6 Breast Cancer

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1 Summary

Breast cancer is the most common cause of death from cancer in women in the UK.

Effective interventions exist:

- population-based breast cancer screening using mammography has been shown to reduce mortality in women aged 50–69 by 25–30%
- breast conservation therapy with post-operative radiotherapy is as effective as mastectomy in prolonging disease-free and overall survival in women with early breast cancer
- adjuvant therapies improve overall survival in women with early breast cancer. After ten years of follow-up adjuvant therapy will have:
  a) prevented ten deaths for every 100 women under the age of 50 treated with chemotherapy
  b) prevented 11 deaths for every 100 women under the age of 50 treated with ovarian ablation
  c) prevented eight deaths for every 100 women over the age of 50 treated with tamoxifen.

Ineffective interventions exist:

- there is no evidence to support the use of routine investigations to detect asymptomatic metastases in the follow-up of women with breast cancer.

The National Health Service Breast Screening Programme (NHSBSP) provides a co-ordinated mammographic breast cancer screening service for women aged between 50–64 years. Issues of relevance to purchasers include:

- the age limits for screening
- the interval between screens.

The diagnosis and treatment of women with breast cancer is often variable. Issues of relevance to purchasers include:

- paucity of information on hospital activity and costing information
- variations in provision leading to sub-optimum care or resulting in inefficient services
- the recommendations of the Report of the Expert Advisory Group on the Commissioning of Cancer Services.

Areas of current research which could have major resource implications for purchasers include:

- primary prevention with tamoxifen
- predictive genetic testing
- annual screening of women aged 40–49
- changes in the indications for chemotherapy in women with early breast cancer
- high-dose chemotherapy with autologous bone marrow treatment.

2 Statement of the problem

Breast cancer is a major public health problem. It is a significant cause of mortality and morbidity and is a national target area in the Government's Health Strategy The Health of the Nation.[1] The Expert Advisory Group on the Commissioning of Cancer Services has recommended the establishment of breast cancer units situated in local trusts for the diagnosis and treatment of breast cancer.[2] Therefore the optimum configuration of services for women with breast cancer must be a prime concern for NHS purchasers.

Scale of the problem

One in 12 women in England and Wales will develop breast cancer during their lifetime. England and Wales have the highest mortality rates for breast cancer in the world.[3] The number of years of life lost in women below the age of 65 is higher for breast cancer than for coronary heart disease.[4]

Strategies to reduce breast cancer mortality and morbidity

There are no proven primary preventive strategies.

Small localized breast cancers have a favourable prognosis.[5] Mammography can be used as a screening test in population settings to detect asymptomatic breast cancers.[6] The NHSBSP aims to reduce mortality from breast cancer by regularly screening women aged 50–64 in order to identify such lesions.[7]

Effective interventions exist for the treatment of women with early breast cancer.[8,9]

Resource consequences

Breast cancer services consume substantial resources. The NHSBSP costs £29 million per annum.[10] Women with breast cancer account for almost 1% of inpatient admissions.[11]

Health care professionals and organizations involved in breast cancer services include family health services authorities (FHSAs), primary health care teams, public health physicians, health promotion officers, surgeons, radiologists, radiographers, breast care nurses, pathologists, medical and clinical oncologists, psychiatrists and palliative care teams. Voluntary agencies and social services provide information, psychosocial care and practical support.

Male breast cancer

Male breast cancer is rare accounting for less than 1% of new diagnoses of breast cancer.[12] Treatment strategies reflect those recommended for women.[13] It is not considered further.

Classification

Appendix I lists the relevant coding classifications related to breast cancer.

Summary

The key issues for purchasers are:

- breast cancer is a significant public health problem
- health gain can be maximized through early detection and appropriate clinical management
- there are major resource implications relating to screening, diagnosis and treatment.

3 Sub-categories

There are four main sub-categories of women accessing breast cancer services:

1 women attending the NHSBSP
2 women with a family history of breast cancer
3 women presenting for assessment of symptoms suggestive of breast cancer
4 women requiring treatment for breast cancer.

Women attending the NHSBSP

The NHSBSP invites all women aged between 50–64 years for breast screening at intervals of three years and is responsible for the assessment and diagnosis of mammographically detected abnormalities.

Family history of breast cancer

Women with a first degree relative with breast cancer have a two- or three-fold increased risk of developing the disease. If two or more relatives are affected the risk of breast cancer may be more than ten-fold that of the general population.[14]

Women presenting with symptoms of breast cancer

The most common presenting symptom is a painless lump. Other symptoms include skin dimpling, bloody discharge from or retraction of the nipple.

A third of all women attending surgical outpatients with a breast-related problem will have a painless breast lump of whom one in eight or nine will have a breast cancer.[15,16,17]

Women with breast cancer

Women with breast cancer can be allocated to one of five clinical staging groups according to the extent the disease has spread at time of presentation (Appendix II). When discussing treatment strategies it is more useful to collapse these into three subgroups:

1 women with ductal carcinoma *in situ* (DCIS), Stage 0
2 women with early breast cancer, Stages I and II
3 women with advanced breast cancer, Stages III and IV.

The distribution of these subgroups in two population-based series of women with breast cancer is outlined in Table 1.

Table 1: Distribution of subgroups of women with breast cancer

	Number of women (%)	
	Wessex[18]	**East Anglia**[19]
1 DCIS	7.3	5.6
2 Early breast cancer	77.0	75.2
3 Advanced breast cancer	15.8	19.2

Ductal carcinoma in situ[20,21]

Ductal carcinoma *in situ* may present as a palpable mass or an asymptomatic mammographic abnormality. It is distinguished from invasive disease by the absence of stromal invasion on histological examination.

The natural history of DCIS has not been adequately clarified. The risk of invasion is not precisely known but there is some evidence that it varies with subtype of DCIS.

Early breast cancer

The majority of women with breast cancer present with early stage disease. Early breast cancer is confined to the breast tissue with or without local spread to axillary lymph nodes on the same side as the tumour. These breast cancers are amenable to local surgical intervention.

The most common invasive breast cancers are infiltrating ductal carcinoma (75% of all invasive tumours) and lobular carcinoma (10–15%). These tumours commonly metastasize to axillary lymph nodes.[22]

Other less common histological types include tubular, mucinous and medullary carcinomas. These are generally associated with a better prognosis.

Advanced disease

Advanced disease includes locally advanced disease and distant metastases.

Locally advanced disease may invade the chest wall and/or overlying skin and involved lymph nodes may be fixed to or invade other structures.

Distant metastases occur most frequently in bone, skin, liver and lung.[23]

4 Prevalence and incidence

Incidence, mortality and survival are used to describe the impact of cancer in a population.

Regional cancer registries collect information on all new cancers occurring in their population and these data are used to estimate incidence rates (the number of new cases per 100 000 population per year). Mortality rates are derived from information contained within death certificates but these have often been shown to be both incomplete and inaccurate.

The incidence of cancer increases with age. In order to compare different populations it is necessary to allow for differences in the age structure. This process is called age standardization and the measure derived the age standardized incidence rate. Directly standardized incidence rates are calculated by applying local rates to a notional (standard) population, e.g. World Standard Population or European Standard Population.

Population based survival rates are derived from matching death registrations with cancer registrations and are expressed as a proportion of patients alive at some defined point subsequent to the date of diagnosis. The 'relative' survival rate allows for deaths from other causes among the population under study and is calculated as the ratio of crude survival to that which would be expected given the general mortality experience of England and Wales.

It is conventional to quote five-year relative survival rates as it is frequently assumed that a person surviving five years from the time of diagnosis is cured. However women with breast cancer may develop local recurrence or distant metastases many years after initial diagnosis and conversely, some women with metastases may survive longer than five years.[24] Therefore it may be more appropriate to report ten-year survival rates.

International and temporal comparisons of population based data sets should be interpreted with some caution due to possible variations in the definition of disease status and the completeness of ascertainment of cases and deaths.

Incidence and mortality

Breast cancer is the most common cause of cancer in women in England and Wales. In 1989 there were 27 768 new registrations of breast cancer[12] and the age standardized incidence rate for England and Wales was 68.2 per 100 000. In 1992 13 663 deaths were attributed to breast cancer.[25]

Breast cancer incidence increases with age (Appendix III). Three-quarters of all registrations occur in women aged over 50 and a third in the age group eligible for screening.

Although nearly 90% of breast cancer deaths occur in women aged over 50 years, it is the most common cause of death in women under 50.

Regional health authorities (RHAs) in Southern England have the highest incidence and mortality rates in the UK.

Temporal trends in incidence and mortality

There has been a steady increase in the incidence of breast cancer over the last two decades (Figure 1). The largest increase has occurred in women aged 50–64 and although recent changes in this age group can be attributed to the NHSBSP the incidence was increasing even before the introduction of screening.[26] It has been suggested that secular changes in the incidence of breast cancer may be due, in part, to changes in the distribution of known risk factors for breast cancer e.g. late age at first pregnancy, early menarche and prolonged use of oral contraceptives.[27]

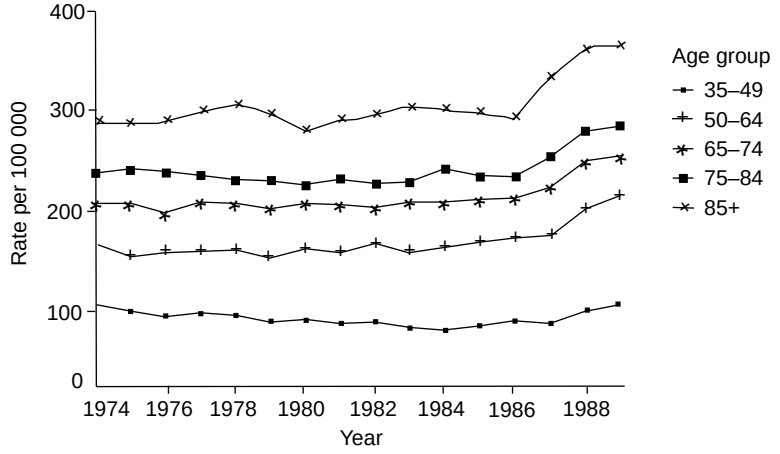

Figure 1: Temporal trends in age-specific incidence rates of breast cancer in England and Wales 1974–89.
(Source: OPCS Series MB1.)

