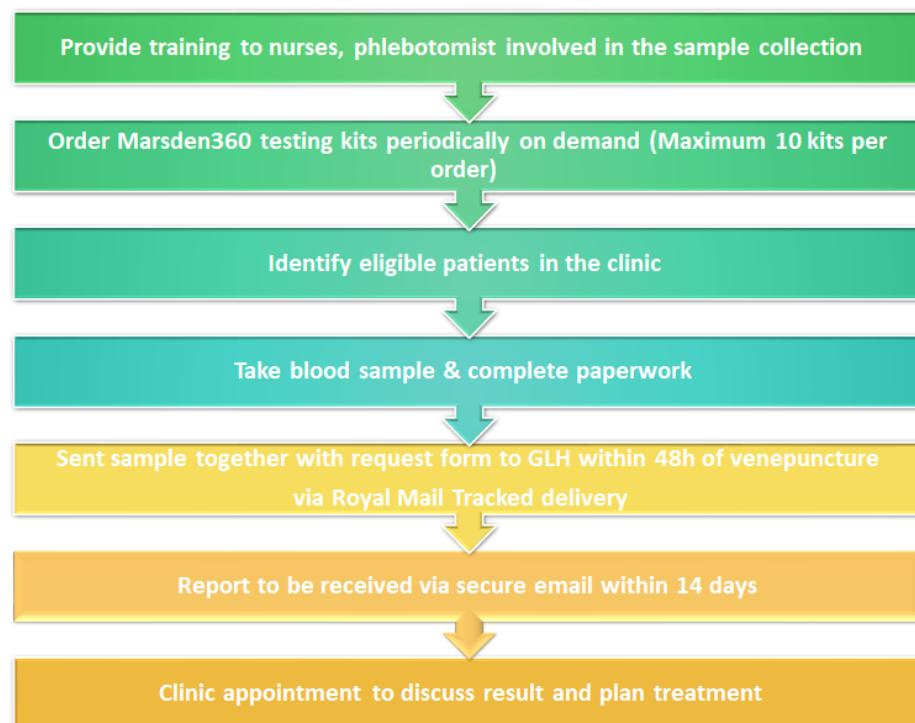
In December 2024, NICE approved the first oral SERD elacestrant. In accordance with an elacestrant SmPC, detection of ESR1 mutations should be performed using ctDNA derived from plasma. The National Genomic Test Directory was updated to reflect this requirement, formally enabling ctDNA-based ESR1 testing within the NHS framework. The recommendation is to test patients whose disease is progressing on first-line endocrine therapy with CDK4/6 inhibitors, having received at least 12 months of this therapy.

This abstract presents a single-centre experience in the development and implementation of a dedicated ESR1 mutation screening pathway.

**Methods:** The pathway was established to operationalise plasma ctDNA testing for eligible patients, ensuring compliance with updated national guidelines, while integrating genomic results into routine clinical decision-making.

Multidisciplinary team was involved in designing pathway for screening patients. MVCC is served by North Thames Genomic Laboratory Hub led by The Royal Marsden and uses the Marsden360 test—a liquid biopsy that analyses ctDNA from a blood sample.

We have analysed retrospectively, patients electronic and physical records treated at MVCC with HR+/HER2- mBC who underwent Marsden360 ctDNA testing between December 2024 and June 2025. The number of patients positive for ESR1 and/or PIK3CA mutations was recorded. The previous number of lines of ET in the metastatic setting was recorded. Please see pathway as figure below.



**Results:** A total of 19 patients were tested. ESR1 mutations were detected in nearly half of the patients 47%(9/19), PIK3CA mutations in 32%(6/19), and 11%(2/19) had both mutations. Regarding lines of metastatic endocrine therapy in the ESR1-positive cohort, 7 patients received one line, 1 patient received two lines, and 1 patient received three lines.

**Conclusions:** Our single-centre experience demonstrates the successful implementation of a structured screening pathway for ESR1 mutation testing. The majority of ESR1-positive patients(7/9) developed mutations after only one line of metastatic endocrine therapy, suggesting early emergence of resistance mutations.

However, tested cohort of patients was limited to patients treated with CDK4/6 inhibitor for at least a year. Therefore, it does not reflect whole HR(+) population. Our findings were consistent with the reported literature. These preliminary results underscore the importance of integrating genomic testing into treatment pathways to enable timely access to targeted therapies such as elacestrant.

# Risk Factor Associations with Distinct Tumor Features in Breast Cancer: A Pooled Analysis from 24 B-CAST Studies

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**Background:** Breast cancers are etiologically heterogeneous, meaning that breast cancer risk factors are differentially associated with tumor subtypes. However, most studies have focused on single markers, particularly estrogen receptor (ER), or clinical classifications based on a combination of tumor features, thereby limiting the ability to identify which of multiple correlated features are most etiologically relevant. We conducted a large, pooled analysis within the Breast CAncer STratification (B-CAST) project to provide conclusive evidence on independent associations between multiple correlated tumor features and breast risk factors.

**Methods:** Analyses included 18,635 invasive breast cancer cases and 56,267 controls from 24 studies in B-CAST. We evaluated associations between established risk factors and six tumor features including immunohistochemistry expression of ER, progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), KI67, and TP53 in tissue microarrays, and tumor grade. Case-case analyses were performed using mutually adjusted models to identify independent associations. Noteworthy associations were identified as having a Bayesian False Discovery Probability (BFDP) < 0.2 in case-case analyses. Case-control analyses in a subset of 10 population-based studies provided relative risk estimates for specific tumor subtypes.

**Results:** In case-case analyses mutually adjusted by tumor features, we identified independent and noteworthy associations for several risk factors with ER, PR, and tumor grade, but not for HER2, Ki67, or TP53. Nulliparous cases were more likely to have ER-positive than ER-negative tumors (OR: 1.81, 95% CI: 1.24–2.65). In premenopausal cases, higher BMI was independently associated with both ER-negative status (OR: 0.89, 95% CI: 0.82–0.96) and higher grade (OR: 1.10, 95% CI: 1.04–1.17). In postmenopausal cases, however, higher BMI was independently associated with PR-positive status (OR: 1.12, 95% CI: 1.06–1.19) and higher grade (OR: 1.11, 95% CI: 1.07–1.16). Cases using combined menopausal hormone therapy were less likely to have higher-grade tumors (OR: 0.61, 95% CI: 0.59–0.72), while later age at menopause was associated with ER-positive status (OR: 1.12, 95% CI: 1.05–1.20). All noteworthy associations with marker status also showed noteworthy log-linear associations with increasing proportion of marker-positive cells. Other risk factors, including age at menarche or first pregnancy, oral contraceptive use, alcohol, smoking, and family history, were not independently associated with any marker at  $BFDP < 0.2$ . Case-control analyses clarified subtype-specific risks; for example, higher BMI was linked to reduced risk of ER-positive and lower-grade tumors in premenopausal women but increased risk of PR-positive and higher-grade tumors in postmenopausal women.

**Conclusion:** This large analysis provides conclusive evidence of independent associations between established risk factors and distinct tumor features, with evidence for dose-response associations with marker expression. By providing a refined understanding of how risk factors relate to tumor features, these findings could inform biologically-targeted prevention strategies.

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### Ethnicity and routes to diagnosis for breast cancer: a population based study in England

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**Background:** Breast cancer is the most common malignancy diagnosed in women of all ethnic groups in the UK, and women from ethnic minority groups have a comparatively lower incidence but observed poorer outcomes. Breast cancer is diagnosed following either referral for symptoms in women of any age (either urgently or routinely), or through population-based screening offered routinely to women aged 50–70, and self-referral in women over 70. Any differences in the route to a breast cancer diagnosis by ethnicity may contribute to observed differences in outcomes. The aim was to investigate the associations of ethnicity and the route to diagnosis for breast cancer in women in England.

**Methods:** Using publicly available data from the National Data Registration Service, a descriptive analysis of the referral rates and conversion rates to a breast cancer diagnosis for urgent and routine referrals in aggregate ethnic groups (Asian, Black and White women) in England during 2009–2023 was conducted.

Data were extracted from the National Cancer Registration and Analysis Service on women registered with invasive breast cancer between 2013 and 2020. Information included age at diagnosis, ethnicity, region of residence, deprivation, route to diagnosis and stage at diagnosis. Logistic regression model was used to estimate the odds ratio (OR) and 95% confidence interval for risk of urgent versus routine referral by ethnicity with adjustments for relevant confounders.

**Results:** Between 2009–2023, there was an increase in the urgent referral rate and a decrease in the routine referral rate in the three ethnic groups examined. Black women have the highest age standardised urgent and routine referral rates compared to Asians and Whites, but the lowest conversion rates to a diagnosis of breast cancer (3.5% versus 4.3% (Asian) and 5.5% (White) in 2023).

Among younger women aged <50 with breast cancer (N=46,882), following adjustment for confounders, broadly similar odds of an urgent versus routine referral were observed in all ethnic groups examined. Among women aged 50–70 with breast cancer (N=134,252), similar proportions of screen-detected cancers were observed for Indian women compared to Whites (53% for both groups), but lower proportions in the other ethnic groups (41% for Black Africans, 43% for Black Caribbeans, 44% for Pakistanis).

Conclusions: This is a large national study using data over several years to report the associations of ethnicity with a route to diagnosis for breast cancer. Overall, the data suggest that the route to diagnosis by ethnicity in younger women are similar, but there may be differences among women of screening age by ethnicity that require further investigation.

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Are there associations between ABCB1 genotypes and deviation from planned taxane treatment due to side-effects in breast cancer patients? - A population-based cohort study

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Background: Taxanes are one of the most prescribed class of chemotherapies used to treat breast cancer in Sweden and worldwide. However, adverse events occur frequently with this treatment. The ABCB1 gene (a.k.a. MDR1) is a molecular transporter responsible for the efflux of taxanes and is involved in multidrug resistance. Moreover, single nucleotide polymorphisms (SNPs) in this gene were suggested to predict taxane-induced adverse events, potentially leading to changes in treatment plans and impacting patient prognosis. Thus, this pilot study evaluated whether three SNPs within ABCB1 gene (rs1045642T>C, rs2032583A>G, and rs3213619T>C) could predict change of treatment plan due to adverse events. Additionally, we explored whether the SNPs or changes in taxane treatment plan altered breast cancer-free interval.

Methods: Taxane-treated patients (n=457) from the Swedish population-based BCBlood cohort were analyzed. The patients, diagnosed with a first primary breast cancer, were included between 2004 and 2016 and followed until 2023. Genotyping of genomic variants from blood samples was performed with OncoArray. "Deviation from planned taxane treatment" included dose reduction, dose delay, switching between taxanes, and early taxane treatment discontinuation due to side-effects. Statistical analysis was conducted in SPSS, using cross-tabulation, frequencies, binary logistic regression, Kaplan-Meier and Cox proportional hazard survival analysis.

Results: Deviation from planned treatment occurred for 106 patients (23.19%) and 78 breast cancer events were recorded. Genotype frequencies for the study population SNPs were 49.0% for rs1045642TC, 19.5% for rs1045642CC, 18.4% for rs2032583AnyG, and 8.5% for rs3213619TC. For the assessed SNPs, there were no significant associations between the presence of polymorphisms and change in treatment plan or breast cancer-free interval, respectively. Also, no significant association between breast cancer-free interval and deviation from planned taxane treatment was observed. However, there was a trend towards a greater frequency of treatment plan deviation in patients with reference alleles in rs1045642 and rs3213619, compared to carriers of the variant allele. Change from the planned treatment was most common (27.3%) in the 143 patients with the diplotype TAT\_TAT and least common (13%) in the 23 patients with the CAT\_CGT diplotype.

Conclusions: Patients carrying reference alleles in the ABCB1 gene displayed a trend towards a higher frequency of treatment deviation. Overall, treatment plan changes were not associated with differential prognosis. While not statistically significant, the influence of patient genotypes on taxane-induced adverse events is an important aspect to be further explored. To achieve this, the present pilot study will be amplified to explore additional SNPs in genes associated with drug metabolism. Such expansion aims at better understanding the genetic makeup of patients affected by severe adverse effects to facilitate clinical stratification of those predisposed to these conditions. This could potentially allow for more personalized and targeted treatment plans to improve patient outcomes and preserve quality of life.

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Omission of sentinel node biopsy in patients with normal axilla at presentation of early breast cancer and complete radiological responses to neoadjuvant chemotherapy

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**Background:** There has been a trend towards de-escalation of axillary surgery over the past decade. With improvements in imaging and systemic treatment, we hypothesise that there is a select group of patients undergoing neoadjuvant chemotherapy (NACT), who have normal appearing axillary lymph nodes on imaging at presentation, in whom sentinel node biopsy (SNB) could be omitted.

**Methods:** A retrospective audit was conducted between January 2019 – December 2024 of all patients presenting to University Hospitals of Derby and Burton NHS Foundation Trust (UHDB) who were undergoing NACT and did not have biopsy proven axillary nodal involvement at diagnosis.

January 2019 was chosen as this was the time at our Trust when we stopped performing upfront SNB in patients undergoing NACT.

**Results:** A total of 177 patients underwent NACT with no evidence of axillary disease at diagnosis, during the time period. The average age at diagnosis was 51 (range 24 – 79). The majority of cases (87%) were detected symptomatically and were unifocal (84%).

Prior to NACT, the average tumour size was 37mm (range 11 – 100mm) and all were grade 2 or 3 cancers. Overall, 31% of cancer were ER positive, 25% PR positive and 45% HER2 positive. Reasons for NACT included: downsizing (36%), favourable receptor profile (35%), to allow for genetic testing (15%), downstaging (10%), other (4%).

At diagnosis 52 cases (29%) had FNA or biopsy of an axillary node with prominent features on ultrasound, all of which had benign histology.

Post-NACT imaging was performed in 150 patients and average size of tumour was 12mm (range 0 -63). Out of the 150 cases, 76 had a partial radiological response (51%), 68 had a complete radiological response (45%), 5 progressive disease (3%), 1 no response. All underwent SNB and the histological outcome is shown in Table 1. No metastasis in SNB were found in patients who had had a complete radiological response to NACT.

	Normal sentinel node biopsy	Fibrosis in sentinel node (no metastasis)	Metastasis in sentinel node
<b>Radiological complete response and normal nodes on imaging at presentation (N=49)</b>	48	1	0
<b>Radiological complete response and abnormal node on imaging at presentation (benign histology) (N=19)</b>	17	2	0
<b>Radiological partial or no response and normal node on imaging at presentation (N=60)</b>	52	5	3
<b>Radiological partial or no response and abnormal node on imaging at presentation (benign histology) (N=22)</b>	18	1	3

*Table 1: Histological outcome of SNB in patients with post-NACT imaging*

**Conclusions:** In patients undergoing NACT with complete radiological response to therapy and normal axillary lymph glands on ultrasound at presentation (not requiring a biopsy), the benefit of performing SNB is small. This may further decrease as reliability of ultrasound and imaging of the axilla increases. Current guidelines recommend axillary radiotherapy if unexpected fibrosis is found at SNB in a clinically node negative patient, however this is likely to change in the coming years once trials such as ATNEC, have been reported.

Assessment of response to neoadjuvant chemotherapy in patients with T1-T3, N0-N1, M0 breast cancer-A single centre experience

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**Background:** The current recommendation for patients with early breast cancer who receive neoadjuvant chemotherapy (NACT) and breast conserving surgery (BCS), is adjuvant radiotherapy. In patients with node positive disease, axillary radiotherapy is an alternative to axillary lymph node dissection. However, both treatments are associated with significant risk of lymphoedema, shoulder stiffness, sensory impairment and pain. Furthermore, meta-analysis has demonstrated low rates of locoregional recurrence in patients with pathological complete response (pCR) who underwent BCS and radiotherapy. In particular for triple negative and HER2 positive disease, pCR has been shown to be a useful surrogate marker for overall survival. The toxicities of radiotherapy and improved apparent survival benefit associated with pCR warrant further investigation into de-escalation of treatment for this patient group. Based on this emerging area of interest, we performed a retrospective analysis at our tertiary centre of response to NACT in breast cancer patients with T1 to T3, N0 or N1 and M0 disease.

**Method:** We performed a retrospective analysis of patients who presented with T1-T3, N0-N1, M0 breast cancer and were treated between 1st Jan 2022 to 31st Dec 2024 at Clatterbridge cancer centre, UK. Data was collected using electronic notes. Patient demographics, disease staging, receptor status, pathological response and nodal fibrosis were outcomes that were.

**Results:** A total of 402 patients were identified with a median age of 53 (range 24-84). 182 patients (45%) were ER +ve, 170 (42%) were HER2 +ve and 149 (37%) had triple negative disease. 289 patients had node negative disease at presentation and 40 (13.8%) had nodal fibrosis at surgery. Node positive patients were only identified from years 2023 and 2024, and 113 patients with N1 disease were identified. At surgery, pCR was found in 57.4% of patients with N0 disease at presentation, and 46.9% of patients with N1 disease. pCR was observed in 65% of patients with triple negative disease, 44% ER positive patients, and 50% HER2 positive patients.

**Conclusion:** Overall, we observed a slightly higher rate of pCR in our patients, when compared with average rates in published clinical trial. In line with current literature, higher rates of pCR were observed in patients with HER2 +ve and triple -ve disease. Interestingly, rates of pCR were similar in N0 and N1 patients. It is hoped that this data will aid in guiding further research into de-escalation of management of patients with pCR in order to optimize quality of life for this patient population.

