SCREENING FOR BREAST CANCER IN ENGLAND: PAST AND FUTURE

Advisory Committee on Breast Cancer Screening*

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*Members of the Advisory Committee on Breast Cancer Screening: Professor V Beral (Chairman), Ms S Cush, Professor IO Ellis, Dr J Emery, Dr K Faulkner, Dr R Given-Wilson, Professor M Law, Ms J Loughlin, Dr MJ Michell, Dr SM Moss, Ms M Noblet, Mrs J Patnick, Professor M Reed, Dr C Rubin, Mrs K Toward, Ms D Winstone.

*Members of the Advisory Committee’s subcommittees contributing to this report: Dr J Austoker, Professor V Beral (Chairman), Dr A Berrington, Dr RG Blanks, Professor NE Day, Ms TJ Day, Professor IO Ellis, Dr K Faulkner, Professor H Møller, Dr SM Moss, Mrs J Patnick (Secretary), Dr M Quinn, Dr MG Wallis, Dr ARM Wilson.
# Screening for Breast Cancer in England: Past and Future

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1. EXECUTIVE SUMMARY

The NHS Breast Screening Programme began in 1988. It aims to invite all women aged 50–70 years for mammographic screening once every three years. The programme now screens 1.3 million women each year, about 75% of those invited, and diagnoses about 10 000 breast cancers annually.

Although some have questioned the value of screening for breast cancer, the scientific evidence demonstrates clearly that regular mammographic screening between the ages of 50 and 70 years reduces mortality from the malignancy.

Screened women are slightly more likely than unscreened women to be diagnosed with breast cancer. The cancers in screened women are smaller and are less likely to be treated with mastectomy than they would have been if diagnosed without screening.

For every 400 women screened regularly by the NHS Breast Screening Programme over a 10 year period, one woman fewer will die from breast cancer than would have died without screening.

The current NHS Breast Screening Programme saves an estimated 1400 lives each year in England.

The screening programme spends about £3000 for every year of life saved.

1.1 History of the NHS Breast Screening Programme

The NHS Breast Screening Programme (NHSBSP) began in 1988, employing single view mammography and inviting women aged 50–64 years for screening once every three years.

By 2005, the programme was using two view mammography and screening 1.3 million women aged 50–70 years annually, about 75% of those invited. Currently, it diagnoses about 10 000 breast cancers annually.

1.2 Trends in breast cancer incidence and treatment

Breast cancer registrations at ages 50–64 years have increased by almost 50% since the NHSBSP began in 1988. About half of this increase is due to screening and about half is due to an increase in the underlying incidence of breast cancer.

Women with symptomatic breast cancer are typically presenting with smaller tumours than was the case before 1988.

Mastectomy rates have fallen since 1988.
A substantially greater proportion of women with breast cancer are receiving chemotherapy and/or hormone therapy than before 1988.

Earlier symptomatic presentation and greater use of adjuvant therapy since 1988 has had a marked impact, reducing mortality rates from breast cancer, in addition to the specific contribution from the NHSBSP.

Although some have questioned the value of screening for breast cancer, the scientific evidence demonstrates clearly that regular mammographic screening between the ages of 50 and 70 years reduces mortality from the malignancy.

The International Agency for Research on Cancer (IARC) concluded that the 25% reduction in mortality seen in the trials of mammographic screening, based on an ‘intention to treat’ analysis, implies a reduction in breast cancer mortality of about 35% for women who are screened regularly.

The effectiveness of screening in the NHSBSP is influenced by programme factors, such as the introduction of two views and the optimisation of optical density, and also by population factors, such as the increasing use of hormone replacement therapy during the 1990s.

The current NHSBSP saves an estimated 1400 lives each year in England.

The NHSBSP now diagnoses about half of all breast cancers found in women in the target age range of 50–70 years, with the remainder occurring in women who do not attend for screening or who present symptomatically in the interval between screens.

Screened women are slightly more likely than unscreened women to be diagnosed with breast cancer. The cancers in screened women are smaller and are less likely to be treated with mastectomy than they would have been if diagnosed without screening.

The current evidence about screen detected ductal carcinoma in situ points to it being an important precursor lesion for invasive disease.

If screening brings forward the diagnosis of breast cancer by an average of three years, this would lead to an apparent 5–10% increase in the incidence of breast cancer in the target age range.

An important priority for the future is for cancer registries and the screening programme to refine their methods for the collection of reliable information on interval cancer rates.

About 1 in 8 women screened regularly by the NHSBSP will be recalled for assessment at least once over a 10 year period.

Factors which affect an individual woman’s likelihood of recall include
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1.6 Screening methods

Film-screen x-ray mammography remains the only single intervention shown in randomised controlled trials to significantly reduce mortality from breast cancer.

Full field digital mammography has been shown to have similar sensitivity and higher specificity than conventional mammographic screening.

Ultrasound is an invaluable technique for further assessment of mammographic abnormalities and for image guided breast biopsy.

1.7 Radiation risk

For every 14,000 women in the age range 50–70 years screened by the NHSBSP three times over a 10 year period, the associated exposure to x-rays will induce about one fatal breast cancer.

1.8 Women at younger and older ages and at high risk of breast cancer

The IARC has concluded that there is only limited evidence that screening women aged 40–49 years by mammography reduces their mortality from breast cancer. Further research on the effectiveness of screening at this age is under way.

For women aged over 70 years, a decision about whether or not to encourage screening should be taken at an individual level, bearing in mind personal circumstances, rather than offering a blanket invitation for screening.

1.9 Communication and anxiety

Few women understand that the risk of getting breast cancer increases with age.

Attendance for screening with a normal outcome causes little anxiety, and there is no difference in anxiety between women whose cancer was detected by screening and women whose cancer presented symptomatically. However, for women who experience a ‘false positive’ recall, there is significant anxiety that may persist for some time.

1.10 Costs

The screening programme spends about £3000 for every year of life saved.

1.11 Benefits versus risks

For every 400 women screened regularly by the NHSBSP over a 10 year period, one woman fewer will die from breast cancer than would have died without screening.

Among women who are routinely screened and diagnosed with breast cancer:

- 1 in 8 women would not have had their breast cancer diagnosed if they had not gone for screening (because screening picks up some
breast cancers that normally grow so slowly that they would not cause symptoms during a woman’s lifetime)

- 1 in 8 women would be spared the need for a mastectomy (because screening detected their breast cancer earlier than it otherwise would have been detected, and before it grew too large or spread so far as to warrant a mastectomy)

- 1 in 8 fewer women will die from breast cancer than would have died had they not been screened (because screening detected their breast cancer earlier than it otherwise would have been found, and before it had spread to other parts of the body).

1.12 Research

An extensive body of research has arisen out of the NHSBSP. The research has contributed to knowledge about screening and also about the causes and treatment of breast cancer.

1.13 The future

The future will see continued improvements in the diagnosis and treatment of breast cancer. There may come a time when mortality rates are so low that the absolute number of lives saved by breast screening becomes smaller and smaller, to the point where screening may no longer be necessary. For the moment, however, this is not a realisable possibility.
2. INTRODUCTION

2.1 Forrest report

In 1985, Mr Kenneth Clarke, then Minister of Health, convened an expert committee chaired by Professor Sir Patrick Forrest and known as the ‘Forrest Committee’ to report on screening for breast cancer. The committee presented its report to ministers in 1986, and concluded that ‘screening by mammography can lead to prolongation of life for women aged 50 and over. There is a convincing case on clinical grounds for a change in UK policy on the provision of mammographic facilities and the screening of symptom-less women.’ It also concluded that the necessary back-up services would need to be provided to assess the abnormalities detected at screening. The NHS Breast Screening Programme (NHSBSP) was established in March 1987 and began inviting women in 1988, aiming to offer routine mammographic screening to each woman in the UK aged 50–64 years once every three years.

2.2 Advisory Committee on Breast Cancer Screening

The Advisory Committee on Breast Cancer Screening was set up in 1986 to advise ministers and the Department of Health on the development of the breast screening programme, to monitor the effectiveness of the breast screening programme and to advise on research concerned with the provision of the breast screening programme. In 1990, the committee reviewed the progress of the NHSBSP and the new evidence on the effectiveness of breast cancer screening that had emerged since 1986. It advised that there continued to be convincing evidence that mammographic screening reduced mortality from breast cancer in women over 50 years of age. Since 1990, further evidence about the effects of mammographic screening has become available, effective treatments for breast cancer have become widespread and screening technologies have changed. The NHSBSP has responded accordingly by changing its guidelines and targets, and the whole programme has been extended to include women aged from 50 up to, and including, 70 years. At the same time, some have called for the NHSBSP to be extended to women younger than 50, whereas others have questioned its value. Consequently, the Advisory Committee on Breast Cancer Screening considered that it was timely to reexamine the evidence of both benefit and harm associated with mammographic screening in the UK, and to look at possible developments for the future.
3. HISTORY OF THE NHS BREAST SCREENING PROGRAMME

3.1 1987–90: setting up the NHSBSP

In March 1987, the establishment of the NHSBSP was announced. In England, each of the then 14 regional health authorities was given the responsibility for setting up the programme in its region. They had to establish their first breast screening unit by 31 March 1988, and to cover their entire region by 31 March 1990. Following closely the recommendation of the Forrest Committee’s report, finances were allocated on the basis of how many ‘Forrest units’ (of half a million people) a region had, and regions received multiples of £206 000 revenue and £155 000 capital per Forrest unit. An advisory committee on breast cancer screening was established with Professor Martin Vessey, then Head of the Department of Public Health and Primary Care at Oxford University, as Chairman and Dr JA Muir Gray as the national training facilitator. By 1988, all regions had at least one functioning breast screening unit, and this is generally taken as the official start date of the programme.

The Forrest report had highlighted a number of outstanding questions about breast screening. In 1988, the UK Coordinating Committee on Cancer Research established trials on whether one view or two views of the breast should be taken and whether screening should take place more frequently than three yearly.

The Forrest report identified the need for high quality mammography as paramount. Since there was little mammography in the UK at the time, this implied that a massive training effort would be needed. The close association between training and quality enabled Dr Muir Gray to establish quality assurance as an underpinning principle of the screening programme. Overall standards for the NHSBSP were set, and the Department of Health supported the need for a quality assurance manager and reference centre in each region. Guidance was issued in a health circular and funding of £100 000 revenue and £50 000 capital was provided to each of the 14 regional health authorities.  

Further investment was made in training. Four training centres were set up (one in Nottingham, one in Guildford, one in Manchester and one at King’s College, London) each of which was associated with a centre of

- The NHSBSP began in 1988 employing single view mammography and inviting women aged 50–64 years for screening once every three years.
- By 2005, the programme was using two view mammography and screening 1.3 million women aged 50–70 years annually, about 75% of those invited. Currently, it diagnoses 10 000 breast cancers annually.
excellence in state of the art treatment. Screening mammography was largely a new technique for radiographers, as was interpretation of the images for radiologists. In the initial years of the programme, the efforts of the training centres were concentrated on defining and developing these key skills in the workforce.

The quality assurance teams and managers supported the evolution of the breast screening programme locally, and professional quality assurance groups were developed with the relevant associations and royal colleges at a national level. In 1990, a new post of national coordinator of the NHSBSP was established, based at one of the regional health authorities. Mrs Julietta Patnick at the Trent Region in Sheffield was appointed, and she is now the Director of the NHS Cancer Screening Programmes, which includes the NHSBSP.