There has also been an increase in registrations of DCIS following the introduction of screening (Figure 2).[25] DCIS accounts for 20% of screen-detected tumours.

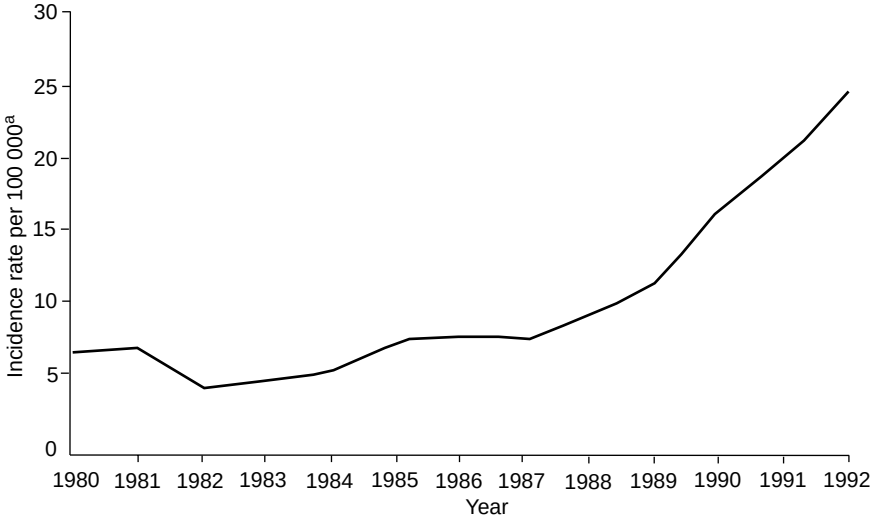

Figure 2: Temporal trends in incidence of *in situ* breast cancer in women aged 50–64 in the UK 1980–92.
[a] Standardized to the 1980 population.
(Source: Regional Cancer Registries.)

All ages mortality rates which rose during the 70s and early 80s have begun to decline in the late 80s and 90s[28] (Figure 3). This decrease predates any impact on mortality that might be expected following the introduction of the NHSBSP.[29]

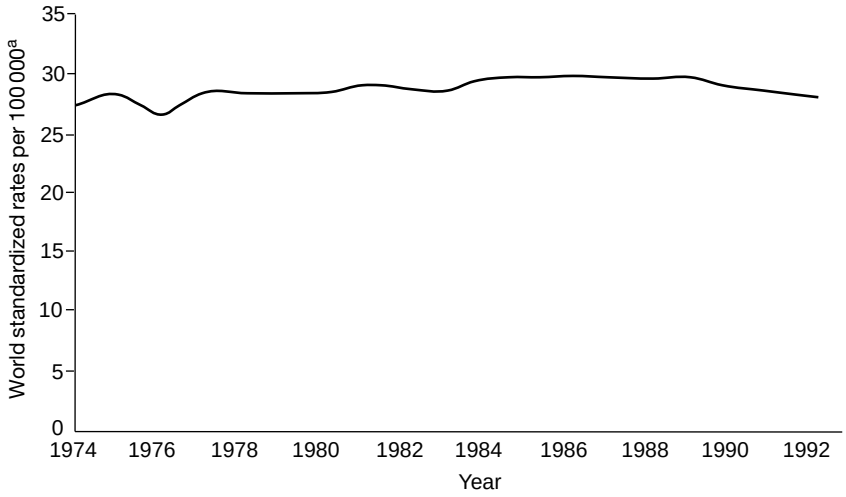

Figure 3: Temporal trends in mortality from breast cancer in England and Wales 1974–92.
[a] Standardized to world population (3 point moving averages).
(Source: OPCS Statistics Series DH2.)

Survival

The relative survival rate for breast cancer has been reported as 63% and 53% at five and ten years respectively.[30] It decreases with age in women over 40 (Figure 4).[31]

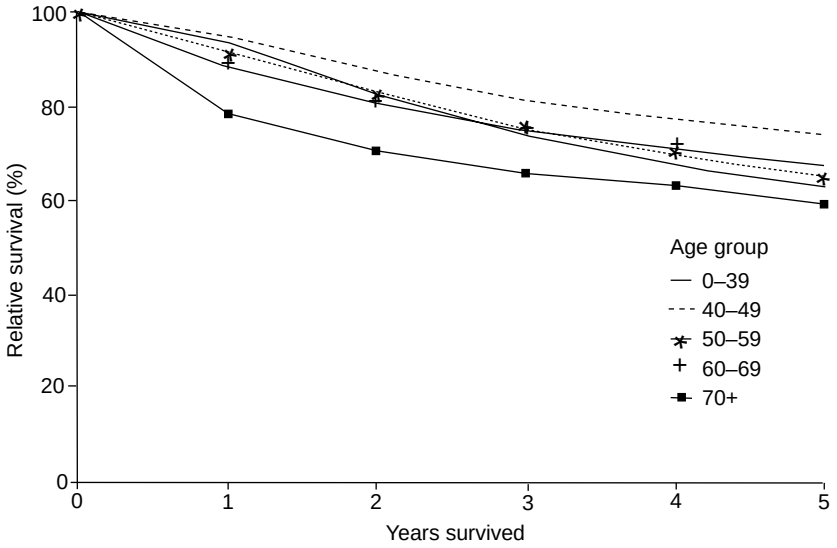

Figure 4: Relative survival rates for breast cancer by age group.
(Source: North Western Regional Cancer Registry.)

International and inter-regional variations in five year relative survival rates are shown in Figure 5 (see page 371).[31–38]

The extent of disease at presentation is an important prognostic indicator. Ten-year relative survival rates for women with no metastases, women with axillary node metastases but no distant metastases and women with distant metastases at presentation have been reported as 65%, 40% and 8% respectively.[30]

In early breast cancer the number of diseased axillary nodes is the most important predictor of recurrence. Large or high grade tumours (WHO pathological grade 3) have a poorer prognosis even in the absence of axillary node metastases.[5,39,40]

5 Service provision

This section describes the current level of provision of breast cancer services. Evidence of the effectiveness and efficiency of specific interventions is discussed in section 6. Palliative care services are not discussed.

The National Health Service Breast Screening Programme

The NHSBSP commenced in 1987. The programme aims to reduce mortality from breast cancer by screening women between the ages of 50 and 64 every three years.[6] The programme has benefited from clear central policy guidance, 'earmarked' funding and a strong quality assurance (QA) structure.[7]

National structure

A national co-ordinating body, with a national co-ordinator, was established at the inception of the NHSBSP. Its role includes training, QA and information systems. Policy and professional advice is supplied by a Department of Health Advisory Committee. Networking and advisory bodies, 'the Big 18s', have been established for the major disciplines within the programme including radiologists, surgeons, pathologists, radiographers, nurses, administrators, regional co-ordinators and QA managers. Each has representation from all RHAs in the UK; the health boards of Wales, Scotland and Northern Ireland and the private sector. There is a National Project Board for information systems.

Regional and district structure

Regional health authorities were responsible for the revenue costs of screening centres. Subsequent to changes in the structure of RHAs, the purchase of screening services became the responsibility of purchasing authorities in 1995.

Regional health authorities were required to nominate a QA manager and establish a QA reference centre to co-ordinate all aspects of the QA programme. The QA team includes a professional co-ordinator from each of the main groups contributing to screening i.e. radiology, radiography, pathology, surgery, nursing, administration and medical physics. Quality assurance was devolved to lead purchasing authorities in 1996.

Local purchasers and providers are required to offer a three-yearly mammographic screening programme and to attain national QA standards.

Quality assurance includes the following functions:

- standard setting (Appendix IV)
- monitoring progress towards meeting these standards
- providing professional advice e.g. QA guidelines for pathologists[41] and medical physics[42]
- co-ordinating professional QA schemes and ensuring they are in place
- local initiatives.

Setting

Breast screening and assessment of screen-detected abnormalities should be undertaken in specifically dedicated centres.

Breast cancer screening involves a core team of radiologists, radiographers, surgeons, pathologists/cytologists and administrative and technical support staff. Primary health care teams, the FHSA, breast care nurses and health promotion officers contribute to the acceptability and uptake of breast screening.

A screening centre is responsible for providing primary mammographic screening and assessment facilities to a defined population. A screening centre consists of the following.

- **Screening office** This is the administrative unit responsible for liaising with FHSAs, inviting eligible women for primary screening, informing women and general practitioners (GPs) of results and recalling women with abnormal mammograms for assessment.
- **Primary mammographic screening unit(s)** There may be one or more units per centre located on permanent sites or on mobile vans. Over 80% of screening centres have a mobile van.[43]
- **Assessment unit(s)** Women with abnormal mammograms are requested to attend for further assessment. This may involve clinical examination, further mammograms and/or ultrasound. Fine-needle aspiration cytology (FNAC) and/or excision biopsy may be undertaken to provide pathological confirmation prior to definitive surgery. Assessment should be by a multi-disciplinary specialist breast team including a radiologist, surgeon and pathologist/cytologist.

Screen-detected lesions may be palpable or impalpable. Impalpable lesions present specific assessment problems and may require the use of stereotactic equipment or ultrasound to guide FNAC. Mammography or ultrasound is required to aid localization of the tumour for excision. The excised area should be imaged to identify completeness of excision of the tumour prior to pathological assessment.