Patient and treatment factors associated with the risk of wound-related complications after breast conservation surgery: A cross-sectional study

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**Background:** Breast conservation surgery (BCS) is an integral component of breast cancer management, offering oncological outcomes comparable to mastectomy while providing superior cosmetic results and patient satisfaction. However, reported rates of wound-related complications after BCS range from 5% to 20%, influenced by patient comorbidities, treatment regimens, and outcome definitions. This study aimed to investigate patient and treatment factors associated with early postoperative complications following BCS in the breast cancer cohort of the international REQUITE study.

**Methods:** Breast cancer patients (n=2,057) were recruited prospectively following breast-conserving surgery (with or without chemotherapy) and prior to radiotherapy across 18 centres in Europe and the US between 2014 and 2016. Complications included haematoseroma, oedema, infection, and delayed healing (>3 weeks), and were assessed at 90 days, usually after completion of radiotherapy. Logistic regression was performed to examine associations between complications and patient (age, BMI, smoking, alcohol, diabetes, cardiovascular disease, rheumatoid arthritis, hypertension), surgical (segmentectomy vs wide local excision, type of axillary surgery), and cancer-related factors (neoadjuvant chemotherapy, nodal involvement, tumour stage).

**Results:** Of patients with available outcome data, 260/2004 (12.97%) experienced haematoseroma, 145/1980 (7.32%) developed postoperative oedema, 91/2013 (4.52%) had infection, and 52/2017 (2.58%) had delayed wound healing. Older age (OR 1.02, p=0.001), Alcohol use (OR 1.35, p=0.040) and segmentectomy versus wide local excision (OR 2.43, p<0.001) increased risk of haematoseroma. Compared with sentinel node biopsy, both axillary dissection (OR 2.86, p=0.003) and axillary dissection following sentinel lymph node biopsy (OR 3.98, p=0.002) were associated with haematoseroma. Diabetes (OR 2.09, p=0.017) was associated with postoperative oedema, as was segmentectomy (OR 2.95, p<0.001). For infection and delayed healing, higher BMI was a risk factor (OR 1.08, per kg/m<sup>2</sup>, p<0.001), while segmentectomy reduced odds compared with smaller resections (OR 0.46, p=0.001). No other significant associations with complications were observed, including for neoadjuvant chemotherapy.

**Conclusion:** This study confirms established predictors of wound-related complications, including age, BMI, diabetes, and axillary surgery, but shows their effects vary across outcomes. By analysing haematoseroma, oedema, infection, and delayed healing separately, we demonstrate how surgical approach and patient factors influence complications in distinct ways. This extends the evidence base beyond prior studies that focused mainly on surgical site infection. Diabetes was associated with oedema but not infection, differing from several large registry studies. Smoking, often reported as a predictor, was not significant here. Segmentectomy showed contrasting effects, raising the risk of haemorrhage and oedema while reducing infection risk. These findings emphasise the need for risk assessment tools that address a wider range of wound outcomes and provide support for developing or validating prediction models to support personalised counselling, surgical planning, and complication reduction.

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### Taking the PROTAC-tical approach against the progesterone receptor in ER+ breast cancer

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Resistance to endocrine therapy remains a major clinical challenge in hormone receptor-positive (HR+) breast cancer (BC), contributing to persistent risk of recurrence and limiting the long-term efficacy of these therapies. While the estrogen receptor (ER) is the primary therapeutic target, increasing evidence suggests significant roles for other hormone receptors, including the progesterone receptor (PR) due to extensive crosstalk within steroid hormone signalling pathways. However, the lack of selective tools has made it difficult to distinguish ER- from PR-driven effects, limiting our ability to fully understand PR's role and therapeutic potential.

Using clinically relevant mammary intraductal (MIND) models, we showed that some HR+ patient-derived xenografts (PDXs) require PR for growth. Moreover, ectopic PR expression can independently drive tumour growth in MCF-7 MIND xenografts, even in the absence of ER signalling and ovarian hormones.

These findings raise the question of whether personalising endocrine therapy by incorporating PR blockade could offer a more effective therapeutic approach.

The clinical use of PR antagonists has been limited by glucocorticoid receptor (GR) cross reactivity and off-target effects. This study aims to use novel PR-targeting PROTAC degraders to investigate the role of PR in HR+ BC and evaluate their potential as a therapeutic strategy.

A panel of first-in-class PR PROTAC degraders were developed in collaboration with the Centre for Protein Degradation (ICR). Mifepristone and Vilaprisan were used as progesterone receptor ligands, with different linkers connecting them to either von Hippel-Lindau (VHL) or cereblon (CRBN) E3 ligase recruiters. PROTAC compounds were tested in T47D human breast cancer cell line in vitro. Four out of nine VHL-based compounds and seven out of twenty-four CRBN-based compounds showed strong PR degradation.

One lead compound showed minimal cross-reactivity with the GR while maintaining robust PR degradation. This was further validated in ex vivo cell line and patient derived MIND xenograft assays to assess tumour response in a physiologically relevant microenvironment. This tool compound will be taken forward in these models to identify responders and non-responders and interrogate mechanisms of PR dependency.

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#### Patient and Public Perceptions of Artificial Intelligence in Breast Imaging and Clinical Decision-Making: A Cross-sectional Survey Study

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**Background:** Artificial intelligence (AI) shows promise in supporting mammography interpretation, triaging referrals, and predicting malignancy risk, potentially enhancing early detection of breast cancer. However, successful integration depends on patient trust and acceptance. This study explores British women's perceptions of AI in breast cancer care to identify knowledge gaps and guide communication about AI-assisted decision-making.

**Methods:** Paper surveys were distributed to women attending the Breast Care Unit at Queen's Hospital, Burton, during autumn 2025. Demographic data, levels of trust and comfort, and concerns about AI were collected. Responses were analysed using descriptive statistics and thematic analysis.

**Results:** Sixty-three participants completed the survey. The majority were female (83.1%), aged 46–74 years (62.5%), and just over half were patients (57.6%). Overall, 59.7% expressed some degree of trust in AI, but awareness was limited: 41.3% had never heard of AI in healthcare, and 79.4% were unaware of its use in breast clinics. Concerns were widespread, with 78.3% worried about misdiagnosis. While 78.7% were comfortable with AI provided a doctor verified its findings, 64.5% were uncertain or uncomfortable about AI involvement in triaging appointment urgency. Thematic analysis highlighted the perceived indispensability of human doctors, and frequent responses of "don't know" reflected uncertainty and knowledge gaps.

**Conclusion:** Although patients were generally receptive to AI, acceptance was conditional on clinician oversight. Limited awareness, accountability and concerns about diagnostic accuracy remain barriers to implementation. Educational initiatives are essential to improve understanding of AI's role in breast care and to support informed acceptance of AI-assisted decision-making.

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## Self-Directed Aftercare (SDA) following breast cancer surgery: What does the evidence say?

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**Introduction:** Self-Directed Aftercare (SDA) following breast cancer surgery has been suggested to deliver individualised care that uses resources efficiently. It is a widespread but under-researched method of aftercare delivery. We conducted a scoping literature review to establish what evidence currently exists regarding SDA, and to identify where research efforts should be concentrated.

**Methods:** 3 databases (Web of Science, MEDLINE and PubMed) were searched using iterative search terms for "breast cancer" "patient-led" and "follow-up". Primary research articles published since 2000 and in English were included, with conferences proceedings, abstracts and review articles excluded. A total of 763 abstracts were screened, and 12 papers (discussing 10 studies) were included in the final analysis. Descriptive statistics and thematic analysis were applied.

**Results:** There was widespread heterogeneity in the design, methods, reporting outcomes and findings of each study. 5 were RCTs with the remainder observational or service evaluation/audit. There was no consensus on inclusion criteria for patient age, stage of cancer or gender. Thematic analysis of reported survey and interview responses demonstrated high levels of unmet need (particularly information and psychological), and a wide spectrum of experience. Some patients reported positive experiences of a prompt and flexible service, whilst others expressed strong feelings of abandonment and uncertainty. An important discord was noted in the responses from surveys alone (largely positive) and responses from free-text and interviews (more frequently reported negative experiences). Although no studies were powered to detect difference in survival, none showed a difference between oncological outcomes. No studies reported the experiences of carers or of patients who developed a recurrence while on an SDA pathway. The experience of staff delivering SDA pathways was not reported in any studies.

**Conclusions:** There is currently no uniform approach to conducting or reporting Self-Directed Aftercare pathways and their outcomes in existing literature. A mixed methods approach is required to establish if such follow-up pathways are oncologically safe, well tolerated by patients and their carers and cost-effective.



## Evaluation of Deep Learning Architectures for Breast Cancer Classification in Mammography Images

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**Background:** Breast cancer remains the leading cause of cancer-related mortality among women, with mammography serving as the primary screening tool. Interpretation is limited by variable sensitivity in dense breasts and inter-reader variability. Deep learning has demonstrated potential to enhance diagnostic accuracy, but challenges remain regarding dataset variability, generalisability, and computational efficiency. This study evaluated state-of-the-art architectures for mammogram classification and compared full-image versus region-of-interest (ROI) approaches.

**Methods:** We used the CBIS-DDSM dataset, comprising 808 patient cases after preprocessing. Splits were performed at the patient level to avoid data leakage, with 55% for training, 23% validation, and 22% test. Preprocessing included ROI extraction and augmentation. Models tested included Convolutional Neural Networks (CNNs), Vision Transformers (ViTs), and hybrid CNN-Transformer architectures. All models were trained with ImageNet-pretrained weights using cross-entropy loss. Performance was assessed using accuracy, area under the ROC curve (AUC), sensitivity, specificity, and computational efficiency.

**Results:** Performance varied across model families and input strategies. On full mammograms, CNNs generally outperformed Transformers, with RepVGG-B1 achieving the highest accuracy (70.8%) and an AUC of 0.74. ROI-based training improved results in 12 out of 19 architectures, reducing background interference and highlighting relevant features. RepVGG-B1 achieved 72.5% accuracy on ROI inputs,

matched by ConvNeXt-Base and MaxViT. The largest gains from ROI processing were observed in DeiT-Small (57.9% → 70.8%) and ConvNeXt-Base (62.4% → 71.9%). Grad-CAM analyses confirmed that ROI-based models consistently focused on lesion areas, whereas full-image models sometimes misallocated attention to pectoral muscle or artefacts. Computationally, RepVGG offered an efficient trade-off between accuracy and training cost, while larger Transformer models required substantially greater resources without consistent performance benefits.

**Conclusions:** Deep learning shows promise for mammogram classification, but performance depends strongly on architecture choice and preprocessing strategy. ROI-guided training improves both accuracy and interpretability across most models. RepVGG-B1 demonstrated the most consistent performance, balancing accuracy with computational efficiency. These baselines provide a foundation for the next phase of this research: a multitask knowledge distillation framework that integrates classification, detection, and segmentation in a unified system, aiming to enhance generalisability and support scalable clinical deployment.

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**AIB1 expression and genotypes in breast cancer – significant interactions between AIB1 genotypes and radiotherapy on prognosis**

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**Background:** Genetic variation in the host can impact mRNA expression and drug response. AIB1 genotypes have been associated with breast cancer risk and AIB1 expression with endocrine treatment outcome. Whether AIB1 genotype impacts radiation response in breast cancer is unknown. Three functional polymorphisms have been associated with altered mRNA expression rs6094752 C>T (low), rs2230782 G>C (low) and rs2076546 A>G (high). We investigated how signaling pathways differed according to AIB1 expression and the impact of AIB1 genotype on breast cancer prognosis in different treatment groups.

**Method:** Gene expression profiles from samples with tumors cells and cells from the tumor microenvironment of unilateral breast cancers from 5326 unique patients with available follow-up for distant metastasis in the SCAN-B cohort were used. Gene set enrichment analysis was performed using 'clusterprofiler' to find the statistically significant, concordant gene sets that differed between the highest and lowest tertiles of AIB1 expression and grouped according to Hallmark Signature annotations. Breast cancer patients included in the BCBlood cohort 2002–2008 in Lund, Sweden with a first invasive cancer (n=576, 503 ER+) were followed until 2019. Clinicopathological factors, treatments and breast cancer events were obtained from questionnaires, patient charts and registry data. Genotyping of genomic DNA was performed with iPLEX™. Univariable and multivariable survival analyses were conducted and adjusted for age, BMI, tumor characteristics, and adjuvant treatments.

**Results:** Gene sets related to Interferon alpha and gamma response, PI3K/AKT/MTOR signaling, IL6/JAK/STAT3 signaling, inflammatory response, and IL2/STAT5 signaling were activated in high vs low AIB1 mRNA tumors irrespective of ER status in SCAN-B. Conversely, genes related to EMT and myogenesis were suppressed in AIB1 mRNA high vs low tumors. In BCBlood, most patients received one or more types of post-operative adjuvant therapy: radiotherapy (60.8%), chemotherapy (18.4%) and for patients with ER+ tumors tamoxifen (62.2 %) and aromatase inhibitors (41.0%). One hundred forty four patients experienced breast cancer events (46 locoregional, 32 contralateral, 96 distant metastasis). CGA\_CGA (61.4%), CGA\_CCA (16.4%), and CGA\_CGG (12.0%) diplotypes were common. Remaining diplotypes were classified as 'Rare'. AIB1 genotypes were associated with prognosis only when treatment was taken into account, with significant interactions between radiotherapy and CGA\_CGA (Pinteraction=0.033) and CGA\_CCA (Pinteraction=0.017). In non-radiotherapy-treated patients, CGA\_CGA conferred half the risk for events, while CGA\_CCA conferred double risk for events compared with other diplotypes. In radiotherapy-treated patients, CGA\_CGA was not associated with prognosis while CGA\_CCA conferred 40% lower risk for events. No other significant interactions between diplotypes and therapies on prognosis were observed. The results remained essentially the same after further adjustment for mastectomy.

Conclusion: Low AIB1 expression was associated with hallmarks indicating higher risk for distant metastasis. AIB1 CGA\_CCA (low expression) carriers appeared to derive the highest benefit from radiotherapy. The impact of pharmacogenetics in radiotherapy needs further study.

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## Menopausal hormone therapy and risk of breast cancer in the Generations Study cohort, UK

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**Background:** Menopausal hormone therapy (MHT) is a commonly used and effective treatment for relief of menopausal symptoms. In 2023/24 there were an estimated annual 2.6 million patients prescribed MHT in England, an increase of 96% from five years earlier. Risk of breast cancer is increased for combined oestrogen plus progestogen formulations of MHT but this risk varies by the type of progestogen used. As new forms of combined MHT become popular the risk profile may change, and women and healthcare professionals will require updated information on the associated risks (and benefits) of MHT use.

**Methods:** The Breast Cancer Now Generations Study is a cohort study involving over 100,000 women from the UK. Formal recruitment began in 2004 and was completed by 2009. Use of MHT was collected by questionnaire at recruitment and updated at follow-up 5 and 13 years later to capture changes in type of MHT use and non-use. Breast cancers occurring in the cohort were ascertained by linkage to national cancer registration. Hazard ratios (HR) and 95% confidence intervals (CI) for (invasive or ductal carcinoma in-situ) breast cancer in relation to MHT use at post-menopausal ages were estimated using Cox proportional hazards regression with age as the analytic time scale, overall and for oestrogen receptor positive breast cancer. Analyses were adjusted for age at menopause and postmenopausal body mass index.

**Results:** 81,473 post-menopausal women were followed up for median 13.5 years with 941,340 person-years, and 3,791 breast cancers occurred at an average age of 65.4 years. Risk of breast cancer relative to non-users was raised modestly in ex-users of any type of MHT (HR=1.12, 95% CI: (1.04–1.21); P=0.003) and current users of oestrogen only MHT (HR=1.24 (1.05–1.47); P=0.013) and raised markedly for combined oestrogen plus progestogen MHT use (HR=2.23 (1.90–2.61); P<0.0001). Risk was raised for combined MHT containing the synthetic progestogens levonorgestrel (HR=3.18 (1.71–5.91); P=0.0003), medroxyprogesterone acetate (HR=2.73 (2.01–3.70); P<0.0001), and norethisterone (HR=2.31 (1.87–2.85); P<0.0001), but less so with dydrogesterone (HR=1.32 (0.77–2.28); P=0.32); these results were more pronounced for oestrogen receptor positive breast cancer: levonorgestrel (HR=4.05 (2.02–8.12); P=0.0001), medroxyprogesterone acetate (HR=3.47 (2.47–4.88); P<0.0001), norethisterone (HR=2.82 (2.21–3.58); P<0.0001), dydrogesterone (HR=0.81 (0.34–1.95); P=0.63). There was too little use of body-identical micronised progesterone (e.g. Utrogestan) during current follow-up to accurately estimate risk for this preparation.

**Conclusion(s):** Dydrogesterone, a synthetic progestogen that is closely related to natural progesterone, may be relatively safer than other types of synthetic progestogens in relation to risk of breast cancer. MHT based on micronised progesterone has recently become popular in the UK and planned continued follow-up of the Generations cohort will enable risks to be estimated for this formulation.

