Institution: Queen Mary University of London (QMUL)

Unit of Assessment: A1 (Clinical Medicine)

Title of case study: Improved sensitivity of breast cancer screening with two-view mammography

1. Summary of the impact

As a result of research at Queen Mary, an estimated 2,500-3,000 additional women per year in UK have a breast cancer detected early through two-view mammography at the NHS Breast Screening Programme, and similar country-wide benefits have occurred abroad. From 1988 the NHS Breast Screening Programme offered women aged 50-64 three-yearly one-view mammography. In 1995, results from the UKCCCR Randomised Trial of One and Two View Mammography (led by Queen Mary researchers) showed that including a second view increased breast cancer detection by 24% and reduced recall rate by 15%. On the basis of this evidence, the Department of Health immediately issued an Executive Letter requiring all breast screening units to move to two-view mammography for the prevalent screen. Changes were rapidly and widely implemented. By 2004, two-view mammography had become the policy at all screens, prevalent and incident. Two-view mammography remains national policy and its benefits continue to the present day.

2. Underpinning research

Breast cancer is by far the commonest female cancer in the UK, accounting for 31% of all new cases of cancer in women; 50,000 new cases are detected annually. Mammography detects most (though not all) breast cancers before they are clinically apparent, allowing treatment to commence earlier and extending long-term survival. Since 1988, the National Breast Cancer Screening Programme has offered three-yearly mammography to women aged 50-64 (more recently, those aged 50-70). Over 2 million such women are screened in the UK annually.

The original National Breast Screening Programme was based on Swedish research that had used one-view mammography. In the early 1990s, the sensitivity, specificity and cost-effectiveness of one- versus two-view mammography was unknown and there was concern to optimise these metrics. Researchers at the Wolfson Institute for Preventive Medicine at Queen Mary, led by Professor Nick Wald, were commissioned by the UK Coordinating Committee on Cancer Research (UKCCCR) to undertake a trial comparing these options in the prevalent round of breast screening.

The UKCCCR Randomised Controlled Trial of One- and Two-View Mammography, which finished recruiting in 1994, was designed to compare one-view mammography (medio-lateral oblique, MLO in Figure 1) and two view (medio-lateral oblique, and cranio-caudal, CC in Figure 1) in breast cancer screening [1]. From nine breast screening centres in England, 40,163 women aged 50-64 attending their first breast screening examination were randomised to have one-view, two-view or two-view mammography in which one view was read by one reader and both views were read by another. Readers were blinded to whether a second view existed (to exclude a possible bias due to the reader knowing that a second view was available if they needed it).

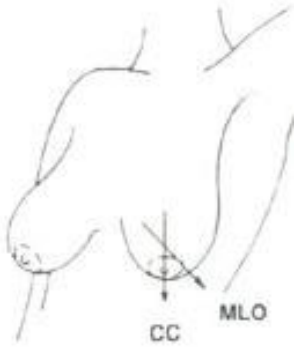

Figure 1: Two different views of the breast taken in mammographic screening: medio-lateral oblique (MLO) and cranio-caudal (CC)

The results, published in 1995, showed that two-view mammography detected 24% more women with breast cancer (95% CI 16% to 31%) than one-view [1]. Prevalence of detected cancer was 6.84 per 1,000 women with two-view and 5.52 with one-view mammography. The proportion of women recalled for assessment was 15% lower (95% CI 6% to 23%) with two-view (6.97%) than with one view (8.16%) mammography. The cost of two-view screening was higher (£26.46 compared with £22 per examination, 1995 prices) but the average cost per cancer detected was similar (£5,330 compared with £5,310) and the marginal cost per extra cancer detected with two views was similar to the average cost (£5,400).

In sum, the study demonstrated conclusively that two-view mammography was medically more effective than one-view; it detected significantly more cancers and reduced recall rates; and it was also similarly cost effective even when only considering short-term costs (ie without taking account of the additional cost savings to the NHS of fewer recalls and fewer late-detected cancers).

In a subsequent study to explore the radiographic reasons why two-view mammography was superior to one-view, mammograms from 110 women whose breast cancer had been detected in the screening programme were retrieved from the screening centres and shown to three consultant radiologists (working independently) [2]. Of the 110 women, 87 had their breast cancer detected by both one and two views and in 23 it was missed by one view but detected using two views. Outcome measures were breast size, location and size of the cancer, mammographic features, presence of micro-calcification and overall radiological assessment. Although 23 cancers were missed in the original trial when one view was used, only two were not visible on the oblique view. Cancers missed using a single oblique view (and only detected if the cranio-caudal view was available with the oblique) tended to be smaller by about 4 mm ($P = 0.05$), centrally located in the breast ($P = 0.16$), not spiculated or round, ($P \leq 0.001$) and lacked micro-calcification ($P = 0.15$). Other variables were non-significant. The authors concluded that the basis of two-view mammography was the added value of the second view for detecting cancers with these features.

More recently, a study led by Queen Mary researchers confirmed that the cranio-caudal view in two-view mammography provides critical information for breast density estimation [3].