Utilization

There are nearly 4 000 000 women eligible for breast screening and 79 screening centres in England. Wales has its own breast screening programme: Breast Test Wales. In 1993/94, 960 678 women aged 50–64 attended for screening.[44]

The Forrest Report recommended that a single assessment team should cover an eligible population of 41 150 women (one million population) in order to maintain sufficient multi-disciplinary expertise in both the assessment of mammographic abnormalities and the management of screen-detected cancers.[6]

There are 93 assessment units in England and Wales. Geographical access, population density and local purchasing decisions account for eligible populations ranging between 12 000 (Isle of Wight) and 130 000 (Greater Manchester).[43]

Funding of the service was based initially on three-yearly recall and the use of single-view mammography (oblique view).[6] All screening centres are now expected to provide two-view mammography (oblique and craniocaudal views) in the prevalent round.[45]

Family history of breast cancer

A family history of breast cancer is given by 20% of all women with breast cancer. An increasing demand for information on individual risk has been reported among young women with a family history.[46]

There has been a stream of experimental work aimed at characterizing and identifying genes responsible for breast cancer. The BRCA1 and BRCA2 genes are likely to cause the vast majority of genetically

determined cases. One to six per 1000 women may carry BRCA1 or BRCA2 genes.[47] The BRCA1 gene has recently been cloned and with this comes the possibility of predictive genetic testing for carrier status.[48] However only 5% of all breast cancer cases are associated with highly penetrant dominant genes.[46]

Setting

Risk counselling is currently provided by GPs, clinicians and an increasing number of specialist genetic clinics. There are 18 such clinics in the UK.[49]

Site specific, familial breast cancer clinics are an alternative to general genetic clinics. These are multi-disciplinary involving surgeons, geneticists, radiologists and specialist nurses. They offer advice on individual risk, clinical examination, teach breast self awareness and may offer specific preventative interventions.[50]

Utilization

The Regional Family History Cancer Clinic based at the Royal Free Hospital saw 851 women between March 1988 and September 1990.[51] 58% of women attending were self-referrals. Of those seen 97% had a risk greater than that of the general population and 23% a specific familial breast cancer syndrome. The compliance rate among those offered screening was 83%.

Symptoms of breast cancer

Services for women presenting outside the screening service are often poorly co-ordinated. It is suggested that the symptomatic service should emulate the multi-disciplinary approach of the NHSBSP.

Setting

The majority of symptomatic women will initially attend their GP and be referred either to a general surgeon, a surgeon with an interest in breast diseases or a surgeon specializing in breast diseases.

Women may be seen in general surgical outpatient clinics, dedicated breast clinics or rapid diagnosis (one-stop) clinics. Rapid diagnosis clinics offer women consultation, investigation and diagnosis on the same day.

Diagnostic services include:

- breast imaging by mammography and/or ultrasound
- pathological assessment by FNAC, tru-cut biopsy and/or excision biopsy.

Some women will present with symptoms suggestive of metastatic breast cancer and require liver scans, bone scans and/or computed tomography (CT).

Utilization

Each year, one in 50 women consult their GP with a breast problem and approximately one in three of these are immediately referred for a surgical opinion.[52–54]

An audit of outpatient surgical workload in two provider units estimated that breast problems account for 20% of all new general surgical outpatient referrals and over 40% of follow-up visits.[17] One in five of the

women referred did not require any investigation and an eighth of new referrals were diagnosed with breast cancer.

Women with breast cancer

The objectives of clinical management vary with the extent of the disease (Table 2).

Table 2: Objectives of clinical management

Subgroup	Objectives
DCIS	Local control of disease
Early breast cancer	Locoregional control Prolongation of disease-free and overall survival
Locally advanced breast cancer	Local disease control In some women, prolongation of overall survival
Metastatic breast cancer	Palliation

Ductal carcinoma *in situ*

Surgical management, mastectomy or breast conservation therapy (BCT), aims to achieve local control.[55] Mastectomy is the removal of the breast with some overlying skin, usually including the nipple, from the chest wall muscles. BCT involves either wide local excision (WLE), removal of the tumour with a 1 cm margin of normal tissue, or quadrantectomy, when a whole quadrant of the breast is excised.

Early breast cancer

Clinical management in women with early breast cancer aims to achieve locoregional control of disease and prolongation of disease-free and overall survival.[22]

Primary surgical treatment may be by mastectomy or BCT with post-operative radiotherapy. Axillary lymph nodes are surgically excised for pathological assessment. Disease in the axillary lymph nodes is treated by surgery or radiotherapy.[56]

Pathological assessment of the tumour and lymph nodes identifies women who would benefit from adjuvant therapy. Adjuvant therapy is administered with the aim of prolonging survival. Adjuvant therapies include chemotherapy, tamoxifen and ovarian ablation.

Ovarian ablation is the destruction of the hormone releasing function of the ovaries by surgery, radiotherapy or gonadotrophin releasing hormone analogue. Only the latter is reversible.

Women undergoing mastectomy require reconstructive surgery or breast prostheses. Reconstructive surgery may be undertaken at the time of the primary surgery or as a delayed procedure.[57,58]

Advanced breast cancer

Treatment strategies for locally advanced disease primarily aim to control local disease and include surgery, radiotherapy and systemic therapy.[59,60] In some women treatment also aims to prolong overall survival.

The management of women with disseminated breast cancer is palliative and aims to ameliorate and control distressing symptoms. Treatments include systemic therapy (chemotherapy or hormone therapy) and radiotherapy.

Approximately 40–70% of women with disseminated disease receive radiotherapy to relieve pain from bone metastases.[61] Orthopaedic intervention may be required to prevent fractures of the long bones or spine.

Setting

The needs of women with breast cancer extend beyond medical care. The clinical, social and psychological management of women during their illness requires a co-ordinated, multi-disciplinary approach involving surgeons, pathologists, clinical and medical oncologists, breast care nurses, psychiatrists, primary health care teams and other agencies from the statutory and voluntary sector.

Women with breast cancer are treated in acute provider units and/or specialist cancer hospitals. Surgery may be undertaken by general surgeons or surgeons interested in or specializing in breast diseases. Reconstructive surgery may be performed by breast surgeons with specific training or plastic surgeons. Pathologists with expertise in the assessment of the pathology of the breast are an essential component of the clinical team.

Breast care nurses can identify significant psychological morbidity,[62] provide information and advice on treatment options and fit breast prostheses.[63] Breast care nurses work within the acute care sector and/or the community.[64]

Radiotherapy requires specialist equipment and women needing radiotherapy are referred to a clinical oncologist in a specialist cancer centre.

Women requiring systemic therapy, e.g hormone therapy or chemotherapy, are usually referred to clinical or medical oncologists in specialist hospitals. Chemotherapy is also administered in acute provider units but this is not always under the guidance of an oncologist.[65]

The majority of women with breast cancer are followed-up after treatment by surgeons or oncologists. Schedules vary but typically may be once every three months for the first two years, every four months for the third and fourth year and then biannually. Women with advanced disease may be followed-up more frequently.

Utilization

Women with breast cancer accounted for 1% of all hospital episodes (46 008 admissions and 17 167 day cases) in the UK during 1991/92. The average length of stay was 8.3 days.[66]

Surgical

10 036 mastectomies (OPCS IV B27: total excision of the breast) and 13 036 BCTs (OPCS IV B28 other excision of the breast (excluding biopsies)) were undertaken for breast cancer. Almost 10% of BCT was performed as day cases.

These statistics should be interpreted with caution. Episodes relate to operations and not women; a woman may have more than one operation either because of bilateral disease or because of incomplete excision of the tumour.

Table 3 suggests there has been an increase in the frequency with which BCT is performed and this may, in part, be attributable to more small cancers detected by the NHSBSP.

It is not possible to identify the current level of breast reconstructive surgery from data collected routinely. Breast reconstructive surgery is not uniformly available in the NHS but an increase in demand from women undergoing mastectomy has been reported.[57]

Table 3: Temporal trends in operative procedures for women with breast cancer

Year	Mastectomy no. of episodes	BCT no. of episodes (% day case)	Ratio of mastectomy: BCT
1991/92	10 036	13 036 (9.4)	1:1.3
1990/91	9284	11 744 (8.0)	1:1.26
1989/90	9001	10 332 (7.7)	1:1.24

Specialist services

The majority of the 218.4 wte clinical and medical oncologists are based in specialist cancer centres.[67] There are 45 such centres in the UK.[68]

The trend toward greater use of BCT compounded by increased detection of small tumours by the NHSBSP will have a substantial impact on radiotherapy workload.[30,69]

Breast care nurses

In 1991 there were 170 breast care nurses employed in symptomatic and/or screening services in England and Wales.[64]

Summary

The key issues for purchasers are:

- quality assurance of the NHSBSP which was devolved to lead purchasers in 1996
- the investigation and treatment of women with breast cancer should be multi-disciplinary.

6 Effectiveness and cost-effectiveness

National Health Service Breast Screening Programme

Evidence of efficacy

Evidence accrued from randomized controlled trials (RCTs) suggests that mammographic screening can reduce mortality from breast cancer by between 25% and 30% in women aged 50 to 69.[70,71] There is insufficient evidence on the efficacy of screening in women over 70 as most trials had an upper age limit of 69.

Randomized controlled trials have failed to demonstrate a significant mortality reduction from the use of mammography in women aged 40–49 but none of these trials were designed to test this specific hypothesis and insufficient numbers in this age group were recruited. The sensitivity of mammography is lower in younger women. Tumours in this age group may be faster growing[72] and therefore younger women may benefit from more frequent screening. The benefit of annual screening in a cohort of women aged 40–41 at recruitment is currently being examined in a RCT (the UKCCCR Age Trial).

There is as yet no evidence of the efficacy of breast self-examination as a population-based screening test[73] but an intervention trial is ongoing in Russia.[74]

Costs

£55 million was initially invested by the Department of Health in establishing the NHSBSP with an additional £16 million developmental costs contributed from regional funds.[7]

In 1993 the revenue costs of the screening programme were £29 million: 90% was allocated for the purchase of breast screening by health authorities, £2 million to regional QA and the remainder to training and national initiatives including the national co-ordinating team.[10]

The Forrest Report calculated the cost-effectiveness of a breast screening programme using information from the Swedish Two Counties and Health Insurance Plan (HIP) trials and assuming:

- a 70% uptake of screening
- a three-year screening interval
- the use of single-view mammography.[6]

The estimate of £3500 per life–year saved (1983/84 prices) compared favourably with the cost-effectiveness of other health service interventions e.g. cervical screening and coronary artery bypass grafts.

Clarke *et al*. calculated the cost-effectiveness of breast screening using data from the Edinburgh Trial assuming a 70% compliance and a three-yearly screening schedule.[75] Their estimate of £8638 per life–year saved (1989 prices) was more than double the Forrest Report estimate. This difference may be due to the poorer outcome of the Edinburgh Trial compared to the Swedish Two Counties and HIP trials and to the inclusion of treatment costs in the calculation.