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# Digital Twins for Mechanistic Investigation of Stress and NF-κB Signalling in Triple-Negative Breast Cancer

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**Background:** Triple-negative breast cancer (TNBC) is an aggressive and molecularly heterogeneous subtype of breast cancer (BC) with high metastatic potential and limited targeted therapies. Psychological stress and glucocorticoid receptor (GR) signalling are linked to poor TNBC outcomes, as dysregulated glucocorticoids (GCs) promote drug resistance, and high GR expression correlates with poor prognosis. The pro-inflammatory transcription factor NF-κB, comprising subunits RelA, RelB, and c-Rel, regulates genes controlling proliferation, metastasis, immune evasion, and drug resistance. However, the relationship between NF-κB and GR modulation remains unclear and may reveal new therapeutic targets. Although computational models have explored NF-κB, proliferation, apoptosis, and therapy responses in other cancers, none have been tailored to TNBC or integrated GR modulation.

**Methods:** This project combines experimental and computational systems biology approaches to develop a novel model of stress-induced GR-NF-κB crosstalk in TNBC. To inform model parameters, experimental work was performed in luminal A (MCF-7), HER2+ (SKBR3), TNBC (MDA-MB-231), brain-tropic TNBC (MDA-MB-231BR), and non-malignant (MCF10A) cells. High-throughput immunofluorescence, flow cytometry, and western blotting were used to assess the abundance and localisation of GR and NF-κB subunits (RelA, RelB, and c-Rel) under untreated and GC treatment conditions. GR knockdowns uncovered how stress signalling alters NF-κB dynamics and refined the computational model. The systems biology aspect includes an established model of NF-κB, the cell cycle and apoptosis in cancer, which were parameterised with breast cancer mRNA and protein abundance datasets from the Human Protein Atlas to create a new TNBC-specific computational model. TNF $\alpha$  signalling and necroptosis were incorporated into computational modelling to capture the multiple competing cell fate outcomes observed in BC. This framework enables the generation of predictive digital twins of tumour responses.

**Results:** High-throughput immunofluorescence and flow cytometry revealed that NF-κB subunits displayed cell line-specific patterns of abundance and nuclear localisation. The RelA subunit demonstrated significantly higher cytoplasmic sequestration and lower abundance in both non-metastatic and metastatic TNBC compared with ER+ and HER2+ cells in the absence of cortisol (MCF-7 vs. 231,  $p = 0.0016$ ; MCF-7 vs. MDA-MB-231BR,  $p = 0.0031$ ; SKBR3 vs. MDA-MB-231,  $p = 0.0077$ ; SKBR3 vs. MDA-MB-231BR,  $p = 0.0163$ ). In contrast, RelB and c-Rel formed nuclear foci across all cell lines without significant cell line specificity in abundance, suggesting selective and constitutive non-canonical NF-κB signalling. Cortisol and dexamethasone treatment did not alter GR or NF-κB localisation, reinforcing that these cell models are inherently stressed. Western blotting confirmed elevated GR expression in TNBC compared to ER+ and HER2+ cell lines, particularly metastatic derivatives, consistent with clinical data.

**Conclusions:** In summary, by integrating experimental data with computational models, this project builds digital twins of TNBC that enable exploration of disease progression under stress and will be able to identify therapeutic strategies targeting GR-NF-κB crosstalk.



Incomplete ovarian function suppression (OFS) in premenopausal patients with oestrogen receptor positive breast cancer receiving GnRH agonists/antagonists whilst being treated with CDK4/6 inhibitors

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**Background:** Ovarian function suppression (OFS) can be given in combination with endocrine therapies to treat premenopausal ER+ breast cancer. GnRH agonists/antagonists (GnRHa) can be used in this context to achieve OFS. E2 measurements are frequently used to monitor OFS, however there is no clear consensus regarding appropriate cut-off levels or assays. Incomplete OFS has important implications on treatment efficacy in the premenopausal setting. We are conducting a systematic review in order to assess the risk of incomplete OFS in premenopausal women with ER+ breast cancer receiving OFS. There have been recent reports regarding possible interactions between CDK4/6 inhibitors and assays used to determine E2 levels, resulting in falsely elevated E2 readings. We therefore present the subset of studies identified in our analysis describing OFS rates in patients receiving GnRHa in combination with CDK4/6i treatment.

**Methods:** The full systematic review protocol has been registered with PROSPERO, and is available at: <https://www.crd.york.ac.uk/PROSPERO/view/CRD42023395920>

In brief, we conducted a search of MEDLINE and EMBASE initially in March 2023, and updated this in June 2024. Eligible studies included premenopausal women with ER+ breast cancer receiving treatment with GnRHa. The outcome of interest was measurement of incomplete OFS based on any definition. 5103 titles and abstracts were initially identified. Following initial screening, 600 full texts were assessed of which 119 studies were included in the full systematic review. Of these, we identified 4 full texts, 2 abstracts and 1 case report which reported hormonal measurements or OFS rates in patients receiving CDK4/6i treatment.

**Results:** Included full texts reported data from the PENELOPE-B, MONALEESA-7 and PALOMA-3 trials. We present the definition and rates of OFS in these identified publications. Importantly, definitions of OFS were often not described, or were based on postmenopausal hormone levels. Despite this, there was evidence of incomplete OFS, with patients having elevated or post-menopausal E2 levels.

**Conclusion:** We summarise the available literature identified in the process of a systematic review in order to further understand current assays in use and rates of incomplete OFS in patients receiving CDK4/6 inhibitors and GnRHa. At least a subset of patients receiving GnRHa have incomplete OFS. Further research is required to determine the most appropriate E2 cut-off and risk of OFS in the context of GnRHa treatment. It will also be important to investigate the impact of concurrent treatment on assays used to determine E2 levels.



# Combined impact of radiation therapy and NCOA3 levels in human breast cancer – Data from a population-based Swedish cohort and in vitro experiments

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**Background:** The nuclear receptor coactivator 3 (NCOA3) protein interacts with nuclear hormone receptors and enhances transcriptional activator functions. NCOA3 thus acts as an oestrogen receptor (ER) coactivator and the gene is overexpressed in some breast cancers, contributing to tumor progression and endocrine resistance. In cervical cancer cells, high NCOA3 was associated with chemoradiotherapy resistance, while NCOA3 knockdown increased treatment sensitivity. However, the role of NCOA3 in radiation response in breast cancer is still unknown. We studied the prognostic impact of tumor-specific NCOA3 protein levels in breast cancer patients treated with or without adjuvant radiotherapy and the effect of NCOA3 expression level on the radiation treatment (RT) sensitivity in two ER-positive breast cancer cell lines.

**Methods:** Between 2002 and 2012, 1018 breast cancer patients were included in the BC-blood cohort in Sweden and followed until 2023. Questionnaires and patient charts were used for clinicopathological data. Tumor-specific NCOA3 levels were annotated in 888 patients using immunohistochemical methods (antibody 61105; BD) on tissue microarrays. NCOA3 intensity (0–3+)  $\times$  fraction (0–100%) yielded Histoscore 300 (H300) and was categorized as NCOA3low (H300 0–99), NCOA3interm (H300 100–249), or NCOA3high (H300 250–300). Univariable and multivariable survival analyses in relation to treatment were performed. NCOA3 was knocked down in MCF7 and T-47D cell lines using human NCOA3 siRNA, with nontargeting siRNA as negative control (siNegative). The effects of RT were assessed in siNCOA3 and siNegative transfected cells via clonogenic assay for 14 days and western blot at different time points. All statistical tests were two-tailed and regarded as statistically significant if nominal  $P < 0.05$ .

**Results:** NCOA3low (n=169) conferred two-fold risks for breast cancer events or distant metastasis at 10 years (both  $P_{adj} < 0.05$ ). Multiplicative interactions between NCOA3low and radiotherapy were found on distant metastasis and overall survival using NCOA3interm (n=439) as reference (both  $P < 0.1$ ) but no interactions with NCOA3high (n=280). Radiotherapy combined with NCOA3low conferred two-fold risks for distant metastasis and death at 10 years (both  $P_{adj} < 0.05$ ). No association between NCOA3low and prognosis was seen in non-radiation therapy treated patients. However, the colony formation ability of both cell lines remained unchanged following the RT of siNCOA3 knocked down cells, compared to RT of siNegative cells. Additionally, NCOA3 knockdown did not significantly affect the radiation response markers (YH2AX and P53).

**Conclusion:** In conclusion, NCOA3low was associated with poor prognosis in general and especially in radiation treated patients. Since downregulation of NCOA3 did not affect RT efficacy in these breast cancer cell lines, the combination of radiation therapy and NCOA3low resulting in poor prognosis in the patients might be due to factors in the tumor microenvironment rather than the NCOA3 level in the tumor cells.

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## Investigating the effects of chronic low dose exposure of bisphenol A on normal mammary epithelial cells

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**Background:** Estrogen influences breast cancer development. The potential role of so-called “forever chemicals” like bisphenol A (BPA), a weak estrogen mimic ubiquitously present in the environment and in many everyday products at low concentrations remains controversial. Classed as an endocrine disrupting chemical (EDC) it can interfere with hormone-regulated pathways. While a single exposure to BPA is

highly unlikely to result in the development of a complex, chronic disease such as breast cancer, sustained exposure to low concentrations over time may have cumulative effects, potentially contributing to carcinogenesis. Models to address this have been imperfect mostly using breast cancer cell lines, varying BPA concentrations (10-3-10-14 M) and short exposures, typically 24-72 hours. This does not reflect realistic physiological conditions. In particular, doses around the European Food Safety Authority (EFSA) approved tolerable daily intake (TDI) of 0.2 ng/kg body weight/day have not been adequately researched. Our aim was to conduct a long-term experiment to assess the potential effects of chronic BPA exposure in mediating breast carcinogenesis using immortalised non-transformed HB2 cells.

Methods: HB2 cells were exposed to 100nM and 200pM BPA over 6 months. The 100nM dose elicited proliferation in a dose-response experiment, while 200pM corresponded to the TDI set by the EFSA. After every month of BPA exposure, assays were performed to assess metabolic activity (MTT), DNA damage (Comet assay), reactive oxygen species (ROS; bioluminescence assay) and expression of DNA damage repair genes (qPCR).

Results: Increased metabolic activity was seen after 3 months BPA exposure and was more pronounced with 100nM. ROS activity increased over time, increasing exponentially for up to 4 months of 100nM BPA. DNA damage was sustained up to 3 months, after which it declined. Hypothesising that DNA-damage repair mechanisms may be initiated, we examined expression of a panel of DNA-damage repair genes. Dose dependent increases in BRCA1 and RAD51 expression were evident after >3 months exposure to BPA. DNA damage quantification ( $\gamma$ -H2AX) and ability of BPA-exposed HB2 cells to form colonies in 3D Hydrogels of different stiffness is being assessed.

Conclusions: Our work suggests adverse effects of BPA on normal mammary epithelial cells in vitro. Limiting exposure is advisable. Steps are being taken to ban BPA use in everyday items, particularly those in contact with foodstuffs. This is already enforced in France. The EFSA has announced a phasing out of BPA and some analogues in food-related items. However, the US Food and Drug Administration TDI is 250,000 times higher than the EFSA TDI. Lingering presence of BPA and other EDCs in the environment remains a cause for concern for human health and, potentially, breast carcinogenesis.

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## Automatic Pipeline for Accurate Breast Volume Assessment

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Breast cancer is the most common cancer in women, with more than 56,000 cases diagnosed annually in the UK. Breast-conserving surgery followed by radiotherapy is a standard treatment, but it often alters breast size, shape, and symmetry, affecting appearance and quality of life.

Current evaluation methods include automatic 2D tools that cannot provide volumetric data, 3D approaches based on MRI or CT that are costly and rarely acquired for cosmetic follow-up, and commercial 3D systems that require proprietary hardware and expensive licenses, limiting accessibility and transparency. As a result, reliable volumetric assessment remains out of reach for most patients and clinicians, despite its clear clinical relevance. Therefore, there is a need for an automatic, accurate, and open-access pipeline for volumetric breast assessment.

Here, we present such a pipeline that can work with 3D surface scans from consumer-level devices, such as iPhones with LiDAR sensors. Our approach combines AI-based breast detection in 2D images with a back-projection method that maps segmentations onto 3D meshes, enabling accurate volume calculation.

The development of this automatic breast-volume assessment pipeline proceeds in three main stages. First, a deep-learning model (YOLOv8) is retrained to teach it to find breast regions in 2D images. Secondly, a back-projection algorithm is implemented to transfer these segmentations onto the corresponding 3D mesh using the ray tracing technique. Finally, all the model's vertices not included in any of the breast segmentation regions are deleted, and the volume of the remaining mesh is calculated.

This strategy is motivated by the lack of large, annotated 3D breast datasets, which makes direct 3D training currently impractical, while large, high-quality 2D datasets remain readily available. By exploiting this abundance of annotated 2D data, we can establish accurate breast delineations and extend them into 3D, accelerating clinical applicability.

The system is currently being trained on more than 8,000 annotated images from the REQUITE dataset ([www.requite.eu](http://www.requite.eu)) to improve generalisability across diverse imaging conditions.

Validation on diverse 3D meshes demonstrates robust performance, opening up prospects for a clinical trial to evaluate accuracy on real scans. Importantly, the pipeline is fully automated, transparent in its intermediate steps, and designed to be adaptable to additional datasets, supporting continuous refinement.

This pipeline is a first step toward objective and accessible breast volumetry. By removing reliance on specialised hardware, costly software, or “black-box” algorithms, it lowers adoption barriers and empowers both patients and clinicians with bias-free measurements. Beyond being part of cosmetic evaluation, such open-source tools could guide reconstruction, enable longitudinal monitoring, and become a backbone for a model capable of predicting future appearance.

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Platelet-derived growth factor-CC expression in triple-negative breast cancer is associated with increased immune cell density and response to adjuvant chemotherapy

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**Background:** Expression of Platelet-derived growth factor-CC (PDGF-CC) is associated with the triple-negative breast cancer (TNBC) subtype. We have previously reported that paracrine PDGF-CC signaling involving cancer-associated fibroblasts is important for maintaining a TNBC tumor cell phenotype. Here, we aimed to characterize PDGF-CC expression in TNBC in detail by combining information from RNA-Seq data and multiplex immunohistochemistry (IHC) with clinical follow-up in patient cohorts.

**Methods:** Tissue microarrays (TMAs) constructed from primary TNBC tumor samples from two cohorts (SCAN-B and Sahlgrenska, total N=589) were stained for PDGF-CC using IHC. Tumor cell-specific expression of PDGF-CC intensity was scored as either absent, weak, intermediate or strong, and associations with clinicopathological variables and outcome were examined. In the SCAN-B cohort, RNA-Seq data was available for N=242 and Gene Set Enrichment Analysis (GSEA) was performed to identify pathways differing between PDGF-CC intensity groups. Deconvolution of RNA-Seq data was performed to infer the abundance of stromal and immune cell populations in each sample, while the immune multiplex IHC panel allowed us to describe cellular neighborhoods inferred from the spatial relationships between immune cell types.

**Results:** Intermediate and strong PDGF-CC intensity scores were associated with increased NHG and Ki-67 percentage. The strong PDGF-CC intensity group was characterized by a higher proportion of PAM50 basal-like tumors and higher immune related GSEA pathways. The effect of adjuvant chemotherapy on recurrence-free interval (RFI) was striking in the PDGF-CC strong patient group (treated vs. untreated, HR=0.21, 95% CI 0.10-0.41, p<0.001) whereas in PDGF-CC intermediate and weak patient groups, adjuvant chemotherapy had no effect (p=0.46 and p=0.12, respectively). Interaction analysis showed that the effect of chemotherapy was due to differences in PDGF-CC intensity (p=0.004). By multiplex image analyses, we identified 10 distinct cellular niches in TNBC; 5 immune-enriched, 3 stroma-enriched and 2 tumor-enriched. B cell- and T cytotoxic cell-enriched neighborhoods were associated with an increased RFI. The strong PDGF-CC intensity group showed higher frequency of these neighborhoods. On

the contrary, lower density of myofibroblast-like cancer-associated fibroblasts (myCAFs) and stroma-enriched niches were found in the strong PDGF-CC intensity group.

**Conclusion:** Strong PDGF-CC intensity identified basal-like TNBCs with an increased immune cell infiltrate, lower myCAF density and stroma-enriched niches, and an excellent response to adjuvant chemotherapy. A window-of-opportunity trial (NCT05722795) has been launched to examine the effect of PDGF receptor inhibition on TNBC phenotype, and the study presented here will aid in interpreting results from the trial.

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Risk of incomplete ovarian function suppression (OFS) using gonadotropin-releasing hormone (GnRH) agonists and antagonists in premenopausal women with estrogen receptor (ER)-positive breast cancer

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**Background:** Ovarian function suppression (OFS) is a key component of treatment for premenopausal women with estrogen receptor-positive (ER+) breast cancer, used in early disease as part of adjuvant strategy with curative intent and in advanced disease to improve survival and quality of life. OFS is typically achieved with gonadotropin-releasing hormone (GnRH) agonists or antagonists, however recent evidence suggests variable rates of associated incomplete OFS. This is clinically important as incomplete OFS can impact the efficacy of breast cancer treatment. The prevalence of incomplete OFS and factors contributing to it remain unclear due to a lack of consensus on what defines adequate OFS, how this may vary in different treatment settings, and inaccuracies associated with assays used to measure ovarian function. We conducted the first systematic review to assess the prevalence of incomplete OFS across treatment settings and identify influencing factors.