3. References to the research

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4. Details of the impact

4a. Change in UK breast screening policy

The Department of Health (which was aware of the findings of the trial some months before the BMJ publication appeared) issued an Executive Letter in early 1995 requiring all breast screening units to move, within 8 months, to two-view mammography for the prevalent screen [4]. There was some uncertainty about whether the full benefit of two views could be realised in practice, especially since the NHS Breast Screening Programme was under workload pressures. For this reason, the introduction of two-view mammography was initially restricted to the prevalent (ie first screening) round while one view was used for incident (ie subsequent screening) rounds [5].

In September 2000, the Department of Health published *The Cancer Plan,* which announced the intention to introduce two views into every attendance at the NHS Breast Screening Programme by December 2003 [6].

4b. Change in clinical practice

Many UK breast screening units adopted the two-view approach back in 1995-96 in accordance with the research findings and Executive Letter [4], and the rest followed. By December 2003, 90% of the programmes had achieved the target set out in *The Cancer Plan*, with the remaining 10% projected to do so shortly afterwards [6]. Two-view mammography is now routine in the UK setting.

4c. Improved sensitivity and specificity of cancer detection

Between 1997 and 2005, the NHS Breast Screening Programme undertook a series of audits of the impact of one- and two-view screening protocols. One audit, for example, compared the cancer detection rates in the incident round of those programmes that had introduced two views at every attendance with the majority of programmes that used single view for the incident round [7]. They found the two-view programmes detected 42% more small invasive cancers (<15mm) – a rate at least as good as, and perhaps even better than, the results obtained from the randomised trial – and also that two views helped to protect against observer error (in which some but not all assessors would be able to detect a small cancer on a single view but far more would detect it on two views). The reduction in recall rate predicted by the trial took some years to establish and may be partly attributable to other influences (eg more double reading of films).

An audit of the NHS Breast Screening Programme in 2000-05 showed a 20% increase in overall incident screen cancer detection rate, with the biggest effect seen for small (<15 mm) invasive cancers [8,9]. This increased detection rate was achieved with an 11% drop in recall rate. Similarly, an audit of the Welsh National Breast Screening Programme between 2000 and 2005 [10] compared 98,752 women who had single-view mammography with 95,464 who had two-view. Five hundred and fifty-five cancers were detected with one view and 744 with two, an increased detection rate from 5.6 to 7.8 cancers per 1000 women screened – a 39% increase (p=0.01) [10]. Two hundred and thirty-nine small (ie early, potentially curable) cancers were detected with one view and 323 with two, increasing the detection rate of these cancers from 2.4 to 3.4 per 1000 women screened – a 42% increase (p=0.05).

In 2004, the Director of the NHS Cancer Screening Programme summed up the benefits of this change in screening practice in the Journal of Medical Screening:

> *"The move from single view at every round to two views at every round has been an evidence-based, cost-effective quality improvement. It has contributed to the high-quality NHS BSP [Breast Screening Programme] operating currently."* (page 56) [5].

4e. Quantified estimates of benefits continuing during the impact period 2008-13

In 2008, a review of advances in breast cancer screening named the introduction of two-view mammography as one of the three most significant advances in breast cancer screening in the previous 20 years [11]. These early improvements in sensitivity and specificity are now beginning to have long-term impacts on morbidity and mortality (because a small breast cancer detected through screening would typically have taken many years to kill the patient had it gone undetected). Thus, whilst the improvements in sensitivity and specificity of national breast screening programmes began before 2008, it has continued and (because of progressively increased uptake around the world) extended further year on year.

Two-view mammography remains the national gold standard and this is a direct result of the UKCCCR trial results published in 1995. It continues to have significant health impacts up to the present day, since the same policy and practice remains in place.

An audit undertaken by Queen Mary researchers in 2010-12, based on the national cohort of women who were first screened with either one-view or two-view mammography in 2003-04 and/or in 2004-05 and who were then followed up for up to three years, showed that there was a highly significant reduction in subsequent interval cancers: the incidence of such cancers with two-view mammography was 0.68 relative to the incidence with one-view mammography [12].

To illustrate the sustained quantitative benefits of this research, we cite figures from 2010-11 [13]. The NHS Breast Screening Programme screened 2,221,938 women in England, Wales, Northern Ireland and Scotland between April 2010 and March 2011. 17,838 cancers were detected in women of all ages; 80% were invasive. Cancer detection rates for all cancers were 8.0 per 1,000

women screened and for small invasive cancers (<15mm in diameter – the ones that are typically too small to be felt) were 3.3 per 1,000 women screened. Using the (relatively conservative) figure of 39% for the incremental detection rate with two-view mammography, it is estimated that around 2,500-3,000 invasive cancers are now detected in UK annually (many of them early and treatable) that would have been missed if one-view mammography remained the norm [13].

4e. Impact on screening programmes and cancer detection beyond UK

The use of two-view mammography in breast screening is now recommended by numerous professional bodies worldwide, including the World Health Organisation's 2006 recommendation, which is still current [14]. The US National Cancer Institute acknowledges the superiority of two- over one-view mammography [15].

Two-view mammography is now practised in almost all screening programmes. In EUNICE, a systematic data warehouse on breast cancer screening in Europe, a review in 2012 of 25 national and regional programmes in Europe found that all used two-view mammography at prevalent screen and 64% (16 out of 25) used two-view at all screens [16].

5. Sources to corroborate the impact

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