Family history of breast cancer

The management of young women with a family history of breast cancer remains problematic. Mammographic screening in this setting is of unproven value.

Prophylactic mastectomy is reserved for women with high risk of breast cancer but its psychological morbidity is unknown. Subcutaneous mastectomy leaves the overlying skin and nipple intact. It may give better cosmetic results but residual breast tissue can potentially undergo malignant change.

Women presenting with symptoms of breast cancer

Current opinion supports a combined modality approach in the assessment of symptomatic women.[76,77] This 'triple assessment' includes clinical examination, breast imaging (mammography and/or ultrasound) and either cytological (FNAC) or histological (tru-cut biopsy) assessment. Triple assessment aims to improve cancer detection rates while limiting the number of unnecessary surgical interventions. However in the presence of clinical uncertainty an excision biopsy is still considered mandatory. Inevitably improvements in sensitivity can only occur at the expense of reduced specificity.

The various estimates of sensitivity and specificity of diagnostic procedures are mainly derived from retrospective analyses (Table 4). The biases introduced by operator competence or experience and case selection may account for the wide variation in reported results.

Although excellent results from FNAC have been reported in some series, a recent review of 9533 consecutive FNACs suggests that results are heavily operator dependent; inadequate rates varied between 6–50% among 31 operators.[84] Errors in reporting may also reduce the effectiveness of FNAC.[85]

Rapid diagnosis (or one-stop) clinics have been introduced following concerns over diagnostic delay and frequency of hospital visits.[86] The costs and benefits of these clinics have not been assessed. Any change in the organization of services has implications for other aspects of the service. Potential disadvantages of rapid

Table 4: Sensitivity and specificity of diagnostic procedures[76–83]

Diagnostic procedure	Sensitivity (%)	Specificity (%)
Clinical examination	86–92	71–90
FNAC	79–99	93–100
Mammography	61–94	55–90
Ultrasound	82–97	84–95
Triple assessment		
clinical examination, FNAC and mammography	93–100	53
clinical examination, FNAC and ultrasound	100	61

diagnosis clinics include relaxation of referral criteria by GPs and increased psychological morbidity secondary to an expedited diagnosis of malignancy.

Routine use of bone, liver or CT scans to detect asymptomatic metastases is not recommended. Detection rates are low and false-positive rates high (7–9% and 22% respectively for bone scans).[87]

Women with breast cancer

Clinical management of DCIS

Mastectomy will cure 98–100% of women with symptomatic DCIS.[55]

Screen-detected asymptomatic DCIS is usually small and localized and there has been a marked shift towards the use of BCT to treat these lesions. However recurrences following BCT are common. In one series 25% of women had recurrences at ten years of which half were invasive.[88] There is increasing interest in identifying those subtypes of DCIS more likely to recur following BCT.[89]

The efficacy of post-operative radiotherapy and adjuvant hormone therapy in reducing recurrence rates following BCT is unproven. A randomized controlled trial under the auspices of the UKCCCR is currently evaluating the use of radiotherapy and/or tamoxifen in preventing subsequent invasion following wide local excision of DCIS.

It is generally considered unnecessary to sample axillary lymph nodes unless disease is extensive or multifocal.

Clinical management of early breast cancer

Clinical management of early breast cancer has four components:

1 primary treatment of the breast and axillary lymph nodes to gain locoregional control of disease
2 pathological staging to direct decisions on adjuvant therapy
3 adjuvant therapy to prolong disease-free and overall survival
4 routine follow-up.

Primary management – surgical treatment

Randomized controlled trials comparing BCT, axillary node dissection and post-operative radiotherapy with total mastectomy and axillary node dissection have demonstrated similar local recurrence-free and overall survival rates (Table 5). Breast conservation therapy is not always considered suitable for women with multifocal disease, large tumours, small breasts or when disease is beneath the nipple.

Table 5: Comparison of results from randomized controlled trials comparing mastectomy and breast conservation therapy

	Fisher *et al.*[90] Follow-up eight years (%)	Lichter *et al.*[91] Follow-up eight years (%)	Veronesi[8] Follow-up ten years (%)
Mastectomy			
disease-free survival	58	76	–
overall survival	71	79	76
BCT			
disease-free survival	59	78	–
overall survival	76	85	79

Primary management of the axilla

Treatment of the axilla, either by surgery (axillary node dissection or clearance) or by radiotherapy is effective in maintaining local control of disease.[92] However there is no convincing evidence of the superiority of any one of these modalities. Side-effects include lymphoedema, limited shoulder movement and inadvertent damage to the brachial plexus. There is some evidence that surgery and radiotherapy combined may increase side-effects without any additional benefit.[93]

Primary management of radiotherapy

Radiotherapy after BCT improves disease-free survival.[94] Routine post-operative radiotherapy following mastectomy has been shown to increase deaths related to cardiac causes.[95] However an updated overview of RCTs comparing survival following mastectomy alone with survival following mastectomy and post-operative radiotherapy has demonstrated that excess cardiac deaths may be offset by a reduction in breast cancer deaths and suggests a small but non-significant advantage from post-mastectomy radiotherapy after ten years of follow-up.[96]

Radiotherapy fractionation schedules for radical treatment following BCT vary in length between three to six weeks.[97] The cost per fraction of radiotherapy varies between £22 and £58.[98,99]

Pathological staging

Adequate pathological staging of early breast cancer is essential to direct adjuvant therapy. Both the tumour and axillary lymph nodes need to be assessed:

1 **assessment of tumour specimen** The histological type, grade and size of tumour provide important prognostic information. Incomplete excision of tumour may necessitate further operative intervention or radiotherapy.
2 **assessment of axillary lymph nodes**[56] Clinical examination is unreliable. Therefore surgical excision of axillary lymph nodes for pathological examination is essential. It is generally agreed that at least four lymph nodes should be available for examination to exclude metastases.

Surgical dissection or clearance, undertaken as part of the primary surgical treatment, usually provides sufficient lymph nodes to stage the axilla but the use of less radical axillary node sampling may reduce operative side-effects.[100] Two small RCTs have demonstrated that well performed axillary sampling is as effective as axillary dissection or clearance in obtaining sufficient lymph nodes for pathological assessment.[101,102] There is some concern that the excellent results of these trials may not be reproducible in all clinical settings.[103]

Adjuvant therapy

A meta-analysis of worldwide trials investigating adjuvant therapy in early breast cancer has produced imposing evidence of the effectiveness of these treatments in improving overall survival. The overview included 133 randomized trials involving 75 000 women.[9] Its conclusions were as follows.

- Tamoxifen
  a) tamoxifen therapy is effective in reducing recurrence and death from breast cancer particularly in women over 50 years of age
  b) tamoxifen therapy lasting at least two years is more effective than shorter term regimens.
- Chemotherapy
  a) chemotherapy is effective in reducing recurrence and death from breast cancer particularly in women under the age of 50
  b) women over 50 respond less well to chemotherapy
  c) chemotherapy regimens involving more than one drug are more effective than those involving single-agent drugs. Cyclophosphamide, methotrexate and fluorouracil (CMF) regimens were studied most often
  d) long-term courses (more than six months) do not confer any additional survival benefit.
- Ovarian ablation
  a) ovarian ablation is effective in reducing recurrence and death from breast cancer in women under 50.

Table 6 illustrates some of the results of the World Overview.[9,104] Estimates of effect are presented as annual odds of death. This is the probability of dying during a year divided by the probability of surviving the year. This can be translated into an absolute benefit and presented as the number of deaths prevented at ten years of follow-up per 100 women treated.

Table 6: Results from the Worldwide Overview of Adjuvant Trials

Adjuvant therapy	Reduction in annual odds of death (%)	Number of deaths prevented per hundred women treated at ten years of follow-up
Tamoxifen in women over 50 years	20	8
Chemotherapy in women under 50 years	25	10
Ovarian ablation in women under 50 years	28	11

Adjuvant therapy in women under 50

The use of adjuvant chemotherapy in premenopausal women is of proven value. Currently consensus opinion supports its routine use in women with node-positive disease.[105]

The absolute and relative benefit of multi-agent chemotherapy is greater in node-positive than

node-negative women. The improvement in overall survival at ten years for node-positive women of all ages was 6.8% (46.6% vs 39.8%) compared to a 4% improvement in node-negative women (67.2% vs 63.2%).[9]

Treatment costs for node-positive premenopausal women receiving chemotherapy are between $4900 per quality adjusted life year (QALY) and $9200/QALY dependent on other risk factors (1989 prices).[106] Chemotherapy for node-negative premenopausal women costs $15 400/QALY (1991 prices).[107]

There are subgroups of high risk, node-negative women in whom chemotherapy may confer substantial survival advantage.[108] Many clinicians support adjuvant chemotherapy in node-negative women with high grade or large tumours.[39,108,109] Only one study has directly compared the effectiveness of chemotherapy and ovarian ablation in the management of premenopausal node-positive women.[110] It did not show a significant difference in survival but the power of the study was low and could not exclude a difference of 10%.

The Nottingham Prognostic Index combines information on several tumour characteristics to aid decisions on the requirement for adjuvant therapy.[111] Other prognostic indicators such as Cerb B2 oncogene, Capthesin D and S phase fraction have been suggested[39,112] but there is no evidence that these contribute sufficient additional prognostic information to support their use in routine clinical practice.

Adjuvant therapy in women over 50

The World Overview suggests that tamoxifen should be considered for node-positive and node-negative women over the age of 50.

Oestrogen and progesterone receptor status may be used to predict response to tamoxifen and other hormone therapies.[39] However even postmenopausal women with oestrogen receptor-poor tumours have a small but still significant survival advantage conferred by tamoxifen.[9]

The overview suggests that combining chemotherapy and tamoxifen (chemoendocrine therapy) may have a greater effect on mortality in women over 50 than tamoxifen alone. This is not based on RCTs directly comparing chemoendocrine therapy with tamoxifen alone but on indirect comparisons using the results of other trials. The results of RCTs of chemoendocrine therapy in postmenopausal women are awaited.