**Methods:** We searched MEDLINE and EMBASE for studies including information on the risk of OFS using GnRH agonists/ antagonists in premenopausal women with ER+ breast cancer. The protocol was registered on PROSPERO (CRD42023395920). We included studies assessing premenopausal women with ER+ breast cancer treated with GnRH agonists/ antagonists for OFS (alone or in combination with other treatments). Only English language articles were included. There were no restrictions on study type. Case reports were included for qualitative synthesis. Studies inducing ovarian ablation using oophorectomy or radiotherapy were excluded. The main outcome of interest was incomplete OFS (any definition). Additional outcomes of interest were serum estradiol (E2), estrone (E1), estrone sulfate (E1S), luteinising hormone (LH), follicle-stimulating hormone (FSH), other relevant hormones, and amenorrhoea.

**Results:** 117 studies met inclusion criteria, including 8 case studies/ series. Treatment settings included adjuvant, neoadjuvant, metastatic and mixed patient populations. Twenty studies explicitly defined incomplete or suboptimal OFS, most commonly with specific estradiol values. Thirty-nine studies assessed suppression using postmenopausal or castrate hormonal ranges, while eighteen studies measured amenorrhoea or vaginal bleeding. Based on these definitions, several studies show that incomplete OFS occurs in a subset of patients, either transiently or persistently. We will present results on the prevalence of incomplete OFS and the influencing factors, including the sensitivity and specificity of hormone assays, treatment setting, and patient factors including BMI and prior chemotherapy.

**Conclusions:** A proportion of premenopausal women with ER+ breast cancer treated with GnRH agonists/ antagonists experience incomplete OFS either transiently or persistently. Further research is needed into the clinical implications of incomplete OFS, the treatment and patient factors influencing its occurrence and the development of clear criteria for its definition. Given the widespread use of GnRH agonists/ antagonists in breast cancer treatment, improved recognition of incomplete OFS and development of treatment strategies to target this will be imperative in improving disease outcomes.

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# 'Accepting your Body after Cancer', a group-based online intervention for women treated for breast cancer: A feasibility randomised controlled trial

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**Background:** While increasing numbers of women are living beyond breast cancer, treatment-related body image concerns are common. The consequences of depression, anxiety, sexual and intimacy issues, poorer quality of life, and shorter survival warrant attention. Nonetheless, rigorously evaluated and effective body image interventions are lacking. We developed 'Accepting your Body after Cancer (ABC)', a seven-session online group intervention based on CBT. This study aimed to examine the feasibility of evaluating ABC in a randomised controlled trial.

**Methods:** We aimed to recruit 120 women who had completed active breast cancer treatment. Participants were recruited from hospitals, cancer charities, and social media across the UK. Using permuted block randomisation, participants were randomised 1:1 to ABC plus a psychoeducational body image booklet or to a control condition receiving only the booklet.

ABC was delivered online over seven weekly two-hour group sessions, co-facilitated by a clinical psychologist and cancer support specialist. The intervention incorporated CBT techniques targeting unhelpful thoughts, anxiety, and avoidance, alongside exploring media literacy, body functionality appreciation, self-care, mindfulness, and relaxation.

Feasibility was assessed via recruitment, retention, and outcome completion at baseline, 1-week, 3-months, and 6-months post-intervention. Acceptability was evaluated through questionnaires and interviews. Proposed candidate primary outcomes were the Kessler Distress Scale (K10), Body Appreciation Scale (BAS), and FACT-B: Breast Cancer Subscale, and secondary outcomes included the Body Image Scale (BIS) and BREAST-Q: Sexual Wellbeing Scale. Health economic measures included the Modified Adult Service Use Schedule (ADSUS), EQ-5D-5L, Recovering Quality of Life-Utility Index-10 (ReQoL), and Work and Social Adjustment Scale (WSAS).

Patient and public involvement and engagement (PPIE) was incorporated in the development of ABC and at every stage of the research. An independent Steering Committee had oversight of the study.

Trial registration number: ClinicalTrials.Gov NCT06412341; ISRCTN ISRCTN88199566; IRAS 327507; REC reference 24/NE/0092; under reference NIHR205415.

**Results:** The recruitment target (N=120; Mage = 51.2; 92% White; 91% heterosexual) was met, with 83.3% retention and no differences in outcome completion or drop-out rates by condition. Sixty percent of intervention participants attended at least six sessions, reporting high satisfaction (M= 4.2/5). Qualitative feedback highlighted shifts toward self-acceptance, shared strength, and practical tools. Participants rated the research experience positively (M=3.9/5). Analyses favoured ABC on the BAS, BIS, FACT-B, WSAS, and ReQoL, with significant differences indicated between the intervention and control arm across all time-points (up to 6 months later).

**Conclusions:** ABC is feasible and acceptable, with promising early benefits, supporting progression to a fully-powered trial. Online delivery offers scalable CBT-informed support for body image concerns in breast cancer survivors, addressing a critical yet underserved need in this population.



## Beyond the Invitation: Women's experiences and perceptions of NHS breast screening in disadvantaged communities in Yorkshire

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**Background:** Socioeconomic inequalities in breast screening uptake remain persistent across the UK, leading to later cancer diagnoses and poorer outcomes. Policy and research often focus on women's awareness or personal choice, but this overlooks how breast screening is negotiated within the pressures of everyday life. Therefore, this study asked: How do women living in disadvantaged areas of Yorkshire experience the NHS Breast Screening Programme, and how do overlapping disadvantages shape their engagement with it?

**Methods:** This study used a qualitative design. Women aged 50–70 (n=33) were recruited through community organisations in socioeconomically disadvantaged areas of Yorkshire. Data were generated through semi-structured interviews (n=12) and focus groups (n=4; 21 participants), including women who had attended breast screening, lapsed in attendance, or never attended. To complement this, a qualitative evidence synthesis (QES) of UK-based studies (n=11; 436 participants) was conducted using meta-ethnography. The primary data were analysed alongside the QES to build a broader understanding of inequalities in breast screening. Analysis was informed by sociological frameworks, with intersectionality providing the overarching lens to explore how socioeconomic disadvantage combines with factors such as ethnicity, disability, or migration status.

**Results:** Breast screening attendance was not a straightforward matter of invitation, personal choice, or behaviour, but a negotiated process shaped by structural, cultural, and psychosocial factors. Women described barriers including language and literacy, transport, work and caring responsibilities, and difficulties navigating appointment systems. Attendance was also influenced by previous experiences with healthcare, including interactions with administrative and clinical staff, as well as community narratives and intergenerational patterns of trust and mistrust in healthcare. Women's sense of whether breast screening was appropriate or intended for them was shaped by perceptions of risk, feelings of entitlement to care, and the availability of emotional and practical resources. Intersectionality highlighted how these factors overlapped to create distinctive and layered barriers. To support translation into practice, the study also developed an innovative, multi-format public engagement tool, the 'Snakes and Ladders to Attending Breast Screening' game. This interactive resource has been used widely across community events to start conversations, challenge misconceptions, and help normalise breast screening within underserved communities. It has also been adapted as a training tool for NHS staff and volunteers, helping them to better understand the everyday barriers women face when navigating breast screening.

**Conclusions:** This study shows that reducing inequalities in breast screening requires more than increasing awareness or providing information. Policies and interventions need to recognise how multiple disadvantages combine and focus on making breast screening services more flexible, accessible, and culturally sensitive. This includes addressing practical barriers such as appointment systems and transport, but also investing in approaches that build trust, reduce emotional burdens, and normalise breast screening within populations most affected by inequalities.

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## Real World Evidence of Adjuvant Ribociclib. In Early Breast Cancer

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**Background:** The phase III NATALEE trial established adjuvant Ribociclib plus aromatase inhibitor, mostly Letrozole, as a new standard for ER+/HER2- early breast cancer, with a 19.5% discontinuation rate due to adverse events (AEs) and high rates of laboratory neutropenia (62.5% any grade; 44.3% grade  $\geq 3$ ). Translating this into real-world practice, tolerability and management patterns may differ.

**Methods:** We retrospectively reviewed toxicity management data from 84 consecutive patients treated at LOC (Leaders in Oncology Cate, part of HCA Healthcare UK, a private oncology outpatient SACT

[systemic anti-cancer therapy] department) with adjuvant Ribociclib. Treatment interruptions, discontinuations, and reasons for dose modifications were compared with reported toxicity outcomes from NATALEE.

#### Results:

- Permanent discontinuation: 4.8% of LOC patients stopped treatment (any reason), versus 19.5% discontinuation due to AEs in NATALEE.
- Interruptions: 45.2% experienced  $\geq 1$  interruption; 21.4% had  $> 1$  interruption.
- Delay reasons: 13.1% of patients required delay for neutropenia, 20.2% for LFT elevations/hepatitis, and 3.6% for infection.
- Comparative profile: Neutropenia was the dominant AE in NATALEE (62.5% any grade, 44.3% grade  $\geq 3$ ), but only 13.1% of LOC patients required action for ANC. LFT related issues were more comparable (20.2% in LOC vs 26.4% in NATALEE).
- QTc prolongation: 2.4% in LOC vs 5.3% (any grade) and 1.0% ( $\geq G3$ ) in NATALEE.
- Other cardiac issues captured within the LOC data included: bradycardia and chest discomfort, which, in turn was linked to MSK and possible endocrine aetiology in the form of Letrozole.
- ILD was not captured in the LOC dataset, whereas, in the NATALEE trial data: Interstitial lung disease / pneumonitis: ~1.5% any grade; ~0% grade  $\geq 3$  in many but some instances.

Conclusions: Real-world tolerability of adjuvant Ribociclib at LOC appears favourable, with lower permanent discontinuation rates than in NATALEE but frequent temporary interruptions. Differences likely reflect shorter exposure, many LOC patients are still on treatment and thus, some toxicity may not have emerged within the dataset yet. Also, differing clinical management strategies, such as, variability in biomarker parameter cut-offs will allow for a disparity between real-life data and formalised trial data. Overall, the AE spectrum aligns with NATALEE, dominated by neutropenia and LFT abnormalities, but the burden of permanent discontinuation appears lower in practice.

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#### Supporting adherence to endocrine therapy: Health Care Professionals' views on the HT&Me intervention and potential for implementation

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Background: Despite the benefits of adjuvant endocrine therapy for breast cancer recurrence and death, many women struggle to take the treatment as recommended. Both HCPs and patients recognise that effective adherence support is urgently required. The SWEET trial (Improving outcomeS for Women diagnosed with early breast cancer through adhErence to adjuvant Endocrine Therapy; ISRCTN Number: ISRCTN24852890) is a large nationwide randomised control trial (RCT) (n=1606) exploring the effectiveness, and cost-effectiveness, of HT&Me, an evidence based, theory informed, patient centred intervention, to reduce poor adherence and improve health-related quality-of-life. Within a mixed-methods process evaluation, we interviewed HCPs involved in delivering the intervention and/or RCT. Here we report the findings from these interviews.

Methods: Semi-structured interviews were conducted, via video call and telephone, with 25 HCPs from across the UK. These include oncologists, surgeons, research nurses, research practitioners, clinical nurse specialists and a Breast Cancer Now (BCN) nurse—all of whom were acting as PI, involved in recruitment or involved in delivering the HT&Me intervention. Interviews explored views and experiences of the intervention and the trial overall, as well as contextual factors, examining what would need to be in place to maintain the intervention within routine care. Interviews were audio-recorded and transcribed. Data was analysed thematically using the Framework Approach.

Results: Findings relate to two main areas, the RCT and implementation. Trial focused themes included: what worked well with regards to the organisation and trial processes, such as having monthly drop-in meetings for site delivery staff to meet with the trial team; recruitment challenges and lessons learned, such as the need for sites to be flexible when contacting participants and to engage all clinical team

members in the research; and methods to improve research inclusion, such as the recruitment animation. Themes relating to implementation of HT&Me into usual care included: the necessity of the intervention, with HCPs stating there was a clear gap to be filled; perceived acceptability, with HCPs highlighting how positively the intervention was received by women, particularly the interactive elements; and workforce capacity issues, such as fear this could increase demands on their time. A potential solution to this was the BCN model, where the intervention was delivered remotely by a BCN nurse instead of by trained site staff locally. Further themes included the benefits of the intervention for HCPs, such as increased understanding of the personal impact of endocrine therapy side effects.

Discussion: SWEET seeks to address a significant issue affecting the growing population of breast cancer survivors: poor adherence to adjuvant endocrine therapy. The HCP focused process evaluation endorses the acceptability of the intervention to HCPs and examines potential challenges of implementation, highlighting solutions to overcome these, such as remote delivery of the intervention by BCN nurses.

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### Listening, Learning, Liaising: Dynamic Public Partnership across the FAST MRI DYAMOND Trial

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**Background:** Women with average breast density (BIRADS B) are being offered an abbreviated breast MRI, called FAST MRI, following their first (prevalent round) screening mammogram within the currently recruiting NIHR and MRC funded FAST MRI: DYAMOND trial (NIHR 150502, ISRCTN 74193022). This group (around 40% of women aged 50–52) has previously been excluded from supplemental screening trials, which focused on women with dense breasts. FAST MRI: DYAMOND aims to discover if FAST MRI can detect cancers earlier in women with average breast density.

Public Engagement was integral to the project's development and Public Partnership is embedded throughout, with Lay Researchers and the wider Public and Patient Involvement and Engagement (PPIE) Group contributing throughout the study and to future dissemination.

We are also undertaking broader Public Engagement to optimise DYAMOND recruitment and inclusion strategies. Developed from the FAST MRI Programme PPIE Strategy, the DYAMOND PPIE Plan provides a specific, formalised framework, designed to be responsive to participant feedback and emerging study needs.

Collaborations with UK-wide and local advocacy organisations such as The Independent Cancer Patients' Voice, Lobular Breast Cancer, Bristol Breast Unit Support Trust, Breast Density Matters and Black Women Rising have been central to this approach.

DYAMOND has six recruiting sites, with engagement activities at each, ensuring regional representation and relevance.

#### Participating NHS Trusts / NHS Foundation Trusts:

- North Bristol
- St George's University Hospitals
- Gloucestershire Hospitals
- Royal Cornwall Hospitals
- Great Western Hospitals
- King's College Hospitals

**Methods:** The DYAMOND PPIE Plan was co-developed with breast cancer survivors, service users, and community stakeholders. Engagement is continually refined, based on lived experience, policy development, and advocacy priorities.

Evaluation is agile and ongoing, using GRIPP2 and COM-B frameworks to explore impact and guide improvements.

Results: DYAMOND has co-developed and deployed a range of engagement activities, often in partnership with Avon Breast Screening Service (see Table 1).

Completed Activities	Planned Activities
Formal PPIE Member Meetings with screening-age women	Ongoing formal PPIE meetings
Stakeholder workshops with screening delivery staff	Breast Screening Health Workshops for underrepresented women
Community outreach: Malcolm X Centre (Bristol)	Joint outreach event for women without stable living arrangements with Gloucestershire Hospitals
Community outreach: Bristol International Balloon Fiesta	LGBTQ+ community outreach, London
Health check days: Chinese communities	Expansion of digital engagement (website, social media)
Health check days: African & Caribbean communities	Outreach at local community centres
Engagement with responses to media coverage	Development of a shortened recruitment video designed for individuals who prefer less information or find detailed content overwhelming.
Community outreach coffee mornings in ethnically diverse areas of Bristol	Training and supporting other researchers in creating high quality PPIE within trials

Table 1

Over 100 participants have engaged directly, with thousands reached through public events.

Feedback from Public Engagement activities has led to:

- Use of animation in the DYAMOND recruitment video
- Revisions to recruitment materials (e.g. subtitles).
- Adjustments to appointment logistics and accessibility.
- Enhanced cultural sensitivity in outreach and communication.
- Identification of operational barriers and enablers.

Conclusion: Our visually engaging poster, developed in partnership with our PPI Group, illustrates FAST MRI: DYAMOND's Public Engagement approach. Structured, yet flexible and responsive, our work integrates inclusive participant, public, and stakeholder feedback and works closely with advocacy organisations to optimise research inclusion, transparency, accessibility, acceptability, compliance and impact.

Future work will focus on sustaining involvement, evaluating long-term impact, and informing policy to reduce health inequalities through widening participation in both research and in breast cancer screening.



Pneumonitis in breast cancer patients treated with adjuvant Abemaciclib- a single centre experience

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Background: Abemaciclib, a CDK4/6 inhibitor, is a recommended treatment in patients with locally advanced estrogen receptor positive (ER+) breast cancers and is an adjuvant treatment given in combination with endocrine therapy. Pneumonitis is not a common side effects of abemaciclib but can occur in some patients. The aim of this study was to analyse the rate of pneumonitis in real life and to study if there is any correlation between incidence of pneumonitis and radiotherapy treatment techniques

due to the increased lung doses associated with volumetric modulated arc therapy (VMAT) in comparison to fixed field intensity modulated radiotherapy (IMRT).

**Method:** Retrospective analysis from January 2023 – March 2025 of breast cancer patients with advanced, locally advanced or high-risk early-stage ER+ HER2- treated with abemaciclib. Clinical notes were reviewed to identify respiratory co-morbidities and radiological diagnosis of pneumonitis was confirmed. The data was analysed using SPSS Version 5, Mann-Whitney U test and Fisher's exact test to determine a correlation between the data sets compared to available literature papers.