Most breast screening units in England had opened by 1990, with the final few opening in 1992. By 1993, most screening units had completed the ‘prevalent round’, ie the first round in which all women were offered screening, and by 1995 all screening units had completed this round. The programme was thus moving from its initial set up phase to the challenging phase of maintaining and improving its performance. The Advisory Committee, which had issued consolidated guidance on breast cancer screening in 1990, followed this up in 1991 by reviewing the evidence and experience gathered since the publication of the Forrest report five years earlier. It remained supportive of breast cancer screening for women aged 50–64.

By 1991, the NHSBSP was inviting over one million women a year for screening. In the autumn of that year, a controversy erupted when the value of breast self examination was questioned by the then Chief Medical Officer. Over the next three weeks, the policy of breast awareness, which had been under development, was hastily polished and delivered. The Department of Health then released the first figures from the breast screening programme showing that it was finding a high rate of cancers and appeared to be on target.

The first major incident involving breast cancer screening occurred in 1994. In a screening unit in the West Midlands, some women had been correctly identified by the radiologists as needing further assessment of an abnormality, but they had not been called for further assessment and, in fact, had received a ‘normal results’ letter. The resulting national press coverage of the incident included the first public criticisms that the NHSBSP had received. Although previously there had been some criticism of breast cancer screening in the medical journals, this debate had now moved into the public arena.

The first NHSBSP results on interval cancers gave rates that were disappointingly high. Interval cancers are breast cancers diagnosed in the period between screens. Their frequency is taken to be indicative of the quality of screening because a high rate of interval cancers may mean that some cancers that should have been identified by good quality screening are presenting instead between screens. Interval cancers were always
anticipated and national publicity materials drew attention to the fact that breast screening is not always accurate and women were reminded to report any changes in their breasts without delay. Expected interval cancer rates had been calculated for the NHSBSP, based on results from the Swedish Two County trial, but, as described below, these were unrealistically low. In 1994, a pathology audit in the NHSBSP showed discrepancies in the measurement of breast cancers and, in 1995, the results of the one view versus two view trial showed that major gains could be made by introducing two views at every round of screening. In anticipation of the publication of the interval cancer results, and before the results of the one view versus two view trial were published, the Department of Health announced the move to two views in the prevalent screen. At the same time, optical density was standardised because evidence had indicated an optimal level, whereas previously it had been left to local discretion.

The influence of the breast screening programme began to extend beyond its target population. An increase in breast awareness led to the earlier presentation of breast cancer at all ages. The de facto existence of a two tier breast cancer diagnostic service was becoming evident in many cities: a first class, high speed screening service and a more traditional service for women presenting symptomatically. By the early 1990s, the latter service was increasingly seen as old fashioned and relatively ineffective, particularly because of the lack of state of the art mammography. From 1992, the Department of Health made specific investment to equip all symptomatic departments with mammography equipment over a three year period. At the same time, multidisciplinary teams were improving diagnostic techniques for women presenting symptomatically, and ‘one stop’ clinics were becoming widespread as this was recognised as a better way of working for both staff and patients.

Despite the apparently high breast cancer detection rates at screening, interval cancers rates were also high. On investigation, it appeared that the expected incidence of breast cancer in England had initially been underestimated, therefore the target rates for screen detected cancers and the expected rates of interval cancer were too low. A further issue was that in situ and invasive disease had been combined together in calculating screen detected breast cancer rates. Revised targets were published, and the concept of the standardised detection ratio introduced. The NHSBSP targets were set such that a 25% reduction in breast cancer mortality should be achieved, based on intermediate markers reported in the Swedish Two County trial.

During this period, public discussion of the NHSBSP was growing, with, on the one hand, claims that the NHSBSP was too costly and ineffective and, on the other hand, calls for its expansion. Concerns were expressed about the potential psychological harm to women recalled for further investigations who turned out not to have breast cancer. At the same time, others argued that screening should be more frequent and that two view mammography should be carried out at each screen. Furthermore, the Health Select Committee induced the government to support piloting of screening for women aged 65–69 years.
In June 1997, another incident occurred and received considerable public attention. This centred on the practices of the breast radiologists in Devon and eventually resulted in their suspension from breast imaging work by the General Medical Council for a period of time. The incident was front page news for a number of days and led to hours of debate in the House of Commons. An inquiry ensued that exposed the fact that the purchaser/provider split, which had been introduced into the NHS and had operated in quality assurance for the previous three years, had undermined the quality assurance structure to the extent that it had been unable to identify some of the problems in the Exeter programme or take action where it knew there to be problems. This led to a major revision of the quality assurance structure and the requirement for the relationship of each breast screening programme to the trust within which it operated to be reviewed and brought in line with the recommendations of the inquiry report (the Exeter report). Quality assurance managers became quality assurance directors and the national coordinator in future was to be accountable to the Deputy Chief Medical Officer.¹⁸

Although the concept of breast awareness was increasingly accepted, clinical breast examination was still being carried out. In 1998, the Chief Medical Officer and Chief Nursing Officer issued guidance that clinical breast examination was not a suitable technique for screening and should not be carried out for this purpose.¹⁹

It had been expected that, by the year 2000, a substantial reduction in mortality from breast cancer would be evident because of the breast screening programme. Breast cancer mortality rates in the UK and USA had fallen by about 25% in women aged 20–69 years.²⁰ Blanks et al²¹ estimated that by 1998 only about a 6% reduction in breast cancer mortality in women aged 55–69 years was attributable directly to the NHSBSP, and concluded that the full effect was still to be seen. The remainder of the decline in mortality was attributed to improvements in treatment, earlier presentation outside the programme and the general improvement in breast cancer services in England. Many observers attributed these developments in part to the introduction of the breast screening programme.

The NHS Cancer Plan,²² which was published in 2000, announced further expansions of the NHSBSP. There would be two view mammography at all screens and the upper age limit for women invited would move from 64 to 70 years. Although the NHSBSP welcomed these improvements, they presented a major challenge in meeting the workload demands that they placed upon its staff. In common with the rest of the NHS, the screening programme was finding it increasingly difficult to recruit staff and, in order to address the need to expand, the screening programme endeavoured to develop new ways of working and new types of staff in order to be more flexible in the ways in which the challenge of programme expansion could be met.

Training centres remained at the forefront of developments in the screening programme by not only training staff new to the service but also developing and updating the skills of those already working in it.
As time has gone on, each of the centres has developed its own special interests. The training centre at Guildford took a special interest in the development of ‘satellite’ training centres that could provide some of the training locally to those regions at some distance from the main centres. One satellite centre in Coventry later became a training centre for use of the breast screening computer and office systems, and another, at St George’s Hospital, London, was developed as a clinical training centre to cope with the demands of the service as it expanded to invite a larger screening population.

The year 2000 also saw two scientists from the Nordic Cochrane Centre claim, in a paper published in the Lancet, that there was no convincing evidence that mammographic screening decreased breast cancer mortality and that the results from the randomised trials that underpinned the scientific justification for the NHSBSP were unreliable. Once again, the professional debate spilled into the public arena and there was discussion in the media. The following year, the same Danish researchers published a Cochrane review in which they argued that screening led to more mastectomies and more aggressive treatment of breast cancer.

The debate continued, but was largely resolved in 2002 by a report from an international working group of the IARC, which concluded that there was indeed sufficient evidence from the randomised trials that mammographic screening in women aged 50–69 years reduced mortality from breast cancer. The IARC working group acknowledged that its conclusions differed from those of the review published by the Danish researchers, and stated that, in particular, it disagreed with the scientific justification given by the Cochrane Centre’s researchers for excluding from their review the results from several of the Swedish randomised trials.

The conclusion of the IARC – that mammographic screening is effective – continues to be supported by most of the scientific community and the general population in the UK, but there are some dissenters. Emphasis has moved from inviting women and promoting the programme to one of promoting informed choice. NHSBSP information leaflets that now accompany letters of invitation include discussion of the limitations of breast screening as well as the positive messages of the benefits of screening. Technical and clinical performance of the programme continue to improve. The programme continues to be evidence based, and will no doubt evolve further in the future.
3.5 NHSBSP performance

The number of women screened by the programme continues to rise year by year, as does the number of cancers detected (Figure 1). In the screening year 2002/3, the programme screened 1.3 million women in England, and among them 9849 breast cancers were diagnosed. Furthermore, the quality of the service continues to improve because, although the cancer detection rate has been increasing, the proportion of women recalled for assessment has remained fairly steady (Table 1 and Figure 2). The chance of that recall leading to a diagnosis of cancer (positive predictive value) has increased from 1 in 12 in the early years of the NHSBSP to 1 in 8 in 2002/3. The sharp rise in the positive predictive value seen in 2002/3 (Figure 2) is attributed to the introduction of two view screening in the incident rounds.

![Figure 1](image_url)

**Figure 1** Cancers detected by NHSBSP in England for invited women aged over 45 years.

*In situ for these years 50–64 only.
Table 1  Screen detected breast cancer rates and recall rates per 1000 women aged 50–64 years: England, 1995/6 to 2002/3

<table>
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<th>Screening year</th>
<th>Cancer detection rates/1000 screened</th>
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<tr>
<td></td>
<td>All (n)</td>
<td>Invasive (n)</td>
</tr>
<tr>
<td>1995/6</td>
<td>4.7 (4370)</td>
<td>NA</td>
</tr>
<tr>
<td>1996/7</td>
<td>5.0 (4768)</td>
<td>NA</td>
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<tr>
<td>1997/8</td>
<td>5.3 (5257)</td>
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<td>2002/3</td>
<td>6.6 (7171)</td>
<td>5.16 (5585)</td>
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NA, not available.

Figure 2  Rate of recall for assessment and positive predictive value (PPV) of recall of NHSBSP in England.
* 92/93 and 93/94 assessment rates are for the UK.
4. **TRENDS IN BREAST CANCER INCIDENCE AND TREATMENT**

- Breast cancer registrations at ages 50–64 years have increased by almost 50% since the NHSBSP began in 1988. About half of this increase is due to screening and about half is due to an increase in the underlying incidence of breast cancer.
- Women with symptomatic breast cancer are typically presenting with smaller tumours than was the case before 1988.
- Mastectomy rates have fallen since 1988.
- A substantially greater proportion of women with breast cancer are receiving chemotherapy and/or hormone therapy than they were before 1988.
- Earlier symptomatic presentation and greater use of adjuvant therapy since 1988 has had a marked impact by reducing mortality rates from breast cancer in addition to the specific contribution from the NHSBSP.