Adjuvant therapy in minimal risk tumours

Small (less than 1 cm) node-negative, low grade or special type (pure tubular or mucinous or papillary) tumours have an extremely good prognosis. They account for approximately 20% of screen-detected lesions.[40] The need for post-operative radiotherapy or adjuvant therapy in these patients[113,114] is being addressed by the British Association of Surgical Oncologists (BASO) II Trial.

Follow-up regimens

Women with early breast cancer may develop local recurrences (9% after ten years) or distant metastases and have a four-fold increased risk of developing cancer in the contralateral breast.[115,116] Post-operative mammographic surveillance is used to detect the following.

1 **Contralateral breast cancer** The increased risk of contralateral breast cancer probably justifies mammographic surveillance in this group of women. However the optimum screening interval is uncertain.
2 **Asymptomatic local recurrences** A difference in overall survival between women with clinically detected recurrences and those with asymptomatic screen-detected recurrences has not been consistently found.[117,118]

The role of post-operative mammographic surveillance needs to be further evaluated.

There is no evidence to support screening for asymptomatic distant metastases during routine follow-up. Two RCTs failed to demonstrate any added benefit, either in overall survival or quality of life, from the routine use of bone scans, liver scans and X-rays.[119,120]

Advanced disease

There are few large RCTs comparing treatment strategies in women presenting with advanced disease and there may be some reluctance amongst clinicians to recruit such patients into trials.[121] There are no trials comparing systemic therapy with supportive care alone in women with disseminated breast cancer and most clinicians would consider it unethical to undertake such a trial.

The mean cost of treating a patient with advanced disease is £7620 (1991 prices).[122]

Locally-advanced breast cancer

It has been suggested that chemotherapy in locally-advanced disease may prolong survival in some subgroups of women but comparisons of chemotherapy and local treatment e.g. surgery or radiotherapy with local treatment alone have produced inconsistent findings. The role of combined chemoendocrine therapy in this setting has not been clarified.[123,124]

Metastatic breast cancer

The management of women with metastatic disease is fairly uniform in the UK. The first-line drug of choice is tamoxifen. Other hormone therapies such as medroxyprogesterone acetate, megestrol acetate, gonadotrophin releasing hormone analogue, aminoglutethemide, androgens and ovarian ablation are used sequentially as breakthrough of disease occurs.[125,126]

Chemotherapy is usually offered when hormones fail. Trials do not demonstrate any benefit of multi-agent chemotherapy over single agent.[127]

High-dose chemotherapy followed by autologous bone marrow treatment or support with haemopoietic factors is used in some centres to treat metastatic disease. There have been no RCTs of this resource intensive treatment and treatment-related mortality is high.[128]

Palliative radiotherapy is useful in the treatment of bone, brain and skin metastases. The average cost per fraction of palliative radiotherapy for bone metastases at Mount Vernon Hospital was calculated to be £37 (1989 prices).[129] Randomized controlled trials have shown that short courses of radiotherapy (one or two fractions) are as effective as longer courses in ameliorating painful bone metastases.[130,131] The shorter regimens potentially represent substantial savings but some radiotherapists are concerned that the 12 week follow-up period of these studies limits their generalizability to breast cancer patients who may survive for several months after treatment. The results of a further RCT with longer follow-up are awaited.[132]

Psychosocial interventions

Psychological morbidity, detectable in 25–30% of women with breast cancer, may have a detrimental effect on treatment compliance.[133] Maguire *et al.* demonstrated in a RCT that a nurse counsellor was successful in identifying psychiatric morbidity in women undergoing mastectomy. Subsequent referral to a psychiatrist resulted in an overall lower level of morbidity in the intervention group a year later.[62] The cost of the nurse

counsellor was offset by savings in psychiatric inpatient care and fewer days off work required by patient and carer.[134]

High levels of psychiatric morbidity have been demonstrated in women who have undergone mastectomy.[135] Women who undergo BCT have a better body image but levels of anxiety are still high.[136,137] Improved psychosexual wellbeing has been associated with breast reconstruction following mastectomy.[138]

There is no firm evidence to support the generally held opinion that offering women a choice of treatment reduces psychological distress. Over half of women with early breast cancer may wish to take a passive role in treatment decisions[139] and the communication style of the doctor may be more important than offering treatment choice.[140] Patients appear to value adequate information on diagnosis and treatment within the context of a caring physician–patient relationship.[141] There has been little formal evaluation of the best way of imparting information and current methods include leaflets, videotapes and written and taped recordings of consultations.[142]

Strength of recommendation

Table 7 summarizes the strength of intervention recommendation.

Table 7: The strength of intervention recommendation

Intervention	Strength of recommendation
Age at screening	
50–64 years	1/a
64–69 years	I/a
<50 years	I/d
>70 years	III/c
Screening interval period less than three yearly	I/b
Two-view mammography	I/b
Breast self-examination	II/c
Diagnostic procedures in assessment	II/b
Pre-operative bone/liver/CT scan	II/e
BCT and radiotherapy	I/a
Adjuvant therapy in early breast cancer	
chemotherapy in women under 50	I/a
ovarian ablation in women under 50	I/a
tamoxifen in women over 50	I/a
Breast care nurse counsellors	I/b
Intensive follow-up regimens	I/e

Key:
I well conducted RCT; II other studies; III opinions of respected authorities based on indirect evidence; a good evidence for acceptance; b fair evidence for acceptance; c poor evidence for acceptance; d fair evidence for rejection; e good evidence for rejection

7 Models of care

Health gain may be maximized through:

- early detection by mammographic screening
- appropriate diagnosis and treatment of women with breast cancer.

National Health Service Breast Screening Programme

Population-based mammographic screening offers the best opportunity of reducing mortality from breast cancer. The cost-effectiveness of the programme will be influenced by the:

- age group invited for screening
- interval between screens
- sensitivity of the test
- compliance.

Age

Despite evidence from RCTs of the efficacy of breast screening in women aged up to 69,[81,82] women aged between 65 and 69 are not routinely invited for screening in this country. There were 12 591 breast cancers diagnosed in women over 65 in 1989.[12]

The Forrest Report suggested that screening would be inefficient in older women due to low compliance.[6] However 61% of Manchester women aged 65–74 responded to an invitation for screening.[143] The cancer detection rate in this population was 11.6 per 1000 screens.

A US economic analysis has shown that raising the screening age to 69 is more cost-effective than only screening women aged 50–64.[144] The model used data derived from the HIP trial and Breast Cancer Detection Demonstration Project and assumed biennial screening with annual clinical examination. A similar evaluation is now underway in the UK.[145]

Screening interval period

The NHSBSP is unique among population-based screening programmes in that the interval between screens is three years. The evidence adduced in support of breast screening effectiveness is mainly derived from trials with shorter screening intervals.

The first population-based report describing the incidence of interval cancers in the NHSBSP revealed that the rate of interval cancers in the third year after screening approaches that which would be expected in the absence of screening.[146] Similar results have been reported from other regional programmes.[147] These suggest that the screening interval may be too long.

The optimum screening interval remains uncertain. The United Kingdom Committee for Co-ordinating Cancer Research (UKCCCR) frequency trial is comparing the benefits of yearly with three-yearly breast screening in a RCT involving 100 000 women. An economic analysis is incorporated in this study.

The cost-effectiveness of screening women aged 50–70 every two years has been shown to be comparable to screening women aged 50–65 every three years. This cost-effectiveness analysis, using a computer simulation model, was based on the results of the Dutch screening programme.[148]

Sensitivity of the test

There are two types of interval cancers; cancers present but not identified on previous screening examinations (false-negatives) or cancers which appear to have arisen *de novo* since the last screening examination (true intervals).

Although not all cancers are detectable by mammographic screening improvement in the sensitivity of the test may identify some cancers which would otherwise have been missed and hence lead to further reductions in the incidence of interval cancers.

It has been suggested that the sensitivity of the screening test can be further improved by optimizing the optical density of the mammographic film,[149] by two radiologists independently reading the mammogram (double reading)[150] and by employing two-view mammography.[151] The NHS Executive has instructed purchasers to fund the first and third of these initiatives.[55]

A RCT suggests that two-view mammography may increase the cancer detection rate in the prevalence round of screening.[152]

Compliance

Programme effectiveness will be adversely effected by low compliance.[153] Factors which may influence compliance include the following.

- **Accuracy of FHSA registers** One of the main reasons for non-attendance at screening is non-invitation due to inaccuracies in the FHSA database.[154]
- **Method of invitation** RCTs have demonstrated that invitation policy can influence compliance. Williams and Vessey demonstrated the superiority of pre-allocated appointments[155] and others have shown the effectiveness of personalized letters of invitation.[156]
- **Accessibility of primary screening facilities** The location of the screening unit may affect uptake.[157] A survey of the Lothian mobile unit in 1988 showed that it cost women 89 pence for every mile travelled to attend for screening and that 'access costs' were directly associated with the uptake of screening.[158]
- **Acceptability of screening** There is no evidence that the screening programme increases psychological morbidity among women invited for screening.[159,160] 90% of screened women will re-attend for further screening; women who do not are more likely to view the previous experience of screening negatively.[161] The majority of women with screen-detected abnormalities will have a benign diagnosis (false-positive). These healthy women undergo unnecessary investigation and occasionally treatment with the possibility of resultant physical and psychological morbidity.[162] Therefore it is important to keep the false-positive rate low. Concerns have been expressed about uptake among ethnic minorities. A RCT of pre-screening visits from linkworkers failed to demonstrate a beneficial effect on subsequent uptake of invitation.[163]

There is a need for more intervention trials of strategies designed to improve uptake, particularly amongst those reinvited for screening.

Diagnosis and treatment

The appropriate management of women with early breast cancer offers additional opportunities to reduce mortality and morbidity.

Variations in quality of care

Comparison of international and inter-regional relative survival rates for breast cancer have raised concerns over poor treatment outcomes in this country (Figure 5). A number of studies suggest that some women in the UK may be receiving less than optimum care.