**Results:** 204 patients were identified. 61 patients (61/204, 29.9%) presented with symptoms of pneumonitis. 30 patients (30/204, 14.7%) had known respiratory comorbidities, of these, 46.7% (14/30) developed symptoms of pneumonitis. Of the 174 patients without known respiratory comorbidities, 27% (47/174) developed symptoms of pneumonitis ( $p=0.028$ ). The incidence of radiological confirmed pneumonitis was 6.9% (15/204). 12 patients did not receive radiotherapy, none of these patients developed pneumonitis. Of the 192 patients who received radiotherapy 7.8% (15/192) developed pneumonitis. There was no significant correlation noted ( $p=0.606$ ). No significant correlation was identified between VMAT and IMRT ( $p=0.741$ ). 36 patients received VMAT, 5.6% (2 patients) developed pneumonitis, 156 patients received IMRT, 8.3% (13 patients) developed pneumonitis. For those who developed pneumonitis, the median time between radiotherapy and abemaciclib was 28 days (range 13-57 days) compared to 38 days (range 5-155 days) for those who did not develop pneumonitis (range 13-57 days) ( $p=0.043$ ). 1 patient was excluded from this analysis as the patient received concurrent treatment.

**Discussion:** The largest clinical trials to date evaluating outcomes for patients receiving abemaciclib is MONARCH 2 and 3. The reported the incidence of pneumonitis was 2.0% and 5.2% in abemaciclib-treated patients in MONARCH 2 and 3, respectively. In both studies, patients who had pneumonitis had history of radiotherapy or metastatic lung disease. Our study identified that the symptomatic presentation as well as the rate of radiological confirmed pneumonitis is higher (29.9% and 6.9% respectively) compared to MONARCH 2 and 3.

**Conclusion:** The incidence of pneumonitis is higher in patients with known lung comorbidities. No significant correlation was found between VMAT treatment and pneumonitis development. Patients who have  $\leq 4$  weeks gap between RT and abemaciclib had higher chances of developing pneumonitis.

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**Counting the Seconds: Frequency and Timing of metastatic breast cancer recurrences after primary breast cancer**

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**Introduction:** At present there is limited data on secondary/metastatic breast cancer (SMBC), preventing adequate planning of treatment and surveillance. There is no standardised ICD10 coding for SMBC and very few population-based cancer registries (PBCR) routinely record SMBC prospectively. The Northern Ireland Cancer Registry (NICR) developed an expert rules-based algorithm to identify SMBC cases from routinely collected healthcare data. However, estimated time to development of SMBC post primary breast cancer (PBC) is still relatively unknown.

**Methods:** This study used algorithm-identified SMBC cases and examined a range of routinely collected clinical and treatment data to estimate time to distant SMBC development including inpatient hospital diagnoses, inpatient procedures, systemic anti-cancer therapy (SACT), radiotherapy, clinical nurse specialist notes, death records and pathology data. A hierarchical model was developed to identify the most accurate estimated date of SMBC development. Patients were excluded if SMBC was identified less than one year from PBC diagnosis as this could represent incorrect PBC staging, if they developed a primary cancer at another site between PBC and SMBC, if they were alive for over 20 years post SMBC or had an ICD10 secondary code before their PBC.

Results: At present we have examined the numbers of patients developing SMBC by stage at diagnosis, with these shown in Table 1.

Stage at primary diagnosis	n	%	Cumulative %
Stage I	185	13.3%	13.3%
Stage II	602	43.3%	56.6%
Stage III	506	36.4%	93.0%
Unknown	97	7.0%	100%
<b>Total</b>	<b>1,390</b>	<b>100%</b>	

Table 1: Number of Patients developing SMBC by stage at primary diagnosis (2009-2020)

We also examined the cumulative hazard of developing SMBC by stage at diagnosis with, as expected, those diagnosed with later stage PBC at higher risk of developing SMBC. For Stage III PBC patients the estimated risk of developing SMBC at 1-year was 7% rising to 28% at 5-years following PBC diagnosis. In contrast, for Stage I PBC patients the estimated risk at 1-year is <1% rising to 2% at 5-years. Further refinement of the hierarchical model is currently being undertaken to further improve estimated time to SMBC development.

Conclusions: For the first time in NI, we provide estimates of time to development of SMBC by stage of primary diagnosis.

Key message 1: Estimating time to development of SMBC at the population level can assist in planning treatment and service provision.

Key message 2: Understanding how time to SMBC development differs by PBC stage allows optimization of surveillance programmes to support those most at risk of developing metastatic disease.

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#### Retrospective Comparative Analysis of Surgical and Patient-Reported Outcomes Following Immediate Pre-Pectoral Implant-Based Breast Reconstruction with Polyurethane Implants Alone vs Micro-textured Implants with Acellular Dermal Matrix

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Background: Prepectoral immediate implant based breast reconstruction (IBBR) is oncologically safe and offers good aesthetic outcomes. This is usually undertaken with an acellular dermal matrix (ADM) or dermal flap to control the implant pocket. We aimed to compare the surgical and patient reported outcomes of immediate IBBR using subcutaneous polyurethane implants alone vs microtextured implants with ADM.

Methods: We evaluated sixty-four pre-pectoral immediate implant-based breast reconstructions (IBBRs) performed in sixty-one patients by a single surgeon between July 2020 and July 2023. Thirty-seven reconstructions used polyurethane implant only, and twenty-seven used an implant with acellular dermal matrix (ADM). Demographic and clinicopathological variables, day-case rates, early surgical complications, radiotherapy-related skin changes, and implant loss were compared using Fisher's exact test. Patient-reported outcomes (PROMs) were obtained by telephone using three individually validated domains of the Breast-Q questionnaire: Breast Satisfaction, Physical Wellbeing, and Radiotherapy side-effects. Rasch-converted scores were analysed with Welch's t-test, while the Radiotherapy domain was analysed on its native 7-point scale. All analyses were performed in RStudio, with statistical significance set at  $p < 0.05$ .

Results: Thirty-seven (57.8%) immediate IBBRs used polyurethane implant alone and twenty-seven (42.2%) had implant with ADM. The mean follow-up period is 42 months. Groups were comparable in demography, clinicopathological features and adjuvant therapies. Day-case surgery was achieved in

62.5% overall (62.2% implant only vs 63.0% ADM). Early complications were low and showed no significant differences: wound dehiscence  $\leq$ 30 days (10.8% vs 18.5%,  $p = 0.48$ ), skin necrosis (2.7% vs 11.1%,  $p = 0.30$ ), seroma  $\leq$ 30 days (5.4% vs 14.8%,  $p = 0.23$ ), wound infection (5.4% vs 11.1%,  $p = 0.64$ ), and implant loss  $\leq$ 30 days (8.1% vs 14.8%,  $p = 0.44$ ). The table below shows a comparison of all postoperative complications between patients undergoing breast reconstruction with implant alone versus implant with mesh.

	Implant alone group (N=37) n (%)	Implant with mesh (N=27) n (%)	Risk Ratio	95% CI	p-value
<b>Wound dehiscence within 30 days</b>	4 (10.8)	5 (18.5)	0.58	0.17-1.97	0.475
<b>Skin necrosis</b>	1 (2.7)	3 (11.1)	0.24	0.03-2.21	0.302
<b>Seroma within 30 days</b>	2 (5.4)	4 (14.8)	0.36	0.07-1.85	0.231
<b>Wound infection within 30 days</b>	2 (5.4)	3 (11.1)	0.49	0.09-2.71	0.642
<b>Implant Loss</b>	3 (8.1)	4 (14.8)	0.55	0.13-2.25	0.443
<b>Wound dehiscence at 3 months</b>	0 (0.0)	3 (11.1)	-	-	0.070
<b>Seroma at 3 months</b>	1 (2.7)	0 (0.0)	-	-	1.000
<b>Radiotherapy related skin damage</b>	2 (5.4)	3 (11.1)	0.49	0.09-2.71	0.642
<b>Capsular Contracture</b>	3 (8.1)	3 (11.1)	0.73	0.16-3.34	0.691

Table 1: Postoperative Complications: Implant Alone vs Implant with Mesh

Patient reported outcome (PROM) response rate was 53% (31/58; 3 patients deceased). Mean Breast-Q scores were similar: Breast Satisfaction  $63.1 \pm 18.3$  vs  $58.4 \pm 21.1$  ( $p = 0.56$ ) and Physical Wellbeing  $81.4 \pm 23.7$  vs  $83.8 \pm 11.8$  ( $p = 0.79$ ). The Radiotherapy side-effects score was slightly higher (i.e. worse) in the ADM group ( $7.4 \pm 0.5$  vs  $6.9 \pm 0.4$ ,  $p = 0.019$ ), but numbers were small.

Conclusions: This study suggests that immediate IBBR using subcutaneous polyurethane implants alone is safe, even in patients receiving adjuvant radiotherapy, and results in high patient satisfaction whilst avoiding the additional cost of ADM. Polyurethane-only IBBR is non-inferior to implant-based reconstruction with ADM in terms of day-case rates, surgical outcomes, and reconstruction failure. Patient-reported outcome measures indicated high satisfaction and physical wellbeing with broadly similar results between the two groups.

Integrative multiomic analysis identifies molecular markers of metastatic spread in ER-positive/HER2-negative breast cancer

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Background: In breast cancer (BC), metastatic spread is the main cause of cancer-related deaths. Despite significant advances in personalised medicine and the molecular profiling of tumours, metastatic disease remains a challenge.

Multiomic profiling is essential in this scenario, improving our understanding and facilitating clinical implementation. We here aim to develop a comprehensive profile of metastatic spread in BC, investigating potential new subtypes and markers in the large and heterogeneous group of patients with ER+/HER2- disease and linking them to clinical outcome.

Methods: We developed a semi-automated protocol for acquisition of proteome and phosphoproteome data via Data Independent Acquisition (DIA) liquid chromatography tandem mass spectrometry (LC-MS/MS) and integration with existing transcriptome and clinical data. We analysed 182 primary BC cases belonging to the Sweden Cancerome Analysis Network – Breast (SCAN-B) cohort (NCT02306096).

Potential markers were identified through differential expression analysis and Multi-Omics Factor Analysis (MOFA) and correlated with disease-specific clinical outcome. Unsupervised consensus clustering was also performed to identify novel potential subtypes.

Results: Comparison of the two main histological subtypes, no special type (NST) and invasive lobular carcinomas (ILC), showed key differences attributed to E-cadherin and other cell adhesion proteins, aligning with the hallmark of ILCs.

We identified a cluster enriched in pathways related to interferon signalling and antigen processing and presentation and associated with worse recurrence-free survival ( $p = 0.09$ ), highlighting a phenotype potentially linked to T-cell exhaustion. This suggests that although BC is typically considered immunologically cold, particularly ER+/HER2- cases, a subpopulation might benefit from immune checkpoint blockade therapy.

We also identified potential markers of both lymph node and distant metastases. The phosphopeptide ES8L2 S570p (HR = 0.61, 95% CI 0.38-0.99, multivariable  $p = 0.005$ ) was associated with improved recurrence-free survival and lower abundance in lymph node positive cases. For distant metastases, the heat shock protein 90 family was associated with worse distant recurrence-free survival (HR = 2.10, 95% CI 1.24-3.55, multivariable  $p = 0.0058$ ) and significantly increased in patients with a distant recurrence event. These findings could be further validated in the Human Protein Atlas and Kaplan-Meier Plotter.

Conclusions: Here, we present the most comprehensive multiomic dataset of metastatic spread in ER+/HER2- BC clinical samples. We identified potential novel subtypes and markers of both LN and distant metastasis, highlighting a possible immune exhausted phenotype and markers which are under active clinical investigation and part of important signalling pathways. Their potential predictive and prognostic roles are currently under investigation.

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#### A systematic review of validated and adapted prediction models for risk of breast cancer

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Background: Breast cancer is the second most commonly occurring form of cancer worldwide and ranks third in leading cancer deaths. Early diagnosis and intervention are key to reducing mortality. This can be facilitated by risk prediction models, which stratify large, asymptomatic populations based on their individual risk to inform further disease surveillance or screening. Many such models exist, and new ones continue to be developed. They incorporate a range of lifestyle and genetic factors, but as they were developed in predominantly Caucasian populations, less is known about their performance in ethnic groups with different risk factors. Beyond external validation, others have also sought to adapt existing models by adding, removing or reweighting factors with an aim to improve performance. Scrutiny of model performance across multiple populations and studies is essential to providing a robust evidence base for their use in clinical practice.

Methods: MEDLINE and Embase were searched from inception to 1st March 2025. After screening, 109 studies were included which validated and/or adapted existing risk prediction models. Information about the models used, population demographics, and model discrimination and calibration – where reported – were extracted and summarised.

Results: For analysis, models were broadly categorised into the Gail (or BCRAT) model; Tyrer-Cuzick; and other models, which included polygenic risk scores, BOADICEA, as well as other mammography-based models. Of the included papers, 48 reported on the Gail model, 33 on Tyrer-Cuzick, and 105 on all other models. Models were extended either by combining with other models, or adding new parameters such as genetic information. Various measures of effect were used for assessing performance, but for the

present study only area under the curve (AUC) or the c-index are shown. Relatively few studies assessed calibration in their cohort, and a small proportion performed subgroup analysis based on age group. Performance varied significantly across cohorts and models, and was synthesised from all studies where it was reported.

**Conclusions:** The summary statistics provided show the performance of models across different validation subgroups and compare genetic and non-genetic models. The presented findings may be of benefit to clinicians in choosing risk scores that demonstrate an acceptable level of discrimination in demographic cohorts of interest, particularly in the context of resource constraints where factors such as genetic information are difficult to acquire.

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### Preventing breast cancer after chest radiotherapy: Developing a national interventional cohort study

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**Background:** Women who received  $\geq 10$  Gy chest radiotherapy under the age of 36 for the treatment of Hodgkin Lymphoma (HL) have elevated breast cancer (BC) risk, at least equivalent to women with a strong family history e.g. 30% lifetime risk. In England, high-risk HL survivors are invited to yearly breast screening, with high uptake, yet no risk-reducing medications are offered. Tamoxifen and anastrozole are licensed for prevention in women with an increased BC risk, reducing risk by 38%-50% (IBIS-I; IBIS-II). This study aimed to characterise the lymphoma survivor population eligible for risk-reducing medication and to engage patients, medical oncologists, and GPs in examining the acceptability of these medications and the experience of their delivery. This will inform a proposed, novel interventional cohort study implementing a shared care model for offering risk-reducing medication to high-risk HL survivors.

**Methods:** Cohort characteristics were obtained from the breast cancer screening after radiotherapy dataset (BARD). BARD is expanded to include non-HL survivors. According to IBIS trial inclusion criteria, BARD women could be eligible for risk-reducing medication if aged 30-70 with no previous BC diagnosis. We conducted a virtual presentations and workshops with BARD women, as well as carers and survivors of other cancer subtypes, at the Royal Marsden Hospital. We undertook 6 focus groups with GPs, medical oncologists and epidemiologists between July-Sept 2025.

**Results:** Of the 4528 BARD women, based on NICE guidance, 3,227 (71%) could be eligible for risk-reducing medication. Mean age and time since radiotherapy was 53 and 28 years respectively. 54% received radiotherapy aged between 20-29 years. Workshop participants had varied understanding of their high BC risk. Some were unaware prior to being invited to screening, and most were unable to describe high-risk. Side effects were frequently mentioned as a barrier to initiating medication, especially in pre-menopausal women. Women felt that knowing their personalised risk would enable informed decision making. Further, women were concerned that GPs don't have the specialist expertise to address side effects appropriately. Following PPIE feedback, GPs and medical oncologists agreed in the importance of personal risk communication prior to offering medication and believed side effects should be co-managed by specialist services and primary care. However, they expressed an unmet need for an effective system to enable this.

**Conclusion:** If informed of their individual risk and all other prevention options, many HL survivors would consider taking BC risk reducing medication, however concern around side effects could prevent initiation. GPs require support from oncologists to manage side effects and highlighted the absence of a system to enable this. To address these issues, we have co-developed a proposed shared-care model for a national centralised service to offer both risk counselling and preventative medication, including centralised side effect management, to BARD women.

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The OxMINT project- improving quality of life and function for breast cancer patients with metastatic bone disease

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In the UK, 25% of patients under Palliative care have metastatic bone disease. A high proportion of these patients have breast cancer. In 2023, the OxMINT (Oxford Metastatic Intervention Team) Quality Improvement project was designed a multi-specialty interest forum with surgeons, interventional radiology and anaesthetics present to hold discussion for patients with complex pain related to patients with metastatic bone disease. Prior to the establishment of the team, discussion about pain and function for patients with metastatic bone disease was disjointed and sporadic.

The OXMINT service supports patients in Oxfordshire, West Berkshire and Buckinghamshire- to date we have had over 300 patients for discussion, 47 of whom are patients with metastatic breast cancer.

47 patients with metastatic breast cancer have now been referred to OXMINT- reflecting 15% of the OxMINT population and age range 40-83.

9 patients were referred for surgery, 6 patients were referred to interventional radiology, 3 patients were referred to the interventional pain team and 15 patients received radiotherapy. 6 remain under surveillance of the orthopaedic team. Only one patient was advised to continue with Systemic Anticancer treatment alone and only five patients continued with best supportive care.

To date, although 22% of breast cancer patients with metastatic bone disease have died since their OxMINT referral. Where surgery has been undertaken, prostheses and intervention has outlived the patient and patients are living more than one year since surgical intervention.

Patients receiving active intervention have been able to reduce their 24h total oral morphine equivalent dose and maintain and or improve their mechanical function and quality of life. Post-operative complication rates remain <10% and inline with national averages.