4.1 **Incidence rates**

Between the late 1980s and early 1990s, registration rates for breast cancer in women aged 50–64 years in England and Wales* increased sharply, coinciding with the introduction of the NHSBSP (Figure 3). Registration rates for breast cancer in women aged 50–64 years reached a peak in about 1991/92, declined rapidly for a few years afterwards and subsequently began increasing again, albeit gradually. The sharp rise in registration rates between the late 1980s and early 1990s for women aged 50–64 years and the rapid decline thereafter do not, however, reflect real changes in the underlying incidence of breast cancer over such a short period. They are due, almost exclusively, to a reservoir of prevalent but clinically unapparent breast cancers, detected at women’s first ever mammogram. Among women aged 55–64 years, most would have had a previous mammogram by 1993, therefore most newly diagnosed cancers at these ages are likely to have arisen in the interval since the last screen – the fall in cancer registrations after about 1993 at these ages probably reflects the change from prevalent to incident cancers, with the maturing of the screening programme. By contrast, only about half of the women aged 50–54 years would have had a previous mammogram in 1993 and thereafter because this age group includes the entry point to the screening programme. Hence, many cancers diagnosed at age 50–54 years would continue to be ‘prevalent’ cases, which may well be why cancer registration rates have not fallen at these ages since 1993. Among women aged 65 and over, breast cancer registration rates increased slightly since the late 1980s, perhaps in part because women of this age can request routine mammography. One interpretation is that the rate, which for some years has been lower than in all the three

*Throughout this section, statistics are given for England and Wales because statistics for England alone were not available until recently.*
screened age groups, is another indication that the screening programme has been successful in bringing forward diagnosis: the cancers not being diagnosed from about 1995 onwards in those 65–69 were diagnosed in the prevalent peak and subsequently, but five years (or more) earlier when the women were five years (or more) younger. It is still too early to evaluate the expected increase in breast cancer registrations in women aged 65–70 years resulting from the extension of the NHSBSP in 2002 to include women up to age 70.

To monitor the effectiveness of the NHSBSP it is important to consider the extent to which the changes in breast cancer registrations over time, especially among women aged 50–64 in the last decade or so, reflect the underlying incidence of breast cancer at these ages. Table 2 shows the observed age specific registration rates for breast cancer in 1988 (when the NHSBSP began operations) and in 2001 (the latest year for which national statistics are available). It also gives estimates of the underlying age specific incidence of breast cancer in 2001, in the absence of screening, based on fitting age cohort models to the data. These results suggest that the registration rate for breast cancer at ages 50–64 years in 2001 was 45% higher than in 1988; about half of this increase is due to screening and about half is due to an increase in the underlying incidence of breast cancer. A large part of the increase in the underlying incidence
4.2 Characteristics of breast cancers diagnosed in women aged 50–64 and their treatment

There are no systematically collected national data on the characteristics of breast cancers diagnosed or their treatment that cover the period before and after the introduction of the NHSBSP. However, data collected by regional cancer registries in East Anglia\(^2\) and Yorkshire\(^3\) show that the breast cancers diagnosed in women aged 50–64 were at a considerably earlier clinical stage if they were diagnosed in the 1990s than if they were diagnosed in the 1980s. Furthermore, data collected by the Yorkshire registry show substantial changes in the use of systemic therapies, especially hormonal therapies (largely tamoxifen), over this period. According to the Yorkshire figures, in 1982–90 about 40% of women aged 50–64 received neither chemotherapy nor hormonal therapy, 5% received chemotherapy only, 45% received hormonal therapy only and 10% received both types of systemic therapy; however, by 1991–99, only about 10% received no systemic therapy, whereas 5% received chemotherapy only, 65% received hormonal therapy only and 20% received both types of therapy.\(^3\) There was a relatively small increase in the use of radiotherapy during this period in women aged 50–64, from about 55% in 1982–90 to about 65% in 1991–99.\(^3\)

The Nottingham group (IO Ellis, RG Blamey and CW Elston, personal communication) has recorded information on the breast cancers this group has treated, and data on 1510 women aged 50–64 diagnosed with breast cancer from 1980 to 2001 have been made available. In keeping with the improvements in the stage of the breast cancers recorded by the cancer registries,\(^2,3\) the Nottingham data show a reduction between 1980/1 and 2000/1 in the average diameter of the breast cancers diagnosed in women aged 50–64 from 2.0 cm to 1.7 cm; during the same period, mastectomy rates fell from 96% to 49% (Table 3). However, historically there has been substantial variation in mastectomy rates and other treatments of breast cancer across the UK,\(^4,5\) and it is not known how typical the practices in Nottingham are.

---

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Age specific rates for invasive breast cancer in England and Wales</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age specific rates for invasive breast cancer per 1000 women, England and Wales</td>
</tr>
<tr>
<td>Breast cancer registrations, 1988(^\ast)</td>
<td>0.5</td>
</tr>
<tr>
<td>Breast cancer registrations, 2001(^\dagger)</td>
<td>0.6</td>
</tr>
<tr>
<td>Estimated ‘underlying incidence’, 2001(^\ddagger)</td>
<td>0.6</td>
</tr>
</tbody>
</table>

\(^\ast\)1988, ie before the implementation of the NHSBSP.  
\(^\dagger\)2001, ie including screen detected invasive breast cancer.  
\(^\ddagger\)Estimated ‘underlying incidence’ of breast cancer in 2001, ie in the absence of screening.  

of breast cancer is the result of the substantial increase in the use of hormone replacement therapy. Use has increased from a prevalence of about 10% in 1990 to about 30% in 2001 for women aged 50–64 with its associated increased risk of breast cancer.\(^30,31\)
Mastectomy rates are lower in women with screen detected breast cancers than in women presenting symptomatically. Since 1996/7, when routine collection of information on treatment in the NHSBSP began, there appears to have been little change in the proportion of screen detected cancers that are treated by mastectomy (Table 4). Over the seven year period from 1996/7 to 2002/3, annual mastectomy rates ranged from 27% to 28% for invasive breast cancer and from 27% to 30% for ductal carcinoma in situ (Table 4). Although there are no national statistics on mastectomy rates for women aged 50–64 years presenting symptomatically with breast cancer, data from 90 centres in the UK indicate that the proportion was 45% in 2001/2.

### Table 3 Averagen diameter of breast cancers and percentage treated by mastectomy in Nottingham: women aged 50–64

<table>
<thead>
<tr>
<th>Year</th>
<th>Average tumour size (cm)</th>
<th>Mastectomy rates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980–81</td>
<td>2.0</td>
<td>96</td>
</tr>
<tr>
<td>1982–83</td>
<td>2.1</td>
<td>94</td>
</tr>
<tr>
<td>1984–85</td>
<td>2.3</td>
<td>86</td>
</tr>
<tr>
<td>1986–87</td>
<td>2.1</td>
<td>85</td>
</tr>
<tr>
<td>1988–89</td>
<td>1.8</td>
<td>60</td>
</tr>
<tr>
<td>1990–91</td>
<td>1.8</td>
<td>52</td>
</tr>
<tr>
<td>1992–93</td>
<td>1.8</td>
<td>52</td>
</tr>
<tr>
<td>1994–95</td>
<td>1.9</td>
<td>46</td>
</tr>
<tr>
<td>1996–97</td>
<td>1.9</td>
<td>55</td>
</tr>
<tr>
<td>1998–99</td>
<td>1.8</td>
<td>48</td>
</tr>
<tr>
<td>2000–01</td>
<td>1.7</td>
<td>49</td>
</tr>
</tbody>
</table>

Source of data: IO Ellis and colleagues, personal communication.

### 4.3 Summary of trends in breast cancer incidence and treatment

Since the NHSBSP was established in 1988, the underlying incidence of breast cancer at ages 50–64 years has increased by about 10% (Table 2). Women are presenting with breast cancer at earlier clinical stages than before, mastectomy rates are falling and a substantially greater proportion of these women are receiving chemotherapy and/or hormone therapy than before 1988. Many of these factors would be expected to have a marked impact on mortality rates from breast cancer, in addition to the specific contribution from the NHSBSP.

### Table 4 Mastectomy rates (%) for women with invasive and non-invasive breast cancer detected during screening by the NHSBSP

<table>
<thead>
<tr>
<th>Screening year</th>
<th>Invasive cancers (%)</th>
<th>Non-invasive (DCIS) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996/7</td>
<td>27</td>
<td>29</td>
</tr>
<tr>
<td>1997/8</td>
<td>28</td>
<td>27</td>
</tr>
<tr>
<td>1998/9</td>
<td>27</td>
<td>30</td>
</tr>
<tr>
<td>1999/0</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td>2000/1</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>2001/2</td>
<td>28</td>
<td>29</td>
</tr>
<tr>
<td>2002/3</td>
<td>27</td>
<td>29</td>
</tr>
</tbody>
</table>

Source of data: Association of Breast Surgery at BASO. An audit of screen detected breast cancers for the years 1996/97 to 2002/3.
5. REDUCTION IN MORTALITY FROM BREAST CANCER RESULTING FROM MAMMOGRAPHIC SCREENING

- Although some have questioned the value of screening for breast cancer, the scientific evidence demonstrates clearly that regular mammographic screening between the ages of 50 and 70 years reduces mortality from the malignancy.
- The International Agency for Research on Cancer concluded that the 25% reduction in mortality seen in the trials of mammographic screening, based on an ‘intention to treat’ analysis, implies a reduction in breast cancer mortality of about 35% for women who are screened regularly.
- The effectiveness of screening in the NHSBSP is influenced by programme factors, such as the introduction of two views and the optimisation of optical density, and also by population factors, such as the increasing use of hormone replacement therapy in the 1990s.
- The current NHSBSP saves an estimated 1400 lives each year in England.

5.1 Efficacy of mammographic screening

In 2002, an international working group of experts convened by the IARC to discuss worldwide evidence on the efficacy of breast cancer screening reviewed the design and results of 10 randomised trials, and concluded that there was sufficient evidence that routine screening with mammography commencing at ages 50–69 years was efficacious in terms of reducing mortality from breast cancer. The IARC working group concluded that, over an average of about 10 years of follow-up, the overall results from the trials suggested a 25% reduction in mortality from breast cancer in women who were first invited for screening mammography between the ages of 50 and 69. The methods of randomisation and analysis of the trials, especially those carried out in Sweden, had been questioned by some. However, further information, along with an extended follow-up of the Swedish trials, showed that many of the allegations of flaws in the design of the trials and potential biases in the analyses were not substantiated.

The new results from the Swedish trials indicated that the main benefit from screening was apparent in the 5–12 years after initiation of mammography. The chief results from the randomised trials were presented, appropriately, using ‘intention to treat’ analyses, in which mortality rates in women are compared according to the group to which they were originally assigned. However, some women who were assigned at random to mammography did not actually attend for screening, whereas some who were assigned to the control group may have had a screening.
mammogram outside the trial. Thus, the reduction in mortality reported from the trials underestimates the true reduction in mortality for women who are screened regularly. In the IARC report, it was estimated that the 25% reduction in mortality found in the trials using an ‘intention to treat’ analysis implied an actual reduction in breast cancer mortality of about 35% for women who are regularly screened. Similar reductions in mortality from breast cancer were observed in the areas of Denmark where routine screening was available.

In the IARC report, it was estimated that the 25% reduction in mortality found in the trials using an ‘intention to treat’ analysis implied an actual reduction in breast cancer mortality of about 35% for women who are regularly screened. Similar reductions in mortality from breast cancer were observed in the areas of Denmark where routine screening was available.

In the Swedish Two County trial, the average time between screens was 33 months. The target screening interval in the NHSBSP, based on the experience of the Two County trial, was therefore fixed at three years, ie 36 months, and has remained so. A randomised trial conducted within the NHSBSP comparing the effect of annual with triennial mammography found little apparent benefit from annual screening, based on surrogate outcome measures. Furthermore, observational data from the USA suggest that, for women aged 50 years and older, there is no difference in the incidence of late stage breast cancer with annual versus biennial mammography. As the numbers of women eligible for screening rises year on year in England, many screening units struggle to maintain the three yearly intervals. Nevertheless, the majority are screening only a few weeks late, and it is estimated that ‘slippage’ at these levels will make little difference to the effectiveness of the overall programme.