Chouillet *et al*. found that of 334 women with breast cancer resident in four RHAs and treated in 81 hospitals, only 46% had undergone axillary node surgery and only 47% of premenopausal women had received chemotherapy.[164] The study predated the World Overview of randomized trials of adjuvant therapy.[9]

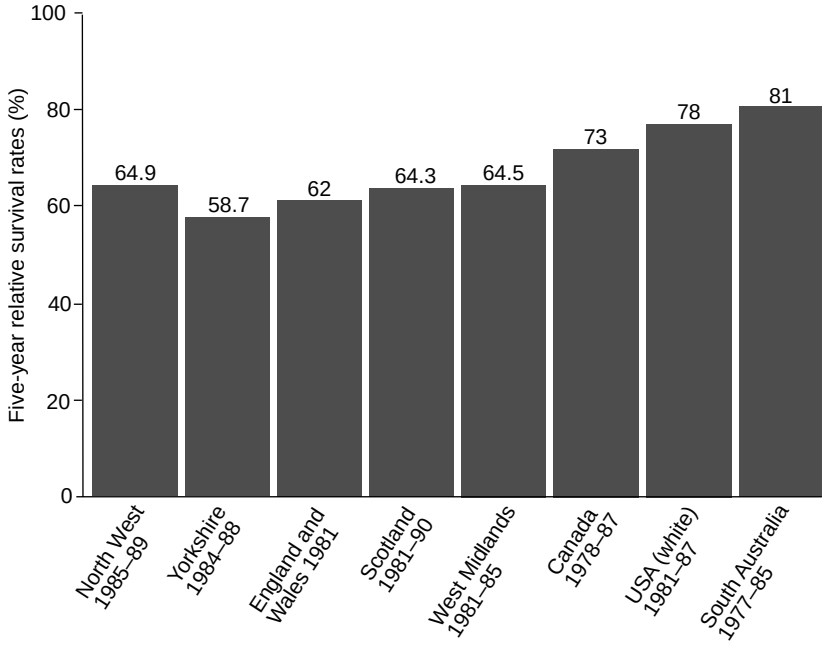

Figure 5: International variations in survival from breast cancer.

(Source: various cancer registries.[31–38])

A population-based audit of the management of 27 216 new cases of breast cancer registered in one RHA between 1978 and 1992 has reported interdistrict variations in the uptake of radiotherapy following surgery and in the use of adjuvant therapies.[165]

A questionnaire survey of surgeons in 1990 showed a marked shift towards BCT as treatment of choice in women with early breast cancer.[69,166,167] However 34% of surgeons would not routinely refer women undergoing breast conservation surgery for radiotherapy and only 74% of surgeons had access to a breast care nurse.

Impact of breast cancer services on outcome

It is important to identify the attributes of a service which may adversely affect the survival of women with breast cancer. Three have been extensively investigated.

Delay in diagnosis

There is no convincing evidence supporting the proposition that delays in diagnosis or referral of the magnitude routinely experienced within the NHS adversely influence survival.[168–170]

Type of hospital

Evidence to support a beneficial impact of specialist hospitals on survival of women with breast cancer is equivocal. Two studies in Italy and Australia have failed to demonstrate a significant difference in survival between women attending private institutions compared to public hospitals.[171,172] Although Karjalainen did find a better survival among Finnish women with breast cancer resident in districts with a university teaching hospital with radiotherapy facilities, this was confined to women with advanced disease.[173]

Lee-Feldstein *et al.* demonstrated a significantly better survival among US women with breast cancer treated in large community hospitals compared to those treated in smaller community and Health Maintenance Organisation hospitals even after adjustment for other factors known to influence survival.[174]

Basnett *et al.* showed that women resident in a London teaching hospital district were more likely to undergo BCT, axillary node surgery and adjuvant chemotherapy.[175] The women in the non-teaching hospital district had a higher risk of death even after adjustment for age and stage at presentation. The conclusions of this study are limited by the small study size and the short period of follow-up.

Workload of consultant surgeons

It is more likely that it is the competence of the treating surgeon which influences survival rather than the type of hospital attended.

There exists a strong belief that only those surgeons with a significant caseload of women have the skills necessary to manage breast cancer.[176] Hand *et al.* reported a significant association between failure to deliver radiotherapy for early breast cancer and number of cases treated.[177]

Uncertainty exists as to the volume of new cases necessary to maintain competence but a notional minimum figure of 50 has been suggested.[178] A population-based audit of breast cancer in Yorkshire has demonstrated that survival was better among women treated by surgeons who had a caseload in excess of 30 breast cancers a year.[179]

In one region with approximately 2000 breast cancer registrations per year analysis of Korner Episode System data for 1992/93 showed that women with breast cancer undergoing surgery were treated in 25 different hospitals. There were only seven consultants in the region treating more than 50 patients (unpublished data).

A Policy Framework for Commissioning Cancer Services

A national Expert Advisory Group was established to consider the organization of cancer care in England and Wales. The report of this group to the Chief Medical Officers of England and Wales, *A Policy Framework for Commissioning Cancer Services*[2] heralds a major reorganization of cancer services. Purchasing authorities will be responsible for securing uniform access to high quality services for their population.

The report recommends a model of care based on the following three levels of service provision.

1 **Primary care** Primary care teams are involved in the initial assessment and referral of patients and in providing ongoing practical and emotional support to patients within the community.
2 **Designated cancer units** Each cancer unit would be responsible for the clinical management of a common cancer, such as breast cancer and would have a lead consultant responsible for co-ordinating care, site-specific specialists and input from non-surgical oncologists.
3 **Cancer centres** These centres would provide specialist services to support cancer units. They would serve a population of between two-thirds of a million to a million and would provide radiotherapy services, specialist diagnostic services, management of rare cancers and intensive chemotherapy regimens.

The report emphasizes the importance of a holistic approach to cancer care from referral through assessment and treatment to palliative care. It stresses integration between primary care, acute providers and specialist services and the co-ordination of surgical and non-surgical expertise with the appropriate specialist backing from support services in radiology, pathology, nursing and palliative care. Key themes in the strategy are adherence to treatment protocols, development of local guidelines on referral practice, clinical audit and continuing medical education.

Levels of service provision

The following section outlines the service requirements of a notional HA with a female population of 150 000 and an age–sex structure similar to that in England and Wales.

OPCS estimates of the incidence of breast cancer in England and Wales for 1992[180] suggest that 172 new breast cancer cases would be expected in this HA per annum; 32 would be screen-detected (Figure 6) and 140 would present symptomatically.

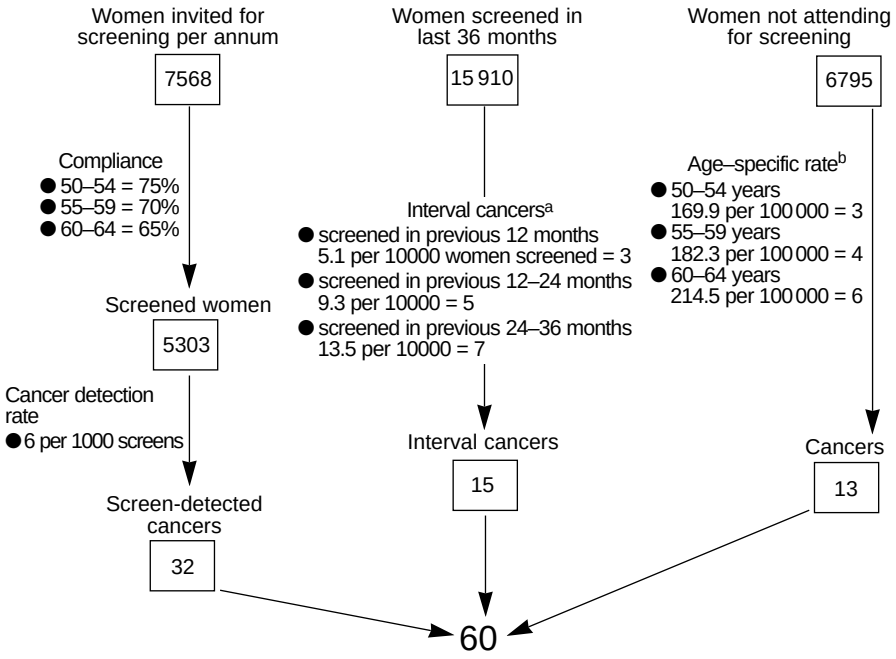

Figure 6: Source of breast cancers detected in the age group eligible for screening. Notional health authority. Population eligible for screening = 22 705.[a] Assuming NWR BSP interval cancer rates.[146] [b]Assuming 1986 OPCS age-specific incidence rates.

The stage distribution of the 172 breast cancer cases occurring in the notional HA has been estimated using 1992 data supplied by the East Anglian Cancer Registry.[10] The proportion of women with stage I high grade tumours has been estimated using unpublished data held by the North Western Regional Cancer Registry. Operative rates were derived from analysis of the Hospital Episode System. These data have been used to suggest a possible treatment profile for these 172 cases (Figure 7).

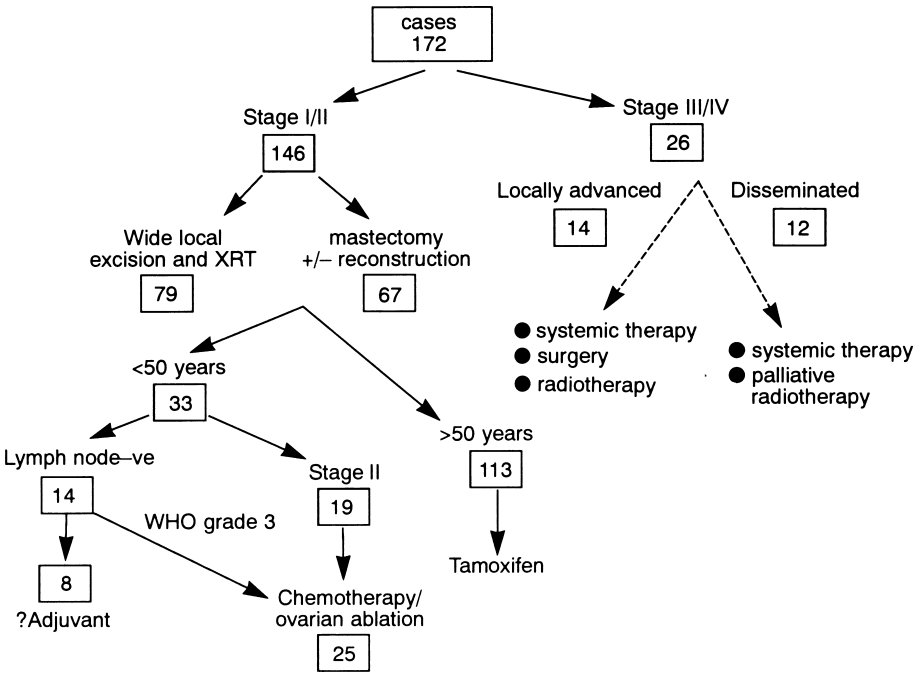

Figure 7: Treatment profile for breast cancer in notional health authority.