The OxMINT forum has galvanised the capacity to offer safe, appropriate and long-lasting effective active and interventional management for patients with metastatic bone disease.



### Trastuzumab deruxtecan for HER2-Positive Metastatic Breast Cancer: The Leeds Experience

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**Background:** Approximately 20% of people with breast cancer have tumours that overexpress the human epidermal growth factor receptor 2 (HER2) and their prognosis has been transformed by HER2 targeted therapies. Nevertheless, metastatic breast cancer remains essentially incurable and a significant unmet need. Trastuzumab deruxtecan (T-DXd), a novel antibody-drug conjugate, was introduced in the UK in 2021 for those with HER2-positive metastatic/unresectable breast cancer following >2 prior anti-HER2 therapies. In 2023, approval was broadened to include those having received >1 prior anti-HER2 therapy. Although the efficacy and tolerability of T-DXd were well-documented in clinical trials, real-world data remain limited. This describes the real-world experience of T-DXd in patients treated at Leeds Teaching Hospitals NHS Trust (LTHT).

**Methods:** A retrospective audit was conducted of patients treated between 26/05/21 and 26/05/25 to:

- Identify and describe the most common adverse effects (AEs) associated with T-DXd.
- Describe the duration of treatment and reasons for treatment discontinuation.
- Evaluate the efficacy of T-DXd

in a real world population.

The medical records of all patients with HER2-positive metastatic breast cancer who received T-DXd after 1 or more prior lines of anti-HER2 treatment outside clinical trials were reviewed. Data were extracted from electronic medical records, including clinic letters and ChemoCare® prescriptions.

Results: Forty-three consecutive patients were identified, with a mean age of 53 years (range 24-73), treated with T-DXd managed according to current guidelines.

The mean number of treatment cycles was >16, median 15 (range 1-50) with 3 patients receiving >50 cycles with 2 patients ongoing. Seven of 43 (16%) patients received a reduced dose on cycle 1 and 17/43 (40%) patients required dose reduction(s) while on treatment.

The most commonly reported AEs (all grades) were nausea/vomiting 19/43 (44%) fatigue, 12/43 (28%), diarrhoea 10/43 (23%) and pneumonitis 5/43 (12%) possibly/probably related to T-DXd. Of these 5 patients, 4 discontinued T-DXd; one, with a history of COPD, died 4 months later with progressive disease.

Treatment was discontinued in 22/43 (51%) patients. Most discontinuations were for disease progression 14/22 (67%), but 4/22 (18%) discontinued due to pneumonitis, or other factors, e.g. patient preference 1/22 (5%) or early clinical deterioration and deterioration in performance status 3/22 (14%).

Efficacy (progression free and overall survival) results will be presented.

Conclusion: In this real-world patient population from Leeds, T-DXd had a generally manageable toxicity profile, although dose adjustments were frequent. The most commonly reported AEs aligned with those observed in the Destiny Breast 03 trial. Pneumonitis remains a concern, but the majority of treatment discontinuations were due to disease progression rather than AEs. The median treatment duration of 1 year suggests significant clinical benefit.

Our findings support the use of T-DXd in routine clinical practice and further evaluation in larger cohorts.

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**PRE-ACT-01: The Prediction of Radiotherapy side Effects using explainable AI for patient Communication and Treatment modification-01 Trial**

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Background: PRE-ACT-01 is a multicentre randomized pivotal stage clinical investigation comparing the use of an individualized explainable AI risk prediction for arm lymphoedema (XAINET) to standard care for breast cancer patients indicated for regional lymph node irradiation (RNI). Primary endpoint is arm lymphoedema at 2 years. Secondary endpoints are the choice of radiotherapy fractionation, technique, and nodal level irradiated, locoregional recurrence, other toxicities, quality of life, and performance of the risk prediction in the trial population.

XAINET, based on gradient-boosted decision trees, was trained in three European breast cancer cohorts (REQUITE, Hypo-G, CANTO, total n=6,361) to predict arm lymphoedema, defined as ≥5% increased arm circumference 15 cm proximal and/or 10 cm distal of the olecranon of the treated side from baseline compared to the contralateral side, with an AUC of 0.84 (±0.003) indicating excellent predictive performance.

Methods: Eligible patients must be over 18 years of age, had surgery (+/-(neo)adjuvant systemic therapy) for cT1-4, cN0-N3, MO breast cancer with either mastectomy or breast conservation, and indicated for RNI to levels I +/-II +/-III +/-IV +/-interpectoral nodes (Rotter) +/-the internal mammary chain. Data on 28 clinical and treatment features will be used for the XAINET risk prediction at enrolment. Patients will be randomized 1:1 between the experimental and the control arm.

The individual risk of developing arm lymphoedema will be presented only to patients in the experimental arm by the physician using the PRE-ACTOR web application, which provides patients with explanations to understand their risk, as well as support to make shared treatment decisions regarding radiotherapy, use of prophylactic arm sleeve, and/or lifestyle changes to mitigate the risk of arm lymphoedema.

Results: A total of 724 patients will need to be recruited, assuming 9% have ipsilateral arm lymphoedema 2 years after radiotherapy and accepting an up to 6% increase in arm lymphoedema (total 15%), based on 80% power, 5% significance level, allowing for 5% annual drop-out. Recruitment is planned over 14 months at 35 centres (29 in France, 3 Netherlands, 3 UK) and commenced in September 2025. Analysis is planned 3.5 years after inclusion of the first patient, stratified by radiotherapy technique, lymph node levels irradiated, and treatment centre.

Conclusions: If the use of XAINET causes less lymphoedema and is non-inferior in terms of oncologic outcomes, this clinical investigation will provide robust evidence for integrating AI-based risk prediction into personalised radiotherapy, potentially reducing side-effects like lymphoedema while maintaining oncologic efficacy. Furthermore, the methodology and approach demonstrated in this study could be extended to predict and mitigate other treatment-related toxicities and applied across various oncology disease areas, offering benefits beyond breast cancer and lymphoedema. This has the potential to broadly transform cancer care by enhancing precision and patient-centred outcomes.

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#### Prediction of sentinel lymph node status in early breast cancer using breast imaging as an alternative to surgical staging – A systematic review and meta-analysis

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Background: Prediction models for sentinel lymph node (SLN) status could serve as an alternative to surgical axillary staging in patients with early breast cancer. Several imaging modalities have been used with various feature extraction and selection approaches. This systematic review and meta-analysis aimed to evaluate prediction models for SLN status based on breast imaging in patients with early breast cancer to summarize the current evidence and to identify areas requiring additional research.

Methods: A review protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42022301852) prior to study initiation. The systematic literature search strategy was based on the Population, Intervention, Comparison, and Outcome (PICO) framework: P: female patients with clinically node-negative invasive breast cancer scheduled to undergo primary surgery; I: breast imaging; C: upfront sentinel lymph node biopsy; and O: prediction model performance regarding SLN status. The search was conducted in the PubMed, Embase, Web of Science, Cochrane, and Cumulative Index to Nursing and Allied Health Literature databases in March 2024. The screening of records, data collection, and bias assessments were performed independently by two reviewers. The risk of bias was assessed via the Quality Assessment of Diagnostic Accuracy Studies 2 tool and the Prediction Model Study Risk of Bias Assessment Tool. A meta-analysis was performed using the random-effects model to assess performance and heterogeneity overall as well as in subgroups. Sensitivity analysis of excluded studies assessed having a high risk of bias was performed, and publication bias was evaluated using Egger's test.

Results: The literature search identified 2706 unique records and resulted in the inclusion of 32 articles, with 11 464 patients in total. Five imaging categories were included: ultrasound (n = 8), magnetic resonance imaging (MRI) (n = 17), mammography (n = 1), positron emission tomography computed tomography (n = 1), and multiple modalities (n = 5). Four studies, assessed as having a high risk of bias, were excluded from the meta-analysis. The meta-analysis revealed heterogeneity in overall performance, except for MRI-based studies, with a pooled area under the curve of 0.85 (95% confidence interval 0.82–0.87). Meta-regression indicated that MRI and model calibration assessment upon validation contributed to heterogeneity. No significant changes in performance were observed in the sensitivity analysis. However, Egger's test indicated significant publication bias ( $p = 0.003$ ).

Conclusions: This systematic review and meta-analysis revealed that prediction models using breast imaging could be potential noninvasive alternatives to SLN biopsy in patients with early breast cancer. The MRI subgroup showed homogeneity and a high pooled AUC, indicating that prediction models using MRI could be superior to other imaging modalities for these patients. The results illustrate the heterogeneity between studies and the need for additional high-quality studies to facilitate the clinical implementation of prediction models.

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### Air Pollution and Breast Cancer Risk in the Generations Study, UK

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Background: Previous studies including predominantly post-menopausal women have reported risk associations between breast cancer incidence and ambient air pollution, notably exposure to nitrogen dioxide ( $\text{NO}_2$ ) and particulate matter  $<2.5\mu\text{m}$  in diameter ( $\text{PM}_{2.5}$ ), with weaker evidence for particulate matter  $<10\mu\text{m}$  in diameter ( $\text{PM}_{10}$ ). We used data from the Generations Study, a prospective cohort of women across the UK with a wide age range at study entry, to evaluate these associations overall and by menopausal status.

Methods: Participants were linked to annual average  $\text{NO}_2$ ,  $\text{PM}_{2.5}$ , and  $\text{PM}_{10}$  via their home address using Expanse air pollution surfaces from 2004-2019. Cox proportional hazards models were fitted to estimate hazard ratios (HR) and confidence intervals (95% CI) for each pollutant at year of recruitment. Subgroup analyses investigated the association between air pollution and breast cancer by menopausal status as a time updated covariate, and differences were tested with likelihood ratio tests (LRT). Sensitivity analyses used time lags of 2 and 5 years between exposure and outcome to look at length of exposure.

Results: The study population included 104,584 women (58% pre-menopausal) at study entry. Within the total follow up of 1,219,232.30 person-years, 3,615 women developed breast cancer. Models adjusted for age and year of entry showed a non-significant 8% increase in breast cancer risk for  $\text{PM}_{2.5}$  [HR(95%CI)=1.08 (0.99, 1.18) per  $5\mu\text{g}/\text{m}^3$ ,  $p$ -value=0.08], and weaker or no evidence of risk associations for  $\text{NO}_2$  [1.02 (0.98, 1.06) per  $10\mu\text{g}/\text{m}^3$ ,  $p$ -value = 0.33] and  $\text{PM}_{10}$  [1.01 (0.96, 1.07) per  $5\mu\text{g}/\text{m}^3$ ,  $p$ -value=0.63]. Adjustment by potential confounders at the individual level (body mass index, alcohol consumption, smoking, education, reproductive history) and small area level (deprivation index) had minimal impact on HR estimates. Subgroup analysis by menopausal status showed similar risk associations for pre-menopausal and post-menopausal women [LRT  $p$ -value= 0.65 for  $\text{NO}_2$ , 0.99 for  $\text{PM}_{2.5}$ , and 0.31 for  $\text{PM}_{10}$ ].

Conclusion: Our analyses are consistent with prior evidence for a breast cancer risk association with exposure to air pollutants, particularly  $\text{PM}_{2.5}$  and  $\text{NO}_2$ , and indicate that associations are similar for pre- and post-menopausal women. Further studies should evaluate risk associations for combinations of air pollutants, by tumour subtype, and the impact of changes in exposures overtime.

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## Longitudinal body mass index patterns and associations with tumour characteristics in breast cancer patients

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**Background:** Excess body weight in adulthood is a known risk factor for breast cancer and may negatively impact treatment response and survival. However, the influence of BMI patterns over time on tumor characteristics remains unclear. Here we explored associations between cross-sectional BMI before and at breast cancer diagnosis, as well as longitudinal BMI change, and tumor biology of prognostic and treatment-predictive relevance.

**Methods:** Malmö Diet and Cancer Study participants diagnosed with first invasive breast cancer 1991-2020 and repeated BMI measures available were included (n=1073). K-means clustering was used to construct longitudinal BMI trajectories based on repeated BMIs and time between measures, together with baseline waist circumference, total body fat, and age. Logistic regression models were used to estimate adjusted odds ratios (OR) with 95 % confidence intervals (CI).

**Results:** Median time to breast cancer diagnosis was 12.9 years (interquartile range 7.2-19). The proportion of women with excess BMI increased from 49.1% at baseline to 53.4% at diagnosis. Cross-sectional overweight at baseline was linked to higher risk of grade II/III tumors and lower risk of luminal A-like subtype, while obesity was associated with increased intermediate/high Ki67 expression. At diagnosis, obesity remained associated with intermediate/high Ki67 and luminal B-like subtype. Six BMI trajectories were identified according to BMI stable (lean, overweight, obesity) or change (loss, moderate gain, major gain). Compared to stable lean BMI, stable obesity was linked to higher Ki67 expression. Moderate weight gain was associated with reduced risk of HER2+ tumors, whereas major weight gain increased the risk of grade II/III tumors and luminal B-like subtype. Weight loss was linked to larger tumors, lymph node positivity, and triple-negative subtype.

**Conclusion:** These findings highlight the clinical relevance of longitudinal BMI patterns, showing that excess BMI and BMI changes over time are associated with distinct breast tumor characteristics and subtypes, which may inform future identification of high-risk women for personalized prevention or treatment strategies.

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## The Influence of PET Scanning in the Management of Patients with Breast Cancer

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**Background:** Positron Emission Tomography (PET) is an established diagnostic tool used for staging of many cancers. The impact of PET scans on breast cancer diagnosis and treatment remains less clear. The Royal College of Radiologists have offered some national guidance with regards to selection criteria. Whilst this helps multi-disciplinary team discussions and commissioning, without the evidence, there is some reluctance to adopt this nationally.

**Method:** Retrospective analysis of 71 breast cancer patients who received a PET scan from 2017 - 2025. Each patient was manually reviewed on Welsh Clinical Portal, searching through patient notes, clinic letters, MDT meetings, histology reports and imaging (CT/MRI/PET) reports.

**Results:** PET scanning upstaged 36 (50.7%) patients, identifying disease not demonstrated on conventional imaging. As a result, it changed the disease management in 24 (34%) and intent from radical to palliative in 20 (28%). We found no statistical correlation with tumour size, immunohistochemistry and nodal stage. Of those where distant metastases and lymph nodes identified on PET, 22 (84.6%) and 36 (65.5%) respectively were not apparent on conventional imaging. Internal mammary lymph node involvement was identified in 15 (21%) patients, 9 (12%) of which were not apparent on prior imaging.

Conclusion: We have demonstrated that PET scanning is an important diagnostic modality for staging locally advanced breast cancer. It directly influences staging by identifying metastatic disease not apparent on conventional imaging and therefore has a subsequent impact on treatment and prognosis. Further work is required to identify which patients benefit most from further imaging.

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A survey of the acceptability of wearing the SENSTM motion exercise tracking device in patients being treated for early and advanced breast cancer

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**Background:** The importance of exercise in breast cancer has been investigated and recognised as improving breast cancer outcomes. Monitoring frequency/intensity and adherence to exercise intervention (EI) remains challenging. This may be improved by tracking the EI and reviewing with patients. A suitable device could also be incorporated into future research studying the efficacy of specific exercise prescriptions on breast cancer outcomes.

The SENSTM motion tracker is a 3cm external, easily applied device that is fixed by a dressing to the skin on the outer thigh. It has been used in several studies in both cancer and other pathologies and can digitally record different types of exercise over 2 weeks. Manufacturer's manual cites water resistance up to 1 hour at 1.5m.

We aim to assess the acceptability of wearing the SENSTM motion tracking device in patients either on or after treatment for early and advanced breast cancer. As the investigation of EI in advanced disease is limited, we concentrated on the views in this group.

**Methods:** A survey of 6 closed and 3 open questions was linked to a QR code. Patients with early and advanced breast cancer were approached at MTW routine clinics and given a patient information sheet. If patients identified as willing to participate, they were shown the device, explained the practicalities of use and given the QR code. The anonymised survey could be completed at any time. The survey was also available to other advanced disease patients through The Make 2NDS COUNT (M2C) patient charity that Dr Harper-Wynne presented at the annual meeting and was then accessible on their website. Quantitative responses were analysed and qualitative comments were thematically reviewed.

**Results:** A total of 47 early and 95 advanced breast cancer patients completed the survey. The median age range for both early and advanced breast cancer was 50-59 years. Recruiting from the M2C conference increased advanced disease participants from 38 to 95. Over 95% of all participants had access to a smartphone or device; 100% in advanced disease patients. Over 98% could download and use an app. 98% in early and 99% in advanced disease were willing to use the SENSTM Motion device with over 98% acceptance of app tracking of exercise data.

The qualitative data collected reflected a positive opinion on the device and the incentive to exercise. The apprehensions focused around the plaster being hypoallergic for sensitive skin and the degree of resistance of the tracker to water-based exercise.

**Conclusion:** The SENSTM Motion tracking device was very well accepted among patients with both early and advanced breast cancer. These findings support potential integration of this device into future research to monitor and encourage physical activity as part of breast cancer management.

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# Diagnosis to Survival: a systematic scoping review of the experiences of Black women with breast cancer in the UK

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**Background:** Ethnic health disparities in breast cancer care and experiences are well-documented, with differences across the various stages of the cancer pathway shaping patient experiences and outcomes. Evidence has shown that women from minoritised ethnic groups have poorer breast cancer outcomes. However, despite growing international evidence, there has been limited synthesis of UK-specific research examining the ethnic health disparities in breast cancer experiences of Black women. This review aimed to synthesise UK-based evidence on diagnosis rates, treatment patterns, experiences of care, and outcomes for Black women with breast cancer.