A randomised trial conducted within the NHSBSP showed that two view mammography is significantly better than one view mammography at detecting breast cancer at women’s first screen. As a result, two view mammography for a woman’s first attendance at screening became policy in 1995. Subsequently, it was shown that two view mammography was particularly effective at detecting small invasive breast cancers, and hence that two view mammography should also increase breast cancer detection at women’s subsequent screens. Since 2003, two view mammography at all screens has been policy in the NHSBSP, and this has had a major

5.2 Effectiveness of the NHSBSP

In the NHSBSP, the main outcome measures that are regularly monitored to assess the quality of the programme are cancer detection rates (measured as standardised detection ratios), percentage of small cancers detected and interval cancer rates. The targets for each are based on the findings from the Swedish Two County trial. The measures are taken to be surrogate markers of the effectiveness of the NHSBSP; if the performance of the NHSBSP is as good as in the trial, then a reduction in mortality of similar magnitude might be expected.

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*In randomised controlled trials, mortality rates for breast cancer in women randomised to be invited for screening and randomised not to be invited can be compared directly. However, once a national screening programme is established, all women of certain ages are routinely invited to screening, therefore no appropriate comparison group exists. Thus, it is not simple to evaluate the impact of a national breast screening programme on mortality. One indirect approach is to use surrogate markers, such as the cancer detection and interval cancer rate, and to assume that, if the values are similar to those achieved by the trials that are known to be efficacious, a reduction in mortality similar to that observed in the trials should be expected. Another approach is to estimate the reduction in mortality expected on the basis of prognostic indicators of the cancers detected. It is unknown whether the predictive value of such surrogate markers varies across populations and over time.
impact on the programme’s cancer detection rate without any increase in the assessment rate.  

Although the NHSBSP aims to deliver a screening programme that is as effective as possible for all women, there is some variation between women in the likely effectiveness of mammography. Increased mammographic density is associated with a reduced sensitivity and specificity of mammography. Both the sensitivity and specificity of mammography in the NHSBSP are reduced in women who use hormone replacement therapy and in women who have a low body mass index or have had breast surgery in the past, each of which is associated with an increase in mammographic density. Furthermore, specificity of mammography is reduced in premenopausal compared with postmenopausal women as well as in users of hormone replacement therapy. These factors may thus reduce the effectiveness of mammography in some individuals, and changes in the prevalence of these factors need to be taken into account when considering the overall effectiveness of the NHSBSP.

5.3 Impact of the NHSBSP on mortality from breast cancer

It is not easy to assess the direct contribution of the NHSBSP to the reduction in mortality from breast cancer. Death rates from breast cancer in England and Wales were fairly constant, or increased slightly, during the 1980s, but since about 1990 they have fallen in all age groups by about 25% (Figure 4). This rapid decline in mortality is believed to be partly the result of earlier diagnosis of breast cancer, which is associated with screening and increasing breast awareness, and partly the result of increased use of hormonal and other effective therapies as well as the direct result of the NHSBSP. Based on findings from randomised trials, the NHSBSP would be expected to show little effect on mortality in the first few years after screening began, with the full impact being evident after 10 or so years and continuing thereafter. However, the longer the interval between screening and its expected impact on mortality and the greater the influence of other factors, the more difficult it is to estimate reliably how much of the decline in mortality from breast cancer could be the result of screening.

Several methods have been used to estimate the reduction in mortality from breast cancer associated with the NHSBSP. One approach is to use surrogate measures of breast cancer mortality based on the tumour characteristics (size, nodal status and grade) of women invited for screening compared with the characteristics of breast cancer in women of the same age who were not invited. Using this approach, McCann et al predicted a 15% reduction in mortality from breast cancer by 2004 among women who were aged 50–64 years when they were screened. These estimates were based on screening performance during the second round of screening, when the detection rates for small invasive cancers were still relatively low and the interval cancer rates were relatively high. Furthermore, many factors have contributed to the decline in breast cancer mortality in England over the last decade, and the relevance of prognostic markers may be changing.

Another approach is to estimate future breast cancer mortality in the absence of screening and use the restricted age range over which screen-
ing will affect mortality to estimate its effect, at the same time allowing for other factors. Blanks et al\textsuperscript{21} used such an approach, fitting age cohort models and carrying out a detailed examination of age specific observed and expected mortality rates from breast cancer in England and Wales. They estimated that screening by the NHSBSP between 1988 and 1995 had resulted in a 6\% reduction in mortality from breast cancer in women aged 55–69 years by 1998.\textsuperscript{21} This comparatively low estimate of the reduction in mortality from breast cancer attributable to screening is in part because 1998 is only a few years after 1995, when full population coverage of the NHSBSP was first achieved, and in part because many deaths in the target age groups were among women who had been diagnosed with breast cancer before the age of 50. Blanks et al\textsuperscript{21} concluded that the full effect of screening on mortality would not be seen until about 2005, but even then it would appear diluted in the 55–69 age range because only about 70\% of deaths in that age range occur in women diagnosed with breast cancer at ages 50–64 years. The use of hormone replacement therapy by a substantial proportion of women aged 50–64 would also have diluted the effects of screening because its use is associated with a reduction in the sensitivity of mammography as well as with an increase in mortality from breast cancer.\textsuperscript{30,47,49} The early detection of small tumours is especially likely to have an impact on mortality from breast cancer, and the recent adoption of two view, rather than

**Figure 4** Age specific breast cancer mortality rates, England and Wales, 1971–2003.

The age groups expected to be most affected by the NHSBSP are shown in bold.
one view, mammography is thus expected to lead to further reductions in mortality in the future as it differentially increases the proportion of small tumours detected.28

An alternative approach is to assume that the reduction in mortality observed in randomised trials would also apply to women screened in the NHSBSP. The results shown in Table 5 use this approach to estimate the number of lives saved (ie deaths prevented) annually among women in England by the NHSBSP, assuming that 75% of the women invited are screened. The calculation of the number of deaths from breast cancers that would be prevented by the NHSBSP exclude deaths from breast cancer in women who would have been diagnosed with the disease before the age of 50 or after the age of 70, ie outside the target age range of the screening programme. Overall, an estimated 1400 lives would be saved each year by the activities of the NHSBSP in England. Among such women, the average age at death would otherwise have been 65.6 years, with 1083 of the deaths prevented (79% of the total) occurring between the ages of 55 and 74 (see Figure 5). Overall, there is an estimated reduction in the cumulative mortality from breast cancer among women screened regularly over a 10 year period between the ages of 50 and 70 years of 2.8 per 1000 (from 8.0 to 5.2 per 1000). This estimate is broadly similar for women screened between the ages of 50 and 60 years and for women screened between the ages of 60 and 70 years.* If the underlying death rate from breast cancer continues to fall in the future, the absolute number of lives saved by routine screening would, of course, also fall. For example, if breast cancer death rates fell by an additional 20% in the next decade, the estimated number of lives saved by screening women aged 50–70 years would be about 1100 annually.

*The cumulative mortality rates from breast cancer are somewhat higher for breast cancers diagnosed between the ages of 50 and 60 (8.2 and 5.3 per 1000 in unscreened and screened women respectively) than between the ages of 60 and 70 (7.7 and 5.0 per 1000, respectively), largely because the rate of death from other causes is greater in older than in younger women. However, the estimated number of lives saved are similar (2.9 and 2.7 per 1000, respectively).
Table 5  Age specific breast cancer deaths among women in England in 2003, and the estimated number of deaths that would be prevented each year by routine screening of women aged 50–70

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of breast cancer deaths in England in 2003</th>
<th>Proportion of breast cancer deaths at each age that were diagnosed at ages 50–70 (%)</th>
<th>Estimated number of breast cancer deaths among women who were aged 50–72 at diagnosis†</th>
<th>Estimated number of deaths prevented each year by screening women aged 50–70*</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–54</td>
<td>757</td>
<td>32</td>
<td>242</td>
<td>86</td>
</tr>
<tr>
<td>55–59</td>
<td>951</td>
<td>74</td>
<td>704</td>
<td>250</td>
</tr>
<tr>
<td>60–64</td>
<td>893</td>
<td>87</td>
<td>777</td>
<td>276</td>
</tr>
<tr>
<td>65–69</td>
<td>952</td>
<td>92</td>
<td>876</td>
<td>281</td>
</tr>
<tr>
<td>70–74</td>
<td>1095</td>
<td>62</td>
<td>953</td>
<td>276</td>
</tr>
<tr>
<td>75–79</td>
<td>1277</td>
<td>27</td>
<td>485</td>
<td>140</td>
</tr>
<tr>
<td>80–84</td>
<td>1304</td>
<td>12</td>
<td>222</td>
<td>65</td>
</tr>
<tr>
<td>Total</td>
<td>7229</td>
<td>52</td>
<td>4258</td>
<td>1374</td>
</tr>
</tbody>
</table>

*Assuming that 75% of women aged 50–70 years in England attend for screening, that breast cancer mortality is reduced by 35% in women screened and that age specific death rates in 2003 apply in the future. The estimates also take into account the reduction in mortality in 2003 that would have resulted from screening women aged 50–64 over the last decade.

†Assuming a lead time of 2.5 years.

Figure 5  Positive predictive value of referral (ppv %) versus referral (%), 1998/99 for women aged 50–64.
6. COMPARISON OF BREAST CANCERS DIAGNOSED AT SCREENING AND SYMPTOMATICALLY

- The NHSBSP now diagnoses about half of all breast cancers found in women in the target age range of 50–70 years, with the remainder occurring in women who do not attend for screening or who present symptomatically in the interval between screens.
- Screened women are slightly more likely than unscreened women to be diagnosed with breast cancer. The cancers in screened women are smaller and are less likely to be treated with mastectomy than they would have been without screening.
- The current evidence about screen detected ductal carcinoma in situ points to it being an important precursor lesion for invasive disease.
- If screening brings forward the diagnosis of breast cancer by an average of three years, this would lead to an apparent 5–10% increase in the incidence of breast cancer in the target age range.
- An important priority for the future is for cancer registries and the screening programme to refine their methods for the collection of reliable information on interval cancer rates.

6.1 Relationship between NHS breast screening and symptomatic services

Mammography in the NHS is provided either as part of the screening programme for asymptomatic women aged 50 and over, or as part of a symptomatic service for women of any age. The symptomatic services perform mammograms for women being investigated for suspected breast cancer, for women followed up after previous treatment for breast cancer and for some women younger than 50 who are under surveillance because they are thought to have an increased risk of breast cancer. Symptomatic services also provide breast cancer services for men where necessary. All aspects of the symptomatic services are solely the responsibility of the providing trust. The NHSBSP is nationally coordinated and locally organised, with a quality assurance mechanism and a structure that enables regular audit of its activities and review of its performance.

There is sometimes confusion in the public mind between ‘having a mammogram’ and ‘being screened’ for breast cancer. The former is available for any woman whose doctor considers it an appropriate investigation, whereas the latter is a routine service for women without symptoms that specifically invites women in a particular age group for routine screening. Where necessary, the screening programme provides the full range of investigations necessary either to confirm normality or to make a diagnosis of breast cancer.
Once a woman is diagnosed through the screening programme as having breast cancer, she is referred out of the screening programme for treatment. However, most breast screening units in England also provide clinics for breast cancer diagnosis in symptomatic women and other services, such as follow up mammography for women who have been treated for breast cancer and surveillance for younger women with a family history of the disease, although a few operate quite separately from local symptomatic provision.