Resource implications for notional health authority

The resource implications for this notional HA which follow from the diagnosis and management of these screen-detected and symptomatic cases are now outlined.

Women attending the National Health Service Breast Screening Programme

Manpower requirements have been estimated by the Forrest Working Party and the NHSBSP for the minimum eligible population of a screening centre.[6,42,181,182]

The notional HA alone would not be large enough to support a screening centre. Its pro-rata contribution to the costs of a screening centre is outlined in Table 8.

Table 8: Manpower requirements for notional health authority

	Manpower recommendations	Notional HA (22 705 eligible women)
Radiologist	0.4 wte/ 41 150 eligible population	0.2 wte
Radiographer	4 wte/ 41 150 eligible population	2.2 wte
Surgeon	0.3 wte/ 41 150 eligible population	0.15 wte
Pathologist	0.2 wte/ 41 150 eligible population	0.1 wte
Clerical	3 wte/ 41 150 eligible population	1.5 wte
Medical physics	1 wte/ 15 screening sets	0.1 wte

Women presenting with symptoms suggestive of breast cancer

Resource requirements for diagnostic services are driven by the number of women referred with a breast-related problem of whom, it must be stressed, only a small proportion will have breast cancer.

It has been estimated that for every breast cancer there are seven or eight new referrals of women with other breast problems.[16,17] If the notional HA generates 140 new cases of symptomatic breast cancer the total number of new referrals to the symptomatic service will be 1120–1260.

An audit of the workload of one consultant undertaking all the breast work within a DGH with a catchment population of 212 000 found that outpatient referrals for breast problems constituted 60% of the consultant's workload (approximately 800 referrals) and 20% of the operative workload.[183] The consultant's workload was in excess of that suggested by the Royal College of Surgeons[184] and the authors concluded that one wte consultant breast surgeon is required per 1000 new referrals. This assumption requires validation.

Summary

The key issues for purchasers are:

- the optimum scheduling of screening visits has yet to be determined
- there is variable service provision for the assessment and treatment of women with breast cancer outside of the screening programme
- the report of the Expert Advisory Group has major implications for the provision of local breast cancer services.

8 Outcome measures

National Health Service Breast Screening Programme

The impact of screening on mortality may not be apparent for at least a decade after its implementation.[29] Four interim measures of programme effectiveness have been suggested:

1 compliance
2 cancer detection rate
3 interval cancers
4 characteristics of screen-detected cancers.

Compliance

The minimum standard for the NHSBSP is an uptake of 70% among women invited for screening. The uptake of primary screening in 1993/94 was 72.1%; this varied from 62% in North West Thames to 79% in East Anglia.[44]

Cancer detection rate

The cancer detection rate is the number of screen-detected cancers per 1000 screens in the eligible population.

The minimum standard for the NHSBSP is five cancers per 1000 screens in the prevalence round and 3.5 per 1000 in the incident round. The overall cancer detection rate for the NHSBSP in 1993/94 was 5.1 per 1000 screens: 5.7 per 1000 in the prevalence round and 3.8 per 1000 in the incident round.[44]

Interval cancers

An interval cancer is a cancer occurring in a woman between screens (see page 369). The NHSBSP standards are 2–3, 4–5 and 7–8 interval cancers per 10 000 screens for the first 12 months, 12–24 months and 24–36 months respectively after screening.

The interval cancer rate in the North Western Regional Breast Screening Programme was 5.1, 9.3 and 13.5 per 10 000 screens at 12, 12–24 and 24–36 months respectively after screening.[146] These rates are substantially higher than the NHSBSP targets.

The NHSBSP standards are currently being revised.

Characteristics of screen-detected cancers

It is hoped that screening will lead to the detection of a higher proportion of prognostically favourable tumours. Generally women with grade 3 tumours have a poor prognosis but this is markedly improved if the tumour is less than 15 mm. Data from the Swedish Two Counties Trial suggests that over 30% of grade 3 tumours should be less than 15 mm.[40]

Analysis of pathology reports from women with screen-detected cancer in the North Western Regional Breast Screening Programme between 1 March 1988 and 31 March 1992 has shown that over 30% of invasive grade 3 tumours were less than 15 mm (unpublished data).

Diagnosis and treatment

There are no routine indicators used to assess the quality, effectiveness and efficiency of diagnostic and treatment services. Standards for the symptomatic service have been set by the Cancer Relief Macmillan Fund[185] and the British Association of Surgical Oncologists.[176]

The following list of audit topics may be helpful in assessing the quality of breast cancer diagnostic and treatment services. Their provenance can be found in the previous discussion on service provision and effectiveness.

Although delays in diagnosis, referral and treatment routinely experienced by women in the NHS are unlikely to effect outcome, they are important QA issues.

The Cancer Relief Macmillan Fund suggests the following standard: 'a firm diagnosis within four weeks of being referred to a hospital by a general practitioner'.[185]

The Joint Committee for Clinical Oncology has set national standards for waiting times for post-operative radiotherapy for early breast cancer of four weeks and for palliative radiotherapy of 48 hours.[186]

Breast imaging

Topics suitable for audit include:

- availability and appropriate use of mammography and ultrasound for the investigation of symptomatic women
- technical performance of diagnostic mammography sets; these are not subject to the strict external QA guidelines found in the NHSBSP.

Adequacy of fine-needle aspiration cytology

Inadequate rates have been shown to vary considerably between operators.

Intraoperative frozen biopsies

Intraoperative frozen biopsies to diagnose clinically suspicious lesions are rarely necessary and are undesirable because they limit the involvement of women in treatment decisions.

Adequacy of pathology reporting

Pathology reports of breast cancer specimens should include, wherever appropriate, a description of:

- histological type, size and grade of tumour
- the adequacy of excision margins.

The rate and adequacy of axillary node surgery

The frequency with which axillary lymph nodes are sampled in premenopausal women is an important indicator of the quality of surgical management. At least four nodes should be available for assessment.

Rate of referral for radiotherapy following BCT

All appropriate women should be referred for radiotherapy following BCT. The need for radiotherapy in 'minimal risk' tumours will be clarified by ongoing trials.

Rate of referral for consideration of adjuvant therapy

All women with high risk early breast cancer should be offered adjuvant therapy. All premenopausal node-positive women should be offered chemotherapy.

Training and qualification of breast care nurses

A survey of breast care nurses in the UK revealed that a significant proportion may not have received recognized training in counselling skills or in oncology.[64]

Screening for asymptomatic metastases

The routine use of liver/bone/CT scans and X-rays in preoperative staging and follow-up regimens is not recommended.

9 Targets

Breast cancer is a key target area in The Health of the Nation.[1] The target is 'To reduce the death rate from breast cancer in the population invited for screening by at least 25% by the year 2000 (baseline 1990)'. A third of breast cancer deaths occur in this age group.[12]

National Health Service Breast Screening Programme

The Health of the Nation target coincides with the target set by the NHSBSP.

Diagnosis and treatment

There are no official targets.

Summary

The key issues for purchasers are:

- the Health of the Nation target is 'To reduce the death rate from breast cancer in the population invited for screening by at least 25% by the year 2000 (baseline 1990)'
- there are four key interim measures for evaluating the success of the NHSBSP
  a) compliance
  b) cancer detection rate
  c) interval cancer rate
  d) characteristics of screen-detected cancers
- there are QA standards for the NHSBSP
- there are a number of areas where clinical audit can be used to assess the quality of local symptomatic services.

10 Information and research

Information

Cancer registries

The importance of cancer registries has been emphasized by the report of the Expert Advisory Group.[2] Cancer registration data allow for:

- description of the burden of disease in the population
- evaluation of the effectiveness of the screening programme
- population-based investigations of variation in the clinical management of breast cancer.

Extent of disease at presentation has not in the past been collected routinely by many cancer registries but is now part of the minimum data set. This will enable cancer registries to contribute more extensively to the evaluation of the screening programme and of diagnostic and therapeutic strategies provided in defined populations.

Changes in the structure of RHAs will result in cancer registry contracts being devolved to lead purchasers after 1996.

National Health Service Breast Screening Programme

Information on the achievement of NHSBSP standards is available at national, regional and screening office level. There are some limitations to the current method of collating screening data particularly in providing district level information and in linking screening related events for individual women. The system is currently being improved.

Hospital information systems

Accurate estimates of resources used in diagnosis and treatment of breast cancer are currently limited by a lack of routinely available hospital activity data and financial information. This may improve following the implementation of the outpatient minimum data set and health care resource groups for radiotherapy.[187]

Research priorities

Primary prevention

There are no proven strategies for the primary prevention of breast cancer although a number are currently under investigation.

Tamoxifen has been shown to reduce the risk of a woman developing a second primary cancer in the contralateral breast by 39%.[9] Randomized controlled trials to assess the effectiveness of tamoxifen in reducing breast cancer in women at increased risk because of a family history or previous breast disease are currently underway in the UK, Europe and the US.[188,189]

Tamoxifen may also reduce the risk of heart disease and osteoporosis but concerns have been expressed following the increased risk of endometrial cancer observed in the ongoing trials of tamoxifen regimens in women with breast cancer.[190]

Family history clinics

The availability of predictive genetic testing following the cloning of the BRCA1 gene has major implications for purchasers.