**Methods:** A mixed-methods systematic scoping review of primary peer-reviewed research and grey literature was conducted. Searches were undertaken across seven databases (CINAHL, EMBASE, MEDLINE, PsycINFO, PubMed, Scopus, & Web of Science) between October and November 2024. Search terms included "breast cancer", "Black women", "UK", "experiences", and "disparities". The search identified 4,973 records, of which 35 articles met the inclusion criteria. Data were extracted using a structured extraction table and synthesised narratively.

**Results:** Evidence was synthesised across four domains: (1) Diagnosis and Incidence, (2) Treatment Patterns and Adherence, (3) Experiences of Care, and (4) Survival and Outcomes. Evidence suggested that Black women are more likely to be diagnosed at a younger age and with more aggressive breast cancer subtypes. Patterns of treatment were inconsistent; while some studies indicated higher rates of chemotherapy or surgical intervention among Black women, no clear overall trends were established, and very few studies specifically explored treatment adherence. Qualitative evidence on experiences of care highlighted accounts of racialised interactions, limited cultural sensitivity within services, a lack of representation in information and support, and differences in communication preferences between Black and white patients. Survival outcomes were often poorer for Black women compared with white women, though findings varied across studies.

**Conclusions:** This review indicates persistent disparities across multiple stages of the breast cancer pathway for Black women in the UK, from diagnosis through to outcomes. The evidence base remains limited, particularly around treatment engagement and adherence, and more robust, longitudinal, and intersectional research is needed. Addressing these disparities is essential to ensuring equitable cancer care and improving outcomes for Black women.

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## Biographical Continuity: A Qualitative Study of the Role of Complementary and Alternative Medicine usage after Breast Cancer Diagnosis

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**Background:** Breast cancer patients frequently use complementary and alternative medicine (CAM) alongside conventional biomedical treatment for symptom relief and to address the disruption caused by diagnosis and treatment. Rates of CAM use appear to be rising. This study explored CAM use in women with breast cancer, focusing on three research questions: Why do women with breast cancer use CAM? In what ways does CAM help maintain or regain a sense of normality? What barriers or tensions do they face when considering or using CAM?

**Methods:** This study used a qualitative interpretative-constructivist research design to analyse the subjective meanings women with breast cancer ascribed to their CAM use during breast cancer treatment. Unstructured interviews were conducted with nine female breast cancer patients undertaking treatment at a major NHS Cancer Centre in Southeast England who were using CAM alongside conventional therapies. The interviews were analysed using a reflexive thematic analysis.

**Results:** These women engaged with a wide range of CAM therapies during their cancer journey. CAM was used not only to alleviate symptoms, but also to restore a sense of 'ordinariness' and biographical continuity amid the disruption caused by disease and treatment. Central to this process were practices of self-care, self-help, and self-management, and the collaboration of CAM practitioners and open-minded medical doctors. Barriers included dominant biomedical approaches, limited information sharing and communication about CAM, financial and geographical constraints, and little clinical validation by medical staff.

**Conclusions:** These women experienced tensions and conflicts when trying to use CAM alongside cancer treatment. They sought overall well-being but often encountered barriers to accessing CAM and sharing their experiences within a biomedical context. Despite this CAM had value for these women by restoring a sense of normality in their lives regardless of any expected or hoped for biological effect.

These interviews highlight a need to raise professional awareness of CAM use by women with breast cancer, to normalise CAM dialogue in the clinical encounter and considering relational care in training.

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## Evaluating Attendance Rates for NHS Breast Screening: A Primary Care Audit in the North East of England

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Evaluating Attendance Rates for NHS Breast Screening: A Primary Care Audit in the North East of England

**Background:** The NHS Breast Screening Programme invites women aged 50–70-years-old for mammography every three years to enable early detection of breast cancer. Attendance at screening is crucial to timely diagnosis and improve survival outcomes, yet uptake varies across socioeconomic status, ethnicity, and other demographic factors, creating health disparities. General Practices (GP) play a crucial role in identifying gaps in uptake, promoting participation, and supporting interventions to improve attendance.

**Aim:** To assess the percentage of eligible women registered with a GP in a deprived area of North East of England, who attended their scheduled breast screening mammograms; and, to identify potential intervention areas to improve uptake.

**Methods:** A retrospective review of 1,147 women invited for NHS Breast Screening between 01/08/2022 and 01/08/2025 was conducted, with data collected on Index of Multiple Deprivation Deciles using postcode, age group, and ethnicity via census records.

**Results:** Overall attendance of the practice was 71% (compared to 70% national target). Socioeconomic status showed the greatest disparity: uptake was 42.5% in the most deprived 1% of the IMDR. Attendance was 64.5% in the two most deprived deciles, compared with 88.8% in the two least deprived decile. Ethnic variation was marked: uptake was highest among Middle Eastern (75.0%) and White British (74.9%), and lowest among White European (41.7%). However, sample sizes between ethnic groups showed large disparities. Age differences were minimal, with 71.9% of 50–59-year-olds attending compared to 71.0% in those aged 60–70.

**Conclusions:** Deprivation is a strong predictor of reduced uptake of breast cancer screening, with additional disparities by ethnicity. Focused outreach in deprived postcodes and targeted at ethnic groups may help reduce inequalities. For example, through culturally sensitive information leaflets, follow-up telephone calls, and personalised reminder texts. A re-audit is planned after implementing the above recommendations.

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## Empowering and educating secondary breast cancer patients through the UK's first Secondary Breast Cancer Patient Summit

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Around 61,000 people are estimated to be living UK with secondary (metastatic) breast cancer (SBC) in the UK . For these people it's important that they receive the kind of educational support that can strengthen their ability to make decisions, feel a sense of control and empowerment, and to live with the disease with more optimism and hope.

A recent LIMBER Study (2022) revealed that 71% of women living with the disease wished they had known more about secondary breast cancer, and a Clinical Trials Study (2021) revealed that patients wanted to understand more about research and clinical trials. In 2024 a collaborative project co-led by a clinician, a patient advocate and a UK charity, Make 2nds Count, organised a Patient Summit, to directly address this need for education and support for patients. A second successful summit was held in June 2025, and there are plans to make this an annual event.

As well as educating, informing and listening to patients, the aim of the Summits is to provide a sense of hope for the future and foster community spirit, for patients who often feel ignored and 'written off'.

The programme is designed with patients at the heart of planning, delivery and evaluation.

In 2025 there were record levels of engagement with 525 patient attendees (109 in person and 416 live online), attendees ranging in age from 29 to 71, and 26 expert speakers. Topics included the latest secondary breast cancer treatments, trials, palliative care, side effects and radiotherapy. All speakers were asked to present using plain English, - with plenty of time for audience interaction as part of each session.

- 97% of patients rated the experience as 'excellent'
- 100% of expert speakers said they gained valuable insights into patient experiences
- 84% said they felt more confident talking to their clinical team
- 70% said they felt less alone

In feedback patients said:

- "It sounds dramatic but attending events like this summit changes lives! I had a voice, I was heard and I felt validated...This was a fantastic opportunity to further my knowledge and to give me confidence to be a better advocate for my future"

In feedback clinicians said:

- "Saw the true value a patient focused event can make to patients"
- "Endless food for thought and some great new contacts for patient advocacy. Helpful shaping of research questions and trial conduct questions form a hugely motivated audience."

Conclusion: This unique patient focused event empowers and educates secondary breast cancer patients, and demonstrates the appetite that MBC patients have to find out more about the disease. Attending an event like this benefits both patients and HCPs – patients feel heard, HCPs gain patient insight.

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## Giving metastatic patients hope through a unique trial matching service

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It is estimated that around 61,000 people are living in the UK with metastatic breast cancer, which can be treated but not cured. For those people timely access to new therapies and trials is critical. For many, clinical trials may offer more treatment options but there are barriers to participation.

Data from a survey of 768 metastatic breast cancer patients<sup>2</sup> reveals that they are interested in taking part in clinical research and trials, but only 23% have discussed clinical trials with their clinician. Of this group only 14% have been accepted onto a trial. Key barriers for patients are a lack of information, their perception of clinical trials and the barriers to accessing trials. As a result of this data, Make 2nds Count, a charity dedicated to supporting patients living with metastatic breast cancer, set up a trial matching service known as the Clinical Trials Service (CTS). This service aims to educate and empower patients around clinical trials.

To develop the CTS, the charity recruited an NHS research nurse to work with a patient to co-design the service, and it was launched as a pilot in 2021 in Scotland. Following a successful pilot, the service has since been rolled out across the UK.

The service allows patients to book dedicated time with a research nurse, to review their medical history and get support navigating the complex information associated with clinical trials. Patients receive a personalised clinical trials search report based on their preferences and eligibility criteria. With patient consent, their clinician is contacted, enabling the patient and clinician to discuss the potential trials list together.

Since the service began, over 1000 patients have used it. Some patients have stable disease and don't need a trial, others have a poor prognosis resulting in being ineligible for trials. Rarely have we been unable to find a trial for a patient.

The service identified eligible trials for 92% of patients, and feedback has been very positive. After using the service:

- 80% of patients plan to speak to their clinician about a trial (compared with 57% previously)
- They rate the service as 'highly effective' in building their knowledge and all would recommend the service to a fellow patient

A clinician said "I have referred many patients to the PTA service and have noted several benefits to the process. Patients share that they feel positive about the future and feel reassured that all options have been explored for them".

Conclusion: This unique to the UK service has given hope to secondary breast cancer patients, who often feel "a little bit written off", and given them the tools and confidence to speak to their clinicians about clinical trials.



# Expanding the spectrum of rare breast cancers – HER2 positive Invasive Lobular Carcinoma with Extracellular Mucin: Histological comparison with other mucin-producing breast cancers to aid diagnosis.

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**Background:** Invasive lobular carcinoma with extracellular mucin (ILCEM), a rare morphological breast cancer subtype, combines features of invasive lobular carcinoma (ILC) with extracellular mucin production – an unusual feature more typical of mucinous or ductal carcinomas. This dual morphology complicates histopathological diagnosis and may lead to misclassification. While classic ILC is oestrogen receptor (ER) positive and HER2 receptor negative, HER2 positive ILCEM is exceptionally rare. Awareness of this entity is critical to ensure accurate diagnosis and appropriate clinical management.

**Methods:** PubMed search keywords “invasive lobular carcinoma with extracellular mucin” with special attention to morphology, receptor status, immunohistochemistry and molecular features revealed 40 cases in English literature. Five cases demonstrating HER2 positivity (12.5% of published cases), suggest this phenotype, while rare, may be under-recognised. We present two HER2 positive ILCEM cases from the UK and Singapore after obtaining informed consent.

**Case 1:** An 84-year-old lady presented with a palpable breast mass and a clinico-radiologically negative axilla. Imaging revealed a 20mm asymmetric density. Core biopsy diagnosed a mixed lobular/mucinous invasive cancer, ER positive, PR negative, Her2-positive. Histology post -mastectomy/sentinel node biopsy confirmed 71mm grade 2 ILCEM with solid and mucinous components. Immunohistochemistry showed ER positivity, PR negativity, E-cadherin loss, and heterogeneous HER2 expression confirmed by FISH amplification. SLNB showed isolated tumour cells only. The tumour reached the posterior margin requiring adjuvant radiotherapy/endocrine treatment, chemotherapy not recommended. Patient remains disease-free at one year.

**Case 2:** A 50-year-old Indonesian woman with a 3-cm spiculate mass in the breast. Biopsy showed two distinct components: classic ILC and areas with extracellular mucin. Both components demonstrated loss of E- Cadherin and HER2 overexpression, confirmed by dual in situ hybridization (DDISH), ER moderately positive, PR negative. No follow up data available as patient returned overseas post-diagnosis.

Both cases highlight the defining features of ILCEM: discohesive tumour cells infiltrating in single file or solid patterns, extracellular mucin deposition, E-cadherin loss, and HER2 amplification.

**Differential diagnosis:** The differential diagnoses of ILCEM include mucinous carcinoma, solid papillary carcinoma, micropapillary mucinous carcinoma, polymorphous adenocarcinoma, and metastatic signet-ring cell carcinoma. These entities often share mucin production but differ in architectural and immunohistochemical features – particularly, retention of E-cadherin expression. Accurate diagnosis relies on identifying features such as single-file growth, discohesive cells, and E-cadherin loss, distinguishing ILCEM from these morphologically similar mucin-producing tumours.

Features	ILCEM	Mucinous carcinoma	Mixed mucinous-NST	Solid papillary carcinoma (SPC)	Micro papillary mucinous carcinoma (MPMC)	Poly morphous adeno carcinoma (PmA)	Metastatic signet ring gastric carcinoma
Extracellular mucin	Present	Present	Present	May be present	Present	Absent (myxo chondroid stroma)	Present
Single file pattern	Present	Absent	Absent	Absent	Absent	Present	Present
Targetoid pattern	Present	Absent	Absent	Absent	Absent	Present	Present
Signet ring cells	Present mostly	Present on occasion	Rare	Present occasionally	Absent	Absent	Present
Fibrovascular cores	Absent	Absent	Absent	Present	Absent	Absent	Absent
E-cadherin	Loss	Intact	Intact	Intact	May show loss of E-cadherin	Intact	Loss
ER/PR	Positive mostly	Positive	Positive	Positive	Positive/Negative	Negative	Negative (positive for CDX2; GATA3 negative)
HER2	Negative Mostly	Negative	Positive/Negative	Positive/Negative	Positive/Negative	Negative	Positive/Negative
NE markers	Absent	Present in type B form	Absent	Present	Absent	Absent	Negative

Table 1: Differential diagnoses of invasive lobular carcinoma with extracellular mucin

Conclusion: ILCEM represents a diagnostically challenging yet clinically relevant breast cancer subtype. Its rarity combined with overlapping features with other mucin-producing tumours, emphasises the need for careful morphological evaluation and confirmatory immunohistochemistry, particularly for E-cadherin and HER2. The HER2 positive cases presented here expand current knowledge highlighting potential for targeted therapeutic strategies. Increased recognition, documentation, and molecular analysis of ILCEM will be essential for refining diagnosis, guiding treatment and improving outcomes.

#### A National Survey of Cavity Shave Practice in Breast Conserving Surgery Amongst UK Breast Surgeons

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Background: Breast cancer (BC) surgery remains the mainstay of treatment, with over 55,000 new diagnoses annually in the UK, including 7,000 cases of Ductal Carcinoma in Situ (DCIS). More than 90% of patients undergo surgical management, typically breast conserving surgery (BCS) or mastectomy. BCS, combined with radiotherapy, has become a standard treatment supported by landmark trials. Advances such as local flaps now allow BCS in many cases where mastectomy was once necessary.

The National Margins-2 audit (2023) reported that 29% of women with DCIS undergoing BCS required margin re-excision, despite over 88% of units adhering to the Association of Breast Surgeons (ABS) guideline of at least 1 mm clearance. These women also had nearly a threefold higher local recurrence risk compared to those with invasive disease. With minimum margin width recommendations now at 2 mm (ABS and NICE), re-excision rates are expected to rise further.

Real-time intraoperative margin assessment techniques are in development but remain costly and technically demanding. Routine cavity shaving—removal of additional cavity margins at initial surgery—has been studied as a simple, low-cost method to reduce positive margin rates. Despite level 1 evidence

published in 2015 by Chagpar et al. supporting this practice, there is currently no national guidance recommending its routine use.

We aim to investigate the current use of cavity shaving in the UK and explore factors that influence surgeons' decisions to adopt or avoid this technique.

**Methods:** We conducted a national electronic survey of UK breast surgeons, targeting consultants, associate specialists (AS), and senior trainees. Consultants and AS were asked about their standard practice for intraoperative cavity shaves in invasive cancer and DCIS, and reasons for not using this technique. Trainees were additionally asked whether their practice aligned with their supervisor and if they would adopt cavity shaving independently.

**Results:** A total of 123 responses were received from 68 units: 91 from consultants and AS, and 32 from trainees. Consultant and AS responses are summarised in Table 1. Among trainees, 97% reported their margin practice matched their supervisor, and 42% indicated they would consider adopting routine cavity shaving in independent practice.

	Margin close-selective shave taken	Routine 4-6 cavity shaves		
Invasive Cancer: What is your standard practice for intra-op cavity shaves?	80 (88%)	11 (12%)		
DCIS: What is your standard practice for intra-op cavity shaves?	75 (82%)	16 (18%)		
	Not necessary	Volume loss-aesthetic outcome	No convincing literature evidence	Other
If you do not perform routine cavity shaves, what puts you off from undertaking this? (74 responses)	17 (23%)	27 (36%)	20 (27%)	10 (14%)

*Table 1 Results of survey from consultants and AS*

**Conclusions:** Despite Level 1 evidence supporting cavity shave practice, fewer than one in five UK breast surgeons routinely adopt this technique. With updated national guidance for DCIS likely increasing re-excision rates, strategies are needed to manage positive margins without exposing more women to margin re-excisions or mastectomies while maintaining the GIFT recommendation of prioritising BCS without compromising oncological safety. A randomised trial evaluating cavity shave in pure DCIS could provide compelling evidence to support wider adoption within the breast surgical community.