The NHSBSP now diagnoses about half of all breast cancers found in women aged 50–64 years, with the remaining half occurring in women who do not attend for screening or in those who present symptomatically in the interval between screens. The cancers diagnosed by the NHSBSP also represent almost 1 in 4 of all breast cancers diagnosed annually, most of which are symptomatic and are discovered and reported by the woman herself.

The introduction of mammographic screening resulted in a large increase in the number of women being diagnosed with ductal carcinoma in situ (DCIS).\textsuperscript{29} DCIS lesions are diagnosed much less often following symptomatic presentation than in a screening programme, where they generally make up about 20% of the breast cancers detected. This is largely because impalpable DCIS lesions tend to have areas of calcification, making them detectable on x-ray mammography. Other impalpable non-invasive carcinomas of the breast, such as lobular carcinoma in situ, are generally not calcified and hence are rarely detected either clinically or at mammography.

Before the advent of mammographic screening, DCIS was sometimes diagnosed in symptomatic women, and about one in three women with biopsy evidence of such lesions went on to develop invasive breast cancer in the same breast during the next 10–20 years if they received no further treatment (which was not unknown during the 1950s and 1960s).\textsuperscript{50–53} This was roughly 10 times the incidence of invasive breast cancer in the general population. The substantial increase in the number of women diagnosed with DCIS following the introduction of the NHSBSP prompted the need to improve understanding of the natural history of this condition, so that women could be offered appropriate information and treatment options. Providing relevant information and treatment options for women with screen detected invasive cancer was expected practice within the programme, and the same standards were required for women diagnosed with DCIS.

The current evidence about screen detected DCIS points increasingly to it being an important precursor lesion for invasive disease. The epidemiological risk factors for DCIS are broadly the same as those for invasive disease, suggesting they have similar causes.\textsuperscript{54–58} Furthermore, the treatment of DCIS with local excision is associated with a substantially increased risk of invasive breast cancer developing in the same breast. In the USA, for example, 8% of women with DCIS treated by lumpectomy alone developed invasive cancer in the same breast within five years,\textsuperscript{58} and in a European treatment trial, 8% of women who had local treat-
ment alone for DCIS developed invasive breast cancer within the next four years.\textsuperscript{59} In other treatment trials, the addition of radiotherapy and/or tamoxifen to breast conserving therapy has been shown to reduce the subsequent incidence of recurrent DCIS or invasive breast cancer.\textsuperscript{60,61} which is further evidence that many screen detected DCIS lesions do not have a benign natural history. The subsequent development of invasive cancer is more likely with high grade than with low grade DCIS lesions.\textsuperscript{58} These observations are supported by studies of the molecular genetics of DCIS, which have shown identical alterations for in situ lesions and related invasive carcinoma that are consistent with precursor status and a common development pathway.\textsuperscript{62}

Some have argued that, if DCIS lesions were left untreated, few affected women would go on to die from breast cancer. However, the probability of death from breast cancer among women treated by lumpectomy alone for DCIS is estimated to be 2\% in the subsequent 10 years, i.e. about 2–4 times the death rate from breast cancer among women in their 50s and 60s in the general population.\textsuperscript{58}

In the UK, 69\% of all screen detected DCIS are high grade.\textsuperscript{63} All women with DCIS diagnosed through the NHSBSP are offered treatment. It would be valuable to be able to identify which women with DCIS would not go on to develop invasive disease, but this is not possible at present. The options that each individual is offered, and chooses, generally reflect the size and location of the DCIS and the woman’s personal values and circumstances. The NHSBSP has recognised that it has a particular responsibility to encourage research where DCIS is concerned. When the programme was first set up, the ‘DCIS trial’ began alongside it. Having found that radiotherapy and tamoxifen reduce recurrence rates in women with DCIS,\textsuperscript{61} a second trial is now being established to build on knowledge from its predecessor. In addition, the ‘Sloane’ audit has been established, funded by the screening programme, which aims to record and investigate all cases of DCIS within the programme over a five year period.

6.3 Overdiagnosis and overtreatment of breast cancer resulting from screening

There is some concern that the detection at routine mammography of DCIS and also of some indolent invasive breast cancers might result in an unnecessary overdiagnosis and overtreatment of breast cancer, since some of these cancers might never become clinically apparent.\textsuperscript{63–65} However, the effectiveness of mammographic screening relies on breast cancers being diagnosed earlier, on average, than they would otherwise have been, so that the associated treatment can prevent deaths that would otherwise have occurred had the cancers presented symptomatically at a later date. Bringing forward the time when a breast cancer is diagnosed is thus a necessary aspect of the screening process if lives are to be saved.

If the NHSBSP brought forward the diagnosis of breast cancer by three years, on average, for women screened at age 50–70 years, this would lead to an apparent 5–10\% increase in the incidence of breast cancer at that age. Thus, some of the observed increase in breast cancer registration rates since the NHSBSP began (Figure 3) is likely to be a consequence of the accelerated diagnosis of breast cancer among screened women, which
the programme aims to achieve. As long as the NHSBSP continues to detect breast cancer earlier than it would otherwise have been diagnosed, age specific breast cancer registration rates will continue to be higher than they were before the programme began. False positive diagnoses of breast cancer are rare in the NHSBSP, as the potential for this happening has been minimised by the activities of the national pathology quality assurance network.

For the reasons given above, it is inevitable that women who are screened regularly will be somewhat more likely than unscreened women to be diagnosed with breast cancer at a given age. Table 6 gives estimates of the number of breast cancers diagnosed over a 10 year period in 1000 women aged 50–70 years in England who do or do not regularly attend for mammographic screening. Slightly more women are diagnosed with breast cancer if they are screened regularly than those who are not screened regularly (30 and 26, respectively, per 1000 over a 10 year period). Among the screened women, 20 out of the 30 cancers would be detected at screening and four of the cancers would be DCIS (Table 6).

For certain individuals, bringing forward the diagnosis of breast cancer would be of little benefit, as they would die from another cause before their breast cancer presented clinically. Such individuals would, in retrospect, have been subjected to overdiagnosis and hence overtreatment of their cancer. It is impossible to predict who would have been overtreated, but in general the longer the woman’s life expectancy when screened,

**Table 6**  Estimated number of breast cancers diagnosed over a 10 year period, and the associated treatment in 1000 women in the age range 50–70 years who do or do not attend for screening*

<table>
<thead>
<tr>
<th>Breast cancers diagnosed over a 10 year period</th>
<th>1000 women aged 50–70, regularly screened over a 10 year period</th>
<th>1000 women aged 50–70, not screened over a 10 year period</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mode of presentation:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screen detected†</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Symptomatic‡</td>
<td>10</td>
<td>26</td>
</tr>
<tr>
<td><strong>Invasiveness:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In situ (DCIS)§</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Invasive</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td><strong>Number treated with:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mastectomy¶</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Breast conserving surgery¶</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td><strong>Total breast cancers diagnosed (over a 10 year period)</strong></td>
<td>30</td>
<td>26</td>
</tr>
</tbody>
</table>

*Assuming that three screening mammograms are performed over a 10 year period, with all screens done in the target population, ie between the ages of 50 and 70 (the 10 year period would need to begin when women were aged between 50 and 60 so that all screens were done at ages 50–70).

†In 2002/3, the cancer detection rate was 6.6/1000; therefore, with three screens, cancers detected per 1000 = 3 x 6.6 = 19.8.

‡For screened women, the cumulative interval cancer rates are assumed to average 1 per 1000 per year (Table 7), ie 10 per 1000 over 10 years. For unscreened women, the underlying incidence in 2001 averaged 2.64 per 1000 per year (Table 2), ie 26/1000 over 10 years.

§Of the 20 screen detected cancers, 20% (four) were DCIS (Table 1).

¶In 2002/3, mastectomy was performed in 27% of screen detected invasive cancer and in 29% of screen detected DCIS lesions (Table 4). For women presenting symptomatically with breast cancer, mastectomy is performed in an estimated 45% of UK women aged 50–64.§

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the less the likelihood of overtreatment. For example, for those women who are screened in their 50s, the potential years of life gained would be 20 or so years longer than for women screened in their 70s.

6.4 Interval cancers

Interval cancers are breast cancers diagnosed in the period between screens, and thus can be defined as occurring only in women who have been screened. Interval cancer rates are important surrogate measures of the quality of a screening programme, and expected rates for the NHSBSP have been calculated according to the interval cancer rates found in the Swedish Two County trial (expressed as a percentage of the underlying incidence rate, and termed the ‘combined proportionate incidence’). In the NHSBSP, interval cancer rates in individual screening centres are inversely related to the screen detected cancer ratios, supporting the view that interval cancer rates reflect the quality of screening. Estimates from various regions of the UK of the interval cancer rate have been published, and are summarised in Table 7. It is difficult to know how to interpret these findings, as it is unclear how much they are affected by geographic variations in the underlying incidence of breast cancer or by other factors. Use of hormone replacement therapy reduces the sensitivity of mammography and increases the interval cancer rates in postmenopausal women (Table 7). Use of this therapy increased rapidly during the 1990s, and this would be expected to result in an increase in interval cancer rates. Of greatest concern, however, is the difficulty in obtaining reliable statistics on interval cancers. There is considerable population movement in the UK, and regional cancer registries may not necessarily have access to data on interval cancers in women who were screened in one region but moved to another region soon after. An important priority for the future is for cancer registries and the screening programme to refine their methods for the collection of reliable information on interval cancer rates.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Place and calendar year of screening</th>
<th>&lt;1 year since screening rate/1000 (n)</th>
<th>1–2 years since screening rate/1000 (n)</th>
<th>2–3 years since screening rate/1000 (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHSBSP expected rates⁹</td>
<td>England, 1995/6</td>
<td>0.45</td>
<td>0.65</td>
<td>1.2–1.3</td>
</tr>
<tr>
<td>Day et al⁷</td>
<td>East Anglia, 1988–94</td>
<td>0.52 (45)</td>
<td>1.28 (61)</td>
<td>1.89 (35)</td>
</tr>
<tr>
<td>Woodman et al⁸</td>
<td>Manchester, 1988–92</td>
<td>0.57 (59)</td>
<td>0.92 (75)</td>
<td>1.51 (57)</td>
</tr>
<tr>
<td>Million Women Study⁴⁷</td>
<td>England, 1996–98</td>
<td>0.82 (97)*</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

*Rates per 1000 were 1.42, 0.77 and 0.45 for current, past and never users, respectively, of HRT.
7. RECALL FOR ASSESSMENT

- About 1 in 8 women screened regularly by the NHSBSP will be recalled for assessment at least once over a 10 year period.
- Factors which affect an individual woman’s likelihood of recall include both the ethos of the screening unit which she attends and physiological factors.
- There is a delicate balance between reducing recall rates so far that small cancers are missed and calling back too many women, which causes anxiety and may reduce reattendance.

7.1 Frequency of recall

Screening tests for any condition are imperfect, and some people who have a positive test result will, on further investigation, turn out not to have the condition for which they were screened. Such individuals are described as ‘false positives’ and, in the NHSBSP, the term refers to women recalled for further investigations in whom no breast cancer is found. The frequency of ‘false positives’ in breast screening varies considerably from country to country and, within the UK, between screening centres. In the NHSBSP as a whole, the false positive rate has remained fairly steady in the last five years at 4–5% (Figure 2). False positive rates are higher at the first screen than subsequently, and are higher in women who have been recalled previously (Table 8). For women who regularly attend for screening, the cumulative probability of being recalled at least once increases over time and, based on national recall rates (Table 1), an estimated 1 in 8 women (13%) would be recalled at least once if they were screened three times over a 10 year period.