Predictive genetic testing is a potentially resource intensive intervention for which the likely demand for services is difficult to predict. While it has been shown that the majority of first degree relatives of women with breast cancer may express an interest in undergoing genetic testing, experience with testing for Huntington's disease has demonstrated that interest is not always followed by demand.[191]

In addition there are ethical, social and public health implications to predictive genetic testing. Effective management options for young women found to be at high risk of breast cancer are not available. The acceptability and long-term psychosexual impact of prophylactic mastectomy and the psychosocial effects of awareness of carrier status are unknown. It is imperative that predictive genetic testing is fully evaluated before it enters routine use.

Screening policy

Issues that remain to be resolved include the cost-effectiveness of raising the age limit of screening or reducing the screening interval to two years.

Breast imaging

New techniques for imaging the breast are being developed. They include magnetic resonance imaging (MRI) and digital mammography.[192]

The usefulness of MRI in the diagnosis of symptomatic breast cancer, identification of recurrences following BCT and monitoring of response to systemic therapy is currently being assessed. At present MRI remains primarily a research tool.

Digital mammography is being evaluated as a screening test and in the localization of impalpable tumours. There is no evidence as yet of the superiority of this technique over conventional mammography although it may provide opportunity for cost savings from the reduced storage space required for optical discs. A full health technology assessment is needed before it is introduced routinely.

Systemic therapy in breast cancer

The World Overview provided valuable information on the role of adjuvant therapy in early breast cancer.[9] However a number of important clinical questions remain, some of which may be addressed by ongoing trials.[193–198] The results of the third World Overview with 15 years of follow-up of trials of adjuvant therapy are also awaited.

- There is a need to clarify which subgroups of node-negative women would benefit from adjuvant chemotherapy (or ovarian ablation). A number of trials are currently ongoing.
- The World Overview suggested that prolonged use of tamoxifen for at least five years may confer additional survival benefit over regimens of two years or less. No firm conclusion could be drawn as the sample size was small and estimates were considered unreliable. Confirmation of the benefit of prolonged use of tamoxifen is awaited from various trials.
- Cyclophosphamide, methotrexate and fluorouracil is the most commonly used regimen in this country. The addition of adriamycin to multi-agent regimens has gained favour with some clinicians. Optimum chemotherapeutic regimens remain to be clarified.
- The role of chemoendocrine therapy in postmenopausal women and of endocrine therapy in premenopausal women also remains to be clarified by ongoing trials.
- Primary treatment with chemotherapy or tamoxifen prior to surgery (neoadjuvant therapy) is an alternative management strategy which aims to downstage large breast tumours and facilitate BCT.[199] The results of ongoing RCTs are awaited.
- A subgroup of high-risk women with ten or more involved lymph nodes has been identified. High-dose chemotherapy with autologous bone marrow transplant or support with haemopoietic factors has been suggested for this group. This resource intensive therapy has a high case mortality rate. Randomized controlled trials are ongoing.[128]

The role of systemic therapy in advanced disease is even less clear and an overview of published trials could aid rational clinical management decisions. Paclitaxel (taxol) is a new chemotherapeutic agent which has been shown in non-randomized studies to reduce symptomatology in women with metastatic breast cancer.[200,201] There is as yet no evidence from RCTs of it superiority over conventional chemotherapeutic agents.

Radiotherapy schedules

Treatment schedules for radical radiotherapy vary from three to six weeks. This variation appears to reflect training and institutional policy rather than patient factors.[107] Shorter regimens can potentially reduce

waiting times and costs. The morbidity of the different schedules is not known and urgent evaluation is required.

Breast cancer in the elderly

Over half of all breast cancers occur in women aged over 70. Advanced disease at presentation is more common in older women (Table 9).

Table 9: Stage of presentation by age

	Less than 50 years (%)	50–64 years (%)	65 years and over (%)
Stages I and II	86	88	69
Stages III and IV	14	12	31

Source: East Anglian Cancer Registry[19]

The relative survival of women with breast cancer in the UK decreases markedly with age. This age differential is not seen in the US and may reflect a reluctance in this country to deliver radical treatment either because of greater comorbidity in older women or the need to ration resources (Figure 8). This is a cause for concern because the average life expectancies of women aged 75 and 85 in England and Wales are 11.2 and 6.1 years respectively.

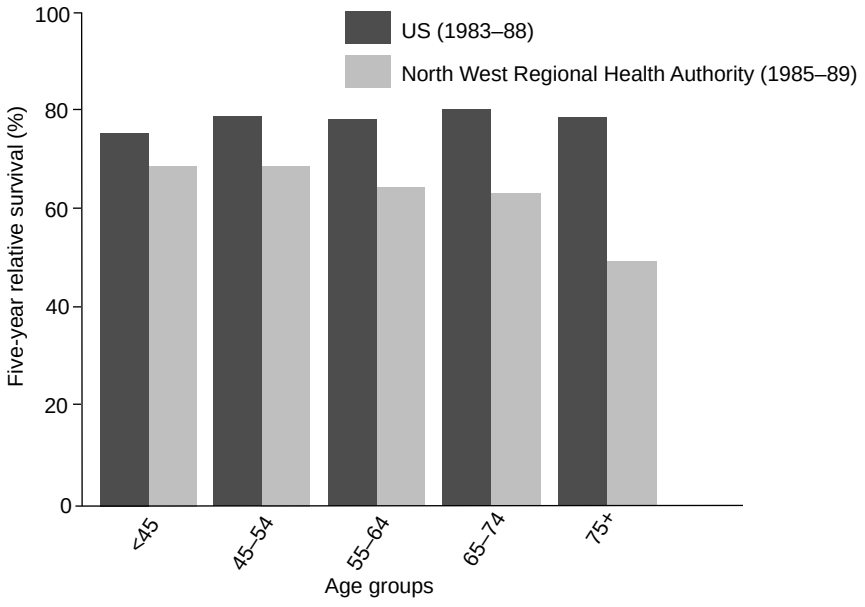

Figure 8: International comparison of age-specific survival from breast cancer.
(Sources: North Western Regional Cancer Registry; Surveillance Epidemiology and End Results programme.[32])

Some clinicians have favoured the use of tamoxifen alone in elderly women with operable tumours. One RCT demonstrated no difference in disease-free survival between elderly women treated with tamoxifen alone and those treated by surgery.[202] However a subsequent RCT comparing tamoxifen alone with

tamoxifen and surgery did demonstrate an increased locoregional recurrence rate in the tamoxifen only group.[203,204] This strategy is no longer recommended.

Elderly women are a heterogenous group. Some will benefit from management regimens at present reserved for younger women. Further evaluation of treatment regimens are required in this age group.

Summary

The key issues for purchasers are:

- information
  a) cancer registration data are essential for evaluation of the screening programme and monitoring of the quality of breast cancer services
  b) there is a paucity of hospital activity and costing information on symptomatic cancer services
- research
  a) current research into lowering the age limit for screening and the primary prevention of breast cancer using tamoxifen may have significant implications for purchasers
  b) the cost-effectiveness of raising the age of the screening programme and reducing the interval of call/recall needs early evaluation
  c) predictive genetic testing has major public health implications and should be fully evaluated before introduction into routine clinical use
  d) more attention should be focused on improving the survival of elderly women with breast cancer
  e) clarification of management strategies requires the recruitment of women into breast cancer trials. This has major resource implications for provider units.

Appendix I Relevant coding classifications

ICD 9

International statistical classification of diseases: injuries and causes of death. Ninth revision.

174	malignant neoplasia of the female breast (excludes: skin of breast)
174.0	nipple and areola
174.1	central portion
174.2	upper inner quadrant
174.3	lower inner quadrant
174.4	upper outer quadrant
174.5	lower outer quadrant
174.6	axillary tail
174.8	other
174.9	breast unspecified
233.0	ductal carcinoma *in situ*

ICD 0

International classification of diseases for oncology.

174	malignant neoplasia of the female breast (excludes: skin of breast)
174.0	nipple and areolae
174.1	central portion
174.2	upper inner quadrant
174.3	lower inner quadrant
174.4	upper outer quadrant
174.5	lower outer quadrant
174.6	axillary tail
174.8	inner breast
	lower breast
	midline of breast
	outer breast
	upper breast
174.9	female breast NOS
233.0	ductal carcinoma *in situ*

behaviour code /3 malignant /2 *in situ*

ICD 10

Tenth revision.

C50	malignant neoplasia of breast (excludes: skin of breast)
C50.0	nipple and areolae
C50.1	central portion of breast

C50.2	upper inner quadrant of breast
C50.3	lower inner quadrant of breast
C50.4	upper outer quadrant of breast
C50.5	lower outer quadrant of breast
C50.6	axillary tail of breast
C50.8	overlapping lesion of breast
C50.9	breast unspecified

ICD 0

Second edition.

C50	breast (excludes: skin of breast)
C50.0	nipple and areolae
C50.1	central portion of breast
C50.2	upper inner quadrant of breast
C50.3	lower inner quadrant of breast
C50.4	upper outer quadrant of breast
C50.5	lower outer quadrant of breast
C50.6	axillary tail of breast
C50.8	overlapping lesion of breast
	inner breast
	lower breast
	midline of breast
	outer breast
	upper breast
C50.9	breast NOS mammary gland

behaviour code /2 *in situ* /3 malignant neoplasia

Diagnostic related groups

DRG	Description of group
257	Total mastectomy for malignancy with CC
258	Total mastectomy for malignancy W/O CC
259	Subtotal mastectomy for malignancy with CC
260	Subtotal mastectomy for malignancy W/O CC
268	Skin, subcutaneous tissue and breast plastic procedures
274	Malignant breast disorders with CC
275	Malignant breast disorders without CC
409	Radiotherapy
410	Chemotherapy

CC = complications or comorbidity

Appendix II Staging classifications

Clinical staging

- **Stage 0** CIS only.
- **Stage I** Tumour 2 cm or less in greatest dimension, no metastasis
- **Stage IIA** Tumour less than 2 cm in greatest dimension, metastasis to movable ipsilateral axillary lymph node(s), no distant metastasis; or tumour more than 2 cm but not more than 5 cm in greatest dimension, no metastasis.
- **Stage IIB** Tumour more than 2 cm but not more than 5 cm in greatest dimension, metastasis to movable ipsilateral axillary lymph node(s); or tumour more than 5 cm in greatest dimension, no metastasis.
- **Stage IIIA** Tumour of any size, metastasis to