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#### Evaluation of Clinic Recalls for Early Breast Cancer patients on a Personalised Stratified Follow up programme

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**Background:** Supported self-management within Personalised Stratified Follow up (PSFU) in early breast cancer patients was implemented at Ashford and St Peter's Hospital (ASPH) in 2016. As of September 2025, there are 926 active patients in the PSFU programme at ASPH. We conducted a snapshot review of patients who were recalled to clinic in one year, which was triggered by patient-related concerns reported to the breast care team. The aim of the review was to assess the effectiveness of PSFU (based

on the proportion of patients booked to clinic) and to identify any patterns or factors which increase the likelihood of clinic recall while on PSFU.

**Methods:** Patients booked to dedicated PSFU clinics at ASPH between July 2024 and July 2025 were identified from the PSFU database. Baseline patient demographics (age, stage, grade, tumour subtype) and treatment details were collected from treatment summary reviews and electronic patient records. PSFU clinic details (timeframe from point of entry into PSFU, reason for clinic review, investigations and outcome) were collected from electronic patient records.

**Results:** 108 patients were included, representing 11.7% of the total number of active patients in PSFU. Median age was 58 years. 65.7% were node negative and 25% node positive. 32.4% received chemotherapy, 83.3% received radiotherapy, and 75.9% received endocrine therapy. 45.4% were in year 1 of follow up in PSFU, 18.5% in year 2, 13.9% in year 3, 14.8% in year 4, 7.4% in year 5 and after. The most common reason for clinic review was breast or axillary symptoms (lumps, pain, skin changes) which were 71.3%. The other reasons included bone pain (16.7%), other lumps or lymphadenopathy (3.7%), follow up on surveillance or other scan results (4.6%) and side effects from endocrine therapy (1.9%). 79.6% underwent further investigations (scans +/- biopsies). 89.8% were referred back to PSFU, and 5.6% referred to other specialists. Recurrences were diagnosed in 5 patients; all presented with symptoms and were within their first 3 years of PSFU.

**Conclusion:** Supported self-management within PSFU at ASPH is effective with a relatively low proportion of patients recalled for clinic review while in the programme. When compared with traditional methods of follow up, it has been effective in reducing the number of routine appointments thereby increasing clinic capacity for new or urgent patients. We did not identify any patient, tumour or treatment-related factors leading to an increased likelihood of clinic recall. Nearly half of the patients were in their first year of follow up in PSFU. The majority were presenting with breast or axillary symptoms and following appropriate investigations, the majority were referred back into PSFU. Further workstreams are ongoing to evaluate patient experience and how they can be better supported especially in their first year of follow-up.

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#### Mainstreaming Genomics in a Breast Cancer Unit, How accurate are the nurse pre-conceptions of Nurse Led Genomic Mainstreaming in practice?

Sara Trotman

**Background:** The NHS ten-year plan follows on from the previous governments preceding plan to introduce and embed Genomics into mainstream clinical and ward healthcare environments by 2035. Nurses are recognised as being an important part of the workforce within this plan, identified in the Nursing and Midwifery framework for best patient outcomes, biologically optimal treatment options, health promotion, screening whilst investing in the future of the NHS. Nurses are best placed to action genomics in the therapeutic setting.

**Method:** A Qualitative pilot study, of Breast Care Nurses, educated to identify, counsel, and test, patients for mainstream genomic testing, deliver results, refer and organise follow up. Using an anonymous online survey aimed to identify attitudes before and after Genomic upskilling. To understand the anticipated vs actual workload and the concept of genomics in healthcare.

A series of 7 closed questions asking about confidence, support and knowledge with 2 open text questions for a deeper understanding of opinion, based on 5 members of a breast care unit, practicing mainstream genomics. Four recipients responded.

An ethical approval was not needed as this is not a cause-and-effect research study on any biological samples or participants or collecting identifiable information (UKRI 2025).

**Results –** BCN's were surveyed for a basic opinion before and after mainstreaming genomics. 50% felt Negative about genomics before undertaking it, however following training and experience, 100% of

nurses felt positive or very positive and confident in genomics. Whilst understanding its importance in healthcare. 100% of nurses felt supported when learning and undertaking mainstream genomic testing.

**Conclusion:** The findings of this local pilot proposal are not unexpected. Knowledge, confidence, workload, time, income, support and adapting to change continues to be negative barriers to change culture in healthcare. However, despite these concerns, the consensus of benefits being patient focused, and all respondents recognised that Mainstreaming and genomics is the future and supports empowerment of patients in their own health salience, regarding health promotion, disease prevention and early diagnosis making treatment more manageable to both patients and the NHS moving forward.

Training and support for mainstreaming genomics in a breast unit has improved patient's outcomes and provided 12% of patients with positive genomic results to be applicable for specialist treatment or prophylactic surgery with improved screening and health education for themselves and their families and this has empowered nurses to upskill and improve their knowledge base whilst feeling supported and recognised in the clinical setting. With national nursing and midwifery competencies developed to reinforce the work in this sector which is recognised by the nursing regulators under extreme current conditions within the NHS.

A larger cohort study is viable as planned Mainstreaming is rolled out throughout the Southwest.

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### Rethinking the message on alcohol and breast cancer: findings from a Delphi Study

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**Background:** Despite the fact that alcohol consumption is a well-established risk factor for breast cancer in women, public awareness of this link is low. Existing communication strategies often neglect the socio-emotional context in which such messages are received. This study therefore sought to provide a novel, participant-informed approach to message development, grounded in public involvement.

**Methods:** A Delphi study was conducted with women aged 40–65 who currently consumed alcohol, or had done so in the past. In the first round, participants were recruited to an online survey using existing national networks relating to alcohol reduction, breast cancer, local patient and public involvement groups, a local library and social media. In rounds 2 and 3, responses were explored in greater depth with a sub-sample of respondents through seven online focus groups (n=33) and a workshop (n=7), to review themes and findings. A reflexive thematic analysis of data was undertaken. A Public Advisory Group of six women provided feedback on all study materials and aided with the interpretation of the findings

**Results:** Two overarching themes were identified: (1) barriers to effective communication, including sub-themes of socio-cultural factors, conflicting messaging and trust concerns, psychological barriers and unintended consequences including fear, stigma and shame ; and (2) messaging strategies for overcoming these barriers, with narrative-based approaches (e.g. personal stories) identified as a promising alternative to hard-hitting or fear-based messaging and the importance of clear and evidence-based information to underpin strategies.

**Conclusion:** The findings from this study offer a framework for constructing public health messages that resonates with diverse audiences while avoiding unintended harms. By foregrounding the emotional and cultural dynamics of risk perception, this research contributes significant and timely evidence to inform breast cancer prevention campaigns.

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## Progress with the SWEET Trial – Supporting women with breast cancer with adherence to adjuvant endocrine therapy

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**Background:** Adherence to adjuvant Endocrine Therapy (AET) in women with early stage breast cancer is a significant problem: approximately 20% of women have poor adherence after two years and around 50% by five years. The SWEET programme has developed an evidence based, theoretically informed and patient centred intervention to support adherence: the HT&Me intervention. A large, UK-wide trial is currently underway to assess the effectiveness of HT&Me in reducing poor adherence and improving quality of life.

**Methods:** The trial is a multi-centre, unblinded, pragmatic randomised controlled trial (RCT) of the HT&Me intervention + usual care compared to usual care alone. The intervention comprises an initial and follow-up tailored consultation with a trained health care professional, access to an interactive website which provides information, advice, support and behavioural strategies to support adherence, and monthly 'nudge' messages for 18 months. The target sample size is 1606 (including 10% over initial target) recruited over a period of 24 months, and followed up for 18 months. Adherence is being measured using a combination of self-report (MARS-5) at 6, 12 and 18 month and monthly community prescription encashment records. Quality of life is being measured using FACT-G. Secondary outcomes include AET-specific HRQoL and cost-effectiveness. Fidelity of delivery of consultations is being assessed by recordings and checklists.

**Results:** We have successfully recruited 1606 women from 66 sites over an 18 month period. 61% sites (40) have delivered the consultations through site staff, 39% (26) sites have had the intervention delivered remotely by a trained Breast Cancer Now nurse, working as part of the trial team. Withdrawals have been low (2.5%). 77% (433/561) of women have completed 6 month questionnaires, and 72% (90/125) 12 month questionnaires to date. Data quality to date is high, with self-reported AET adherence and HRQoL able to be calculated for 99% of women who have completed questionnaires.

A qualitative and quantitative process evaluation is underway. Initial qualitative feedback on the intervention from women and healthcare professionals is very positive. Interim examination of web analytics reveals that the majority of women in the intervention arm have accessed the web-app (76.9% (574/746)), with 86.8% (249/287) of participants to date still active on the website six months after their initial visit.

**Conclusion:** The SWEET trial has successfully recruited to target, including women with ER +ve early stage breast cancer recruited from a range of hospital sites from around the UK. Follow-up is underway and the trial will report in early 2028. An implementation workstream is preparing for roll out of the intervention if the trial shows the intervention to be effective and cost-effective.

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## Patients with breast cancer have elevated plasminogen activator-1 and delayed fibrinolysis

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**Background:** Cancer associated thrombosis (CAT) is the second leading cause of mortality in cancer patients. Due to the high prevalence of cancer, these patients account for a high incidence of CAT. Tumour cells release procoagulant factors and promote hyperactivation of platelets which promote the

development of CAT. However, the clinical significance of a thrombus is dependent on both coagulation and breakdown (fibrinolysis). The fibrinolytic system involves the activation of the zymogen plasminogen into plasmin which cleaves the fibrin clot into degradation products. This is regulated by plasminogen activators/inhibitors including plasminogen activator inhibitor-1 (PAI-1). Here, we aim to determine whether patients with breast cancer have dysregulated fibrinolysis which may contribute to increased risk of CAT.

**Method:** Citrated (3.2 %) blood from healthy volunteers (n = 26) or patients (n = 100) with breast cancer was collected via NHS Grampian Biorepository prior to initiation of treatment. Platelet poor plasma was collected by centrifugation at 1860 x g for 30 min 4 °C. Clot formation was monitored as change in absorbance at 405 nm in plasma (30 % + 16 µM phospholipids) clotted with CaCl2 (10.6 mM) and tissue factor (1 pM) in the presence or absence of tissue plasminogen activator (tPA). PAI-1 activity was measured by ELISA.

**Results:** Patients had a median age of 60 (IQR 51 – 88), BMI of 27 (23.5 – 32.9) and 99 % were female. The lag time for clot formation was shorter in patients with breast cancer compared to the healthy controls (108.1 (74.0 – 141.6) vs. 149.6 (90.0 – 201.3)). However, the maximum absorbances did not differ between groups. The time to 50 % clot lysis with tPA was delayed in patients with breast cancer compared to healthy controls (95.9 (81.9 – 126) vs. 87.1 (76.9 -99.9) min). PAI-1 activity was 2-fold higher in patients with breast cancer compared to healthy controls (3.5 (2.1 – 6.5) vs 7.1 (4.1 – 12.9) U/mL). At present, 3/100 patients have had a significant thrombotic event.

**Conclusions:** Patients with breast cancer have faster clot formation, delayed fibrinolysis and elevated PAI-1 activity. Attenuated fibrinolytic potential could predispose patients to CAT and warrants further investigation.

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Development and evaluation of a one-day communication workshop for healthcare professionals working in a metastatic breast cancer (MBC) setting

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**Background:** Numerous reports and surveys have revealed many criticisms about the quality and content of communication between people living with metastatic breast cancer (MBC) and their health care providers (HCPs). The paucity of specific communication skills training (CST) and high levels of burnout contribute to this dissatisfaction. Based on these findings and an in-depth patient survey we developed and evaluated the impact of a CST workshop for HCPs.

**Methods:** The 6-hour small group, facilitator-led workshops included:- didactic presentations, exercises about issues such as disclosing prognosis and group discussions about filmed verbatims from patients with MBC as to what HCPs did or said that helped or hindered understanding and satisfaction. HCPs were recruited via websites and academic organisations. Prior to attendance they completed online:- General Health Questionnaire(GHQ12) a screening measure of psychological morbidity; Standford Fulfilment Index (SFI) examining work exhaustion & burnout; and a navigating professional boundaries questionnaire (NPB). Self-confidence when discussing 9 MBC issues was assessed pre- and post-workshop.

**Results:** Twenty surgeons, 26 oncologists, and 20 nurses participated in 5 workshops. Overall 14/66(21.2%) had GHQ12 scores of 4 or more indicating heightened anxiety and psychological concerns, 21/66(31.8%) were experiencing burnout and merely (21/66(31.8%) felt professionally fulfilled by their work. Higher anxiety levels (GHQ-12  $\geq$  4) were associated with increased odds of burnout (OR = 6.0, 95% CI: 1.7 to 21.0, p = 0.0057) and also reduced odds of professional fulfilment (OR = 0.12, 95% CI: 0.015 to 1.00, p = 0.052). Metastatic and specialist nurses were less fulfilled (16.7% & 14.3% respectively) compared with surgeons and oncologists (50% & 30.8% respectively). The primary outcome of overall self-confidence when communicating about different issues across 9 areas including patients from varied socio-educational backgrounds, different ages and diagnosed with MBC either de-novo or following

recurrence, improved significantly post workshop (mean change = 1.5, 95%CI:1.14 to 1.81). Workshops were rated highly by all participants who would encourage colleagues to attend.

**Conclusion:** The dissatisfaction with HCPs' communication reported by patients with MBC is multifactorial. Bespoke small-group workshops using patient verbatims, that help address psychological and practice constraints inhibiting effective communication, were shown to improve HCPs' self-confidence when discussing challenging areas during MBC consultations.

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## The Power of Less: Evidence-Based De-escalation of Denosumab for Optimal Patient Outcomes and Resource Utilisation

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**Background:** Conventional protocols for bone-modifying agents (BMAs) suggest dosing at 3-4-week intervals diagnosis of following bone metastases. The long-term dosing schedule raises concerns about toxicity, patient inconvenience, and healthcare costs, has prompted studies into extended-interval dosing. Despite widespread BMA use, optimal dosing frequency remains uncertain.

A 2021 survey by Alzahrani et al., revealed that 82.5% (33/40) of oncologists already practice de-escalation approaches, with 60% uncertain about the benefits of BMAs beyond two years. Ibrahim et al.'s (2015) systematic review and meta-analysis demonstrated no significant difference in Skeletal-Related Events (SRE) rates between standard (q4w) and de-escalated (q12w) regimens (RR 0.90, 95% CI 0.63-1.29) suggesting non-inferiority of extended-interval dosing. The REDUSE trial showed significantly lower incidence of hypocalcaemia with Q12W dosing (15.8% vs 31.6%), with more patients improving after transition (57.8% vs 27.4%). A practice-changing approach to managing patients with BMAs was adopted locally with following aims:

1. To implement a standardised, evidence-based protocol for denosumab de-escalation from q4w to q12w dosing for eligible patients
2. To reduce patient hospital visits while maintaining clinical efficacy
3. To quantify environmental and economic benefits of extended-interval dosing

**Methods:** Following formal governance approval and agreement from all tumour site consultants (February 2025), implementation began March 2025. Eligibility criteria included: adults with radiologically confirmed bone metastases who had received denosumab at standard dosing for  $\geq 12$  months, stable disease, and adequate calcium levels. Exclusion criteria included: active/recent SREs, progressive bone metastases, and unstable disease.

Each eligible patient underwent clinical assessment and received standardized counselling explaining the rationale, risks, and benefits of transitioning to q12w dosing. Prescriptions were adjusted following informed consent to reflect the de-escalated interval. Ongoing clinical reviews and monitoring continue for all patients who transitioned to ensure patient safety and clinical efficacy.

**Results:** De-escalation was successfully implemented in 86/89 eligible patients (97% uptake). Patient demographics: average age 67 years (range 32-90), mean travel distance 7.02 miles (maximum 48.54). The initiative eliminated 688 hospital visits and blood tests annually, reducing patient travel by 4,828 miles (1.95 metric tons CO<sub>2</sub>). Financial analysis demonstrated annual savings of £213,183.68 (£2,478.88 per patient based on BNF pricing).

	<b>Age</b>	<b>Distance in miles</b>
<b>MIN</b>	32	0
<b>MAX</b>	90	48.54
<b>AVERAGE</b>	67	7.02
<b>MEDIUM</b>	68	5.38
	8	less injection per year
<b>Total cost saving</b>	£2,478.88	per patients
	£213,183.68	per annum
<b>Total number of reduction of visit</b>	688	
<b>Total number of reduction of blood tests</b>	688	
<b>Reduction in patient travel in miles</b>	4828.08	per annum
<b>Average passenger vehicle emits about 404 grams of CO2 per mile (EPA figure)</b>		
<b>4,828.08 miles × 404 g/mile = 1,950,544 grams of CO2</b>		
<b>Converting to metric tons: 1,950,544 g ÷ 1,000,000 = 1.95 metric tons of CO2</b>		

Table 1 Analysis of Denosumab Extended Interval Dosing on Cost Savings and Hospital Visits

**Discussion:** This initiative demonstrates significant sustainable value across clinical, environmental, economic, and social domains. By reducing required hospital visits by two-thirds, patients experience less disruption to daily routines and fewer travel burdens, in particularly valuable for our elderly population and those traveling longer distances. Informal feedback indicates enhanced patient satisfaction. The approach aligns with emerging evidence while generating substantial cost savings that can be redirected to other areas of patient care. This readily implementable protocol offers a model for other centres to adopt evidence-based de-escalation of BMAs, optimising resource utilisation without compromising clinical outcomes.

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