7.2 Factors affecting recall

The principal determinant of recall is previous attendance at screening, with recall rates for the first (prevalent) screen being more than double that at subsequent (incident) screens. The recall rate in England of 7.6% for the first screen, which is usually at age 50–52 years, is lower than in the USA (range 12.5–14.6%). The overall recall rate for England disguises a wide range of performance, with rates in individual screening units varying from 4% to 19% at the prevalent round in 2002/03 (RG Blanks, personal communication). The reasons for this range are manifold and reflect the ethos of each screening unit, which usually settle at a rate they feel comfortable with by balancing the need to find small cancers with the anxiety induced by false positive recalls. This is affected by the

Table 8  False positive recall rates for women in West Midlands and Yorkshire

<table>
<thead>
<tr>
<th></th>
<th>Women not recalled previously</th>
<th>Women recalled previously</th>
</tr>
</thead>
<tbody>
<tr>
<td>First invitation</td>
<td>6.9% (2995/43 269)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Second invitation</td>
<td>2.5% (932/38 031)</td>
<td>4.6% (121/2619)</td>
</tr>
<tr>
<td>Third invitation</td>
<td>2.9% (1072/37 054)</td>
<td>4.9% (176/3585)</td>
</tr>
</tbody>
</table>

Source of data: MG Wallis and K Faulkner, personal communication.
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number of views, number of readers and reading protocols as well as unit size and experience of readers. The characteristics of the women screened that increase their likelihood of being ‘false positive’ are premenopausal (rather than postmenopausal) status, prior breast surgery and use of hormone replacement therapy.

7.3 Investigation at recall

At recall, women undergo some or all of the following investigations: further mammography with specialised views, clinical examination, ultrasound and needle sampling according to local protocols based on national guidelines. Before 1996, fine needle aspiration cytology was the main tissue diagnostic technique used. There were wide differences across England in the non-operative diagnosis rate of breast cancer and in the open surgical biopsy rates. In 1996, the radiology and pathology national quality assurance groups undertook a joint audit through the quality assurance network, and a formal decision was made to increase non-surgical diagnosis through greater use of needle core biopsy (which does not require skilled cytopathology interpretative skills and has been shown to be of value through increase in tissue sample yield). By 1997, training centres were specifically commissioned to run courses in image guided needle biopsy sampling technique and interpretation, and radiologists and pathologists were actively encouraged to attend. Over time, the switch away from fine needle cytology to needle core biopsy techniques resulted in a dramatic increase in the percutaneous biopsy rate, a rise in non-operative diagnoses (from 61% in 1997 to 91% in 2003) and a corresponding fall in the number of women subjected to surgical diagnostic procedures (open biopsy rates declined from 3.5 to 1.8 per 1000 over that time). Further refinements have occurred since then, with the use of digital stereotaxis, with or without prone tables, and the increasing use of larger and more sophisticated needle biopsy systems.

7.4 Optimising recall

Recall rates should be neither too high nor too low. There is a delicate balance between reducing recall rates so far that small cancers are not missed and recalling too many women, which causes anxiety and reducing reattendance. Film readers must be involved in breast screening assessment and pretreatment clinical management meetings that provide each member of the team with information on their performance. The positive predictive value (PPV) for recall, particularly when used in a PPV recall diagram (Figure 5), is a powerful audit tool to demonstrate the relationships between cancer detection and recall and can be used to suggest ways to improve performance. The increase in breast cancer detection rates since 1992/3, shown in Figure 1, has not been accompanied by an increase in the false positive recall rate.
8. SCREENING METHODS AND IMAGING

- Screening with film-screen x-ray mammography remains the only single intervention shown in randomised controlled trials to significantly reduce mortality from breast cancer.
- Full field digital mammography has been shown to have similar sensitivity and higher specificity than conventional mammographic screening.
- Ultrasound is an effective technique for further assessment of mammographic abnormalities and for image guided breast biopsy.

8.1 Film x-ray mammography

Screening with film-screen x-ray mammography remains the only single intervention shown in randomised controlled trials to significantly reduce mortality from breast cancer. Various new technologies have been developed (and are discussed below). Any new technology considered for use in the NHSBSP goes through both a technical assessment by the King’s Centre for the Assessment of Radiological Equipment (KCare), as well as an evaluation in a clinical setting. This is part of the ongoing formal evaluation programme organised by the NHSBSP in conjunction with KCare.

8.2 Full field digital mammography

Currently, the most promising development is full field digital mammography. A number of manufacturers now market mammography x-ray equipment that acquires and displays the mammography image in digital format. The introduction of such equipment into the screening programme can take place only if it is shown to improve the existing system or, at the least, is equal to the existing system.

Direct digital mammography has been shown to have similar sensitivity and higher specificity to conventional film x-ray mammography for screening. It also has a number of potential advantages, including:

- reduced radiation dose, with equipment delivering less dose by making more effective use of the x-rays
- reduction in the need for repeated images
- better visualisation of the dense breast
- instant information transferred electronically across single or multiple organisations
- no chemicals are required (COSHH), thereby reducing the hazard to staff and reducing costs as well as improving the clinical environment
- images available to clinicians at any destination
- ease of consultation between clinicians, with clinicians in different places able to view images simultaneously
- image manipulation, allowing the reporting clinician more versatility for image viewing for diagnosis, eg edge enhancement, electronic magnification
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- reduction in storage space needed
- reduction in manual handling by radiographers
- potential for remote workstations and thus less travel between installations.

These potential advantages mean that estimated additional costs of digital compared with conventional mammography for screening are likely to be minimal, provided the images are not routinely printed since printing digital images substantially increases costs.\(^79\)

8.3 Computerised radiography

Computerised radiographic mammography could be useful and shares many of the advantages of digital mammography at lower cost. However, systems are of variable quality and performance.\(^80\) In particular, there have been concerns over loss of definition for smaller abnormalities. The NHSBSP is currently considering its appropriateness in the screening situation.

8.4 Computer aided detection

Computer aided detection (CAD) can be applied to digital mammographic images, and advantages may include improved sensitivity and a reduction in the number of human readers needed per film. Work is continuing to evaluate newer CAD systems as they develop. However, current systems often slow the film reader down and, as yet, no clear benefits from this technology have been demonstrated.\(^81,82\)

8.5 Ultrasound

Ultrasound is accepted as a very effective technique for further assessment of mammographic abnormalities and for image guided breast biopsy. There is some evidence of the benefit of ultrasound as a secondary adjunct to screening the mammographically dense breast, and also some evidence of its benefit in the primary screening of younger women at increased risk.\(^83\) Some studies have reported a significant increase in cancer detection using ultrasound in women whose mammograms show a level of background density that is likely to reduce sensitivity for the changes of early breast cancer.\(^83–85\) Breast ultrasound is widely available and is inexpensive compared with other imaging techniques such as nuclear medicine and magnetic resonance imaging; however, it is time-consuming and there is a shortage of radiologists and radiographers with the necessary skills to carry out breast ultrasound screening.\(^79\) While ultrasound may improve invasive cancer detection in dense breasts, it has poor sensitivity for DCIS and has high false positive rates.\(^83\)

8.6 Magnetic resonance imaging

Magnetic resonance imaging has the highest sensitivity for invasive breast cancer of all currently available imaging techniques.\(^83,86,87\) However, it is expensive and, although the equipment required is available in the NHS, there is limited experience in breast magnetic resonance imaging interpretation and guided biopsy. Breast magnetic resonance imaging also has higher false positive rates than x-ray mammography. Although it promises to be the technique of choice for screening women younger than 50 who are at an extremely high risk of breast cancer,\(^83,86,87\) further information is needed on its performance in a screening setting and its cost-effectiveness.

8.7 Other imaging techniques

Although some other imaging techniques, such as scintimammography, computerised tomography and positron emission tomography, are useful
for further assessment of symptomatic breast problems, these techniques have no proven benefit in the screening setting. New breast imaging techniques, such as elastography, optical imaging, electrical impedance imaging, microwave imaging, Hall effect imaging and thermography, are either not yet available for clinical assessment or have no proven use as part of screening.

Cohort studies show that clinical examination of the breast for screening does not affect mortality from breast cancer. Clinical examination was included in the UK Trial of Early Detection of Breast Cancer (UKTEDBC) and was shown to have an inferior sensitivity and specificity compared with mammography and to add only marginally to the overall cancer detection rate of a breast screening programme that incorporates routine mammography. Similarly, routine breast self-examination does not significantly influence breast cancer detection rates or mortality from breast cancer. Trials in the former USSR and Shanghai have both demonstrated no benefit in terms of a reduction in mortality from breast cancer, as did the UKTEDBC. However, in order to maximise early detection of all breast cancers and to facilitate the availability of a range of treatment options, it is considered good practice to advise women to be ‘breast aware’ and present to their general practitioners should they notice any change in their breasts, whether or not they have attended for screening and, if they have, whatever the result of that attendance was.

8.8 Clinical examination and breast self-examination

Cohort studies show that clinical examination of the breast for screening does not affect mortality from breast cancer. Clinical examination was included in the UK Trial of Early Detection of Breast Cancer (UKTEDBC) and was shown to have an inferior sensitivity and specificity compared with mammography and to add only marginally to the overall cancer detection rate of a breast screening programme that incorporates routine mammography. Similarly, routine breast self-examination does not significantly influence breast cancer detection rates or mortality from breast cancer. Trials in the former USSR and Shanghai have both demonstrated no benefit in terms of a reduction in mortality from breast cancer, as did the UKTEDBC. However, in order to maximise early detection of all breast cancers and to facilitate the availability of a range of treatment options, it is considered good practice to advise women to be ‘breast aware’ and present to their general practitioners should they notice any change in their breasts, whether or not they have attended for screening and, if they have, whatever the result of that attendance was.
9. RADIATION RISK

- For every 14,000 women in the age range 50–70 years screened by the NHSBSP three times over a 10 year period, the associated exposure to x-rays will induce about one fatal breast cancer.

9.1 Estimated exposure to ionising radiation

The use of ionising radiation for mammography carries with it a small risk of inducing breast cancer at a later stage. For a screening programme to be justified in radiation protection terms, the benefit of breast screening must be greater than the risk of inducing cancer by the use of ionising radiation. Optimisation implies maximising the numbers of cancers detected, which can in turn be increased by improving image quality. As image quality and radiation dose are linked, optimisation has implications for the balance between benefit and harm. There are, in effect, conflicting objectives which need to be considered if an objective decision is to be made about mammographic screening.

There is evidence of the induction of breast cancer by ionising radiation, and the probability of induction of breast cancer at low doses can be estimated using various models of the dose–response relationship, assuming no threshold. There is some uncertainty in the estimates of radiation induced breast cancer. Nevertheless, the risk of breast cancer induction per unit dose of x-rays is age dependent and is lower in older than in younger women. This age dependence is partly because younger women are more susceptible to the induction of breast cancer by x-rays and partly because they have a longer life expectancy after they are exposed to x-rays, and hence a longer time to develop radiation induced breast cancer.

It is accepted that the glandular tissue of the breast is sensitive to radiation. A woman’s radiation dose is also affected by breast size and the proportion of fat and glandular tissue in the breast. Larger breasts attenuate radiation more than smaller breasts and, as a consequence, require more radiation to create an image on film. The mean glandular dose to a standard phantom is monitored routinely as part of a quality assurance programme. In addition, surveys of doses received by patients are performed on a regular basis; technique factors and compressed breast thickness are also recorded for a series of women attending each NHSBSP screening unit. Radiation doses in the NHSBSP have been analysed, and the mean glandular dose for a typical woman attending the breast screening programme for two view mammography is about 4.5 mGy,* using the latest conversion factors for glandular dose. Factors which may be used to estimate mean glandular dose for a range of breast compositions and sizes have also been published.

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*milliGray, a measure of radiation dose.
9.2 Breast cancer risk associated with x-ray mammography

For women in England who are screened by the NHSBSP over a 10 year period using two view mammography, the risk of a radiation induced fatal breast cancer is estimated at 0.1 and 0.04 per 1000 women aged 50–59 and 60–69 years respectively (an average of 0.07 cancers per 1000 women screened at age 50–70). Thus, for every 14000 women aged 50–70 screened by the NHSBSP over a 10 year period, about one fatal breast cancer will be induced by the associated x-ray exposure.
10. WOMEN AT YOUNGER AND OLDER AGES AND AT HIGH RISK OF BREAST CANCER

- The International Agency for Research on Cancer has concluded that there is only limited evidence that screening women aged 40–49 years by mammography reduces their mortality from breast cancer. Further research on the effectiveness of screening at this age is under way within the NHSBSP.
- For women aged over 70 years, a decision about whether or not to be screened should be taken at an individual level, bearing in mind personal circumstances rather than offering a blanket invitation for screening.

10.1 Younger women

The IARC working group on breast cancer screening concluded that there was only limited evidence that screening women aged 40–49 years by mammography reduces their mortality from breast cancer.25 and pointed out that the observed reduction in mortality seen in some trials in women who entered the trials when they were aged 40–49 may well be the result of the known benefit from mammograms performed after the women reached the age of 50. The IARC working group drew attention to the biological plausibility that mammography may be less effective before age 50 because the mammographic density of breast tissue in premenopausal women (usually aged under 50) is greater than in postmenopausal women (usually aged over 50). The IARC working group concluded that there needed to be direct evidence comparing the effect of initiating routine mammography before age 50 with waiting until age 50.

The ‘Age Trial’ was set up in the UK in 1991 to evaluate whether offering women annual mammography from age 40 to 47–48 years leads to an additional reduction in mortality from breast cancer compared with offering women triennial screening beginning at age 50.98 The trial involves 160,000 women in total, with 54,000 in the intervention group. Preliminary results, based on prognostic indicators of the breast cancers detected so far, predict about a 10% reduction in mortality from breast cancer among women first invited for routine screening at age 40 compared with age 50.99,100 Results on mortality from breast cancer in women participating in this trial should be available in the next year or so, and will inform UK policy on screening women younger than 50.

Another consideration is that younger women are more susceptible to the carcinogenic effects of x-radiation on breast tissue than older women.92 The younger women are at mammography, the fewer cancer deaths are prevented by screening but the more cancers are induced by radiation.95 This is largely because breast cancer incidence is much lower at younger than at older ages (Table 2). For women in their 20s and 30s, the number...
of breast cancer deaths induced by radiation associated with annual mammography is likely to be greater than the number prevented by screening. However, for women in their 40s, the overall balance between the risks and benefits is unclear, given the uncertainty of the estimated effects of radiation and of the efficacy of screening. This balance will need to be examined in detail when the results of the Age Trial are available.

### 10.2 Older women

Incidence rates for breast cancer rise with age, and the underlying rates are greater for women in their 70s than at 50–69 years (Table 2). The IARC working group concluded that there was ‘limited evidence’ that screening women beginning at age 70 or older was effective in reducing mortality. This conclusion was based on the findings from trials that randomised women for their first screen ever when they were aged 70 or older. In the trials where women were offered their first screen at ages 50–69 years, many would have been aged over 70 during the trial, and the results of these trials showed significant benefit. The Advisory Committee on Breast Cancer Screening therefore considers that there would be a benefit to women who wish to continue being screened after the age of 70. A survey conducted on behalf of the NHSBSP in May 2004 found that 74% of women in England aged 71–80 years had been screened previously, and that 66% said that they would attend for screening if invited.

For women to benefit from breast screening, they must be in good health and have a life expectancy of at least about 10 years. For most women aged 50–70 years in England, this is a fair assumption. As women age, however, they become more heterogeneous in this respect, and attendance rates fall with increasing age. Therefore, at this stage it seems appropriate that a decision about whether or not to be screened is taken at an individual level, bearing in mind personal circumstances, rather than offering all older women a blanket invitation to attend for screening. While routine invitations cease after the age of 70, there is, in fact, no upper age limit for screening. Women aged over 70 can continue to request routine mammography every three years as part of the breast screening programme. As long as breast screening continues to be regarded by a woman as worthwhile for her, she is encouraged to be screened.

### 10.3 Women at greater than average risk of breast cancer

The NHSBSP does not attempt to identify those women who are at higher risk of breast cancer. An important consideration is that the strongest ‘risk factor’ for breast cancer is a woman’s age, and other factors, including having a family history of the disease, predict very poorly those individuals who will develop breast cancer and those who will not. As almost 90% of women who develop breast cancer do not have affected first degree relatives, concentrating resources on women with a family history would exclude the majority of those who develop the malignancy. The National Institute of Clinical Excellence has recommended annual mammographic surveillance for certain women aged under 50, if they have a relevant family history, provided that they are properly counselled about the fact that at present there is no evidence of benefit. This surveillance is not part of the NHSBSP. The risks of radiation induced breast cancer are greater the younger women are at exposure, and it...
has been suggested that women with a family history of breast cancer have increased susceptibility to the effects of radiation. Even if there is no increased susceptibility, it is unclear, however, whether the extra breast cancer deaths caused by the radiation exposure associated with annual mammography would be outweighed by the potential benefits of screening for women younger than 50 years.

For carriers of BRCA mutations and other genetic disorders that put them at an extremely high risk of developing breast cancer before the age of 50, there is at present no evidence that regular mammography before age 50 would be any more effective at reducing mortality than it is for women who are not carriers. Alternative approaches to screening, such as the use of magnetic resonance imaging, show promise.
11. COMMUNICATIONS AND ANXIETY

- Few women understand that the risk of getting breast cancer increases with age.
- Attendance for screening with a normal outcome causes little anxiety, and there is no difference in anxiety between women whose cancer was screen detected and women whose cancer presented symptomatically. However, for women who experience a ‘false positive’ recall, there is significant anxiety, which may persist for some time.

11.1 General communications

At one time, breast cancer might have been regarded as a taboo topic, whereas it is now a subject frequently discussed in magazines, on television and radio programmes and over a cup of coffee between friends. Campaigns from various charities have also lessened the taboo surrounding breast cancer.

Although increased awareness, encouraged by the introduction of a breast screening programme, has led to earlier presentation of women with symptoms, it has not occurred hand in hand with greater understanding of the disease. The lifetime risk of developing breast cancer of one woman in nine is well recognised. However, among women aged between 40 and 80 years who were questioned in 2004 and 2005 (ONS Omnibus survey; unpublished data), about half replied that the risk of getting breast cancer did not vary with age, and only 2% – very few – correctly picked the oldest group of women (aged 70 or older) as being at greatest risk.

Symptomatic clinics are reported as having ever increasing numbers of relatively young ‘worried well’ being referred, thus leaving fewer resources for the decreasing proportion of attendees who are diagnosed with breast cancer. Furthermore, the public are confused about the distinction between the breast screening programme and symptomatic mammography.

11.2 Public relations

Collaboration between all those with an interest in breast cancer is needed to encourage women to have a correct understanding of the disease and to understand who is at greatest risk, as well as understanding the likely symptoms and the need for breast awareness.

Almost since its inception, a formal public relations initiative has been found necessary by the NHSBSP in order to promote new initiatives (such as the introduction of the informed choice policy), to correct inaccurate information in both the professional and lay press and to counter unjustified attacks on the programme because they might inappropriately reduce women’s confidence in the service provided. In this way, women and the media might increase their understanding of the disease, and the staff providing the service are defended when appropriate.
11.3 Informed choice

When the screening programme began, the emphasis was to persuade women to comply with their screening invitation. Since November 2001, however, the strategy has officially been one of ‘informed choice’. This reflects changing attitudes among the public to public health recommendations, increasing awareness about the fallibilities of screening programmes and also changing guidance to doctors from the General Medical Council in particular. In its guidance on consent, the General Medical Council points out that doctors must ensure that anyone considering whether to accept an invitation for screening makes a properly informed decision. A standard invitation leaflet had not been used in the screening programme before 2001, but a national leaflet became necessary to explain clearly the purpose of screening, the likelihood of positive/negative findings and the possibility of false positive/negative results. It also needed to include information about the uncertainties and risks attached to the screening process and cover some data handling issues such as audit by quality assurance teams.

The national leaflet, which was developed in collaboration with Cancer Research UK, now accompanies every invitation for breast screening and sets out not only the benefits of screening but also its limitations. These include the possibility of an interval cancer, and the leaflet also mentions overdiagnosis. A more detailed booklet has been produced with CancerBacup for those women who require more information, either at the initial invitation stage or when recalled for assessment. This booklet goes into detail about assessment procedures and outlines the issues associated with a diagnosis of DCIS. There is also a great deal of further information on the programme’s website, the address of which is given in the leaflet. The leaflet is designed to be accessible by people with a low reading age and low level of educational attainment. As such, it is relatively limited in the detail it can contain. Particular difficulties were encountered when developing the leaflet in trying to communicate numerical information. By making further information available on the website and in the CancerBacup booklet, women who wish to obtain further detail before they can make an informed decision about whether or not to attend can do so, whereas those for whom it would be superfluous or even overwhelming need not encounter it. If a woman does not attend for screening when invited, a second invitation is sent. However, if there is still no response, no further correspondence is sent to the woman until her next screen is due. If a woman indicates that she wants to remove herself from the invitation process altogether, her wishes have always been respected.

11.4 Anxiety and breast screening

A number of studies have shown that women experience adverse psychological consequences as a result of the breast screening process. The main reasons cited for anxiety are fear of the procedure, in particular the fear of the anticipated pain, and fear of cancer.

For women attending for breast screening, studies have found that those receiving a clear result following mammography experienced little or no adverse psychological consequences. This outcome has been observed both in studies where validated measures of anxiety were used and in studies using other indicators of psychological consequences. However,
for ‘false positive’ women, ie women recalled for further investigation and then found to be clear of cancer, several studies have shown that the psychological consequences are significantly higher than for those receiving negative results following mammography. Significant levels of anxiety have been found before the recall visit, during further investigations and immediately after recall. The existence of anxiety in the period between receiving the recall letter and attending for the recall appointment illustrates the importance of minimising the waiting time in this period.

There is conflicting evidence as to whether the psychological consequences experienced by women who have undergone a false positive examination continue as a long-term effect. Some studies have shown that significantly increased levels of anxiety remain at one month, at 5–6 months, and at 11 months following the recall appointment. A multicentre UK study has shown that the psychological consequences experienced as a result of recall process may even be evident immediately prior to a woman’s next routine mammography appointment, ie 35 months after the last screen, and adversely affect subsequent attendance for routine breast screening. However, another study in one screening unit in London found no difference in the rates of attendance for subsequent routine mammography between women with a previous screen negative or false positive result.

Minimising the delay in obtaining results has also been demonstrated to be important in reducing the potential psychological consequences for recalled women. In comparing women given results at the recall clinic and those referred on for surgical biopsy, significantly reduced levels of anxiety and depression were reported in the former group while remaining relatively high in the latter.

Looking specifically at women diagnosed with breast cancer, it has been indicated that no significant differences in psychiatric morbidity were evident between women diagnosed via breast screening and those diagnosed symptomatically. Predictors of psychiatric morbidity (such as depression or anxiety) were found to be patient related factors, rather than due to the method of diagnosis, the disease or its treatment.
12. COSTS

- The screening programme spends about £3000 for every year of life saved.

Breast screening in England for women aged 50–70 years costs around £75 million per year. The programme is estimated to save about 1400 lives per year. Without screening, the average age at which these women would have died is 67 years old. Life expectancy at this age is a further 18 years. Hence, each woman whose life is saved by the programme can be expected to live, on average, about an additional 18 years, and the cost of the breast screening programme is thus about £3000 per year of person–life gained. This cost compares favourably with many other health interventions currently undertaken in the NHS, including screening for cervical cancer.117
13. BENEFITS VERSUS RISKS

- For every 400 women screened regularly by the NHSBSP over a 10 year period, one fewer will die from breast cancer than would have died if they had not been screened.
- Among women who are routinely screened and diagnosed with breast cancer:
  - 1 in 8 women would not have had their breast cancer diagnosed if they had not gone for screening (because screening picks up some breast cancers that normally grow so slowly that they do not cause symptoms during a woman’s lifetime)
  - 1 in 8 women would be spared the need for a mastectomy (because screening detected their breast cancer earlier than it otherwise would have been, and before it grew too large or spread so far as to warrant a mastectomy)
  - 1 in 8 fewer women will die from breast cancer than would have died had they not been screened (because screening detected their breast cancer earlier than it otherwise would have been, and before it had spread to other parts of the body).

13.1 Reduction in mortality

The purpose of screening for breast cancer is to reduce mortality from the disease. As described in Chapter 5, the totality of the evidence from randomised trials shows that regular mammographic screening commencing at ages 50–69 years reduces mortality from breast cancer by about 35%. In England, with 75% of women aged 50–70 attending regularly for screening, this amounts to about 1400 lives saved annually by the activities of the NHSBSP (Table 5). This is equivalent to a reduction in mortality from breast cancer from 8.0 to 5.2 per 1000 women in the target age range if they are regularly screened over a 10 year period (Table 9).

The benefit of regular mammographic screening in reducing mortality needs, of course, to be considered in the context of any associated adverse effects. In Table 9, the frequency of various beneficial and adverse effects are compared for 1000 women aged 50–70 years who are regularly screened over a 10 year period with 1000 women who are not screened. Women who are regularly screened have slightly more breast cancers diagnosed because of the accelerated diagnosis of breast cancer associated with screening (30 and 26 per 1000 in screened and unscreened women, respectively, over a 10 year period). However, screened women are less likely to have a mastectomy than unscreened (10 and 12 per 1000, respectively over 10 years). The earlier diagnosis of breast cancer is an integral part of successful screening, and it will never be possible to devise an effective screening method that does not result in more breast cancers being diagnosed in screened than in unscreened women (albeit at an earlier stage, with fewer mastectomies and fewer deaths subsequently).
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Table 9  Estimates of the number of events relating to breast cancer screening in 1000 women in the NHSBSP target population who do or do not attend for screening over a 10 year period*

<table>
<thead>
<tr>
<th>Event</th>
<th>For 1000 women aged 50–70, regularly screened over a 10 year period</th>
<th>For 1000 women aged 50–70, not screened over a 10 year period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of breast cancers diagnosed (from Table 6)</td>
<td>30</td>
<td>26</td>
</tr>
<tr>
<td>Cumulative number of deaths attributed to breast cancer among women aged 50–70, diagnosed with breast cancer over a 10 year period (derived from Table 5)†</td>
<td>5.2</td>
<td>8.0</td>
</tr>
<tr>
<td>Number of radiation induced breast cancer deaths due to mammography (from Table 9)</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td>Number of mastectomies (from Table 6)</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Number false positive recalls for assessment (adapted from Table 8)</td>
<td>130</td>
<td>0</td>
</tr>
<tr>
<td>No invasive procedure performed</td>
<td><strong>121</strong></td>
<td>Unknown</td>
</tr>
<tr>
<td>Biopsy performed but benign lesion found</td>
<td><strong>9</strong></td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*Assuming that three screening mammograms are performed over a 10 year period, with all screens done in the target population, i.e between the ages of 50 and 70 (the 10 year period would need to begin when women were aged between 50 and 60 so that all screens were done in the target population).

†Cumulative number of deaths from breast cancer per 1000 women who were diagnosed with breast cancer at ages 50–70 (allowing for the fact that, for women diagnosed with breast cancer at ages 50–70, the distribution of their ages at death is as shown in Table 5).

Among women in England who are not screened, about 8 in every 1000 aged 50–70 years would die from a breast cancer diagnosed over a 10 year period, and, within this age range, the number does not vary much according to the exact age at diagnosis. Screening itself would reduce the death rate to 5.2 per 1000, but an additional small number of screened women (0.1 per 1000) would develop a fatal, radiation induced, breast cancer. On balance, an estimated 2.7 (8.0 minus 5.2 minus 0.1) lives are ultimately saved per 1000 women aged 50–70 years if they are regularly screened over a 10 year period. This means that about 1 in 400 fewer women would die from breast cancer if they were regularly screened. These estimates are based on the most recently published mortality rates for breast cancer in England, and could well change over time.

The results in Table 9 can also be interpreted as showing that, among women who have been screened and are diagnosed with breast cancer, about 18% (5.3 out of 30) would ultimately die from the disease, whereas the corresponding figure for unscreened women is 31% (8.0 out of 26).

13.2 Recall for assessment

Because some women have mammographic findings that are difficult to interpret, they can be recalled for further assessment, which mostly involves clinical examination and further mammography, and rarely includes an operative biopsy being taken. It is estimated that about 1 in 8 women (130 in every 1000) screened are recalled once or more often over a 10 year period of regular screening, and about nine of them have a biopsy performed that showed benign lesions only. It is difficult to obtain comparative figures for women who do not attend for screening, as some may well present clinically with suspicious lesions of the breast.
and some may have biopsies performed that show benign lesions only. The numbers undergoing such procedures would probably be smaller among unscreened than screened women. Again, recalling women with ambiguous mammographic findings for further assessment is an integral part of a successful screening programme.

13.3 Statistical summary

The statistics in Table 9 can be summarised as follows:

- 1 in 400 women aged 50–70 who are regularly screened over a 10 year period will be prevented from dying from breast cancer
- 1 in 8 women diagnosed with breast cancer by the screening programme will be prevented from dying from breast cancer (because screening detected their breast cancer earlier than it would otherwise have been, and before it had spread to other parts of the body)
- 1 in 8 women diagnosed with breast cancer by the screening programme will be prevented from having a mastectomy (because screening detected their breast cancer earlier than it would otherwise have been, and before it grew too large or spread so far as to warrant a mastectomy)
- 1 in 8 women diagnosed with breast cancer by the screening programme would not have had their breast cancer diagnosed if they had not gone for screening (because screening picks up some breast cancers that normally grow so slowly that they do not become clinically apparent during a woman’s lifetime).

13.4 Individual benefits and risks

The figures quoted above are statistical summaries. For an individual woman, however, it is impossible to predict in advance whether or not she will be the one woman in 400 who has her life saved by regular screening. And, for a woman who has a breast cancer picked up at screening, it is impossible to know whether she is the one woman whose cancer was found early enough for it not to have disseminated, or whether she is the one whose cancer would have remained undetected had she not been screened.

It is important that women attending for screening, and the general public, understand that mammographic screening does save lives and spares some women the need to have a mastectomy; however, it is an inevitable consequence that some women will be recalled for further investigation who do not have cancer and that slightly more women are diagnosed with breast cancer, although mostly at early stages that can be treated by local excision.
14. RESEARCH

- An extensive body of research has arisen out of the NHSBSP. The research has also contributed to knowledge in other areas of screening activity and about the causes and treatment of breast cancer.

14.1 Breast screening trials

The NHSBSP has always considered research as central to its goal to provide a service based as much as possible on the best available evidence. Three randomised trials were started at the beginning of the programme looking specifically at screening questions: the age trial, the frequency trial and the one view versus two views trial.\(^{11,39,96-100}\) The first two trials\(^{11,39}\) are already complete, and the age trial has produced its preliminary results.\(^{99,100}\) A trial looking at the treatment of DCIS\(^{61}\) has now been followed by a second study and a major audit – the ‘Sloane’ project.

14.2 Treatment and other trials

Beyond this, however, a depth of research has come out of the screening programme that has developed knowledge in other areas of screening activity and about the treatment of breast cancer. The large numbers of women with breast cancer who are all managed according to similar protocols provides an opportunity to acquire knowledge that could not have been acquired by any single unit. This may cover issues such as the BASO II trial of treatment of early invasive breast cancer and also various more professionally specific questions for pathologists or physicists. In addition to this, the psychological effects of screening have been studied, as have factors influencing the decisions that women make about screening.\(^{101,108,111,118-121}\)

14.3 Programme evaluation

The routine statistics produced by the programme are the subject of research activity carried out by the Cancer Screening Evaluation Unit. This has yielded data about the effects of changes in the programme and also about its operation, such as the effect of size of unit on performance.\(^{14,21,42,44,66,68,69}\)

14.4 Research collaboration

The screening programme regularly works with academic institutions to investigate various aspects of breast screening, mammography and the causes and treatment of early breast cancer. This will continue as long as the screening programme operates in order to refine the programme, to take advantage of new knowledge and techniques and to improve the treatment of women with screen detected disease.
15. THE FUTURE

- The future will see continued improvements in the diagnosis and treatment of breast cancer. There may come a time when the mortality rates are so low that the absolute number of lives saved by breast screening becomes smaller and smaller to the point where screening is no longer necessary. For the moment, however, this is not a realisable possibility.

The NHSBSP has, in its 17 year life, undergone a number of changes. It has moved from single view to two view mammography. The majority of films are now double read, and the upper age for invitations has been raised from 64 to 70 years. As technology develops, further refinements of the screening process will, no doubt, be suggested and debated. However, caution should be used because further refinements will most probably bring increasingly marginal additional benefits. Resources may be better spent in extending the age range of the screening programme than in further refining the process for women already served.

The future will, undoubtedly, see continued improvements in diagnosis and treatment. Indeed, there may come a time when, despite the proportionate benefit in terms of the relative risk reduction in mortality remaining the same as in randomised trials, mortality rates and thus the absolute number of lives saved by breast screening may become smaller and smaller. At that point, providing this achievement could be maintained in the absence of screening and its ‘halo effect’, the screening programme might no longer be thought worthwhile. For the moment, however, this is not a realisable possibility, and screening is likely to remain an important tool in the armamentarium against breast cancer deaths for decades to come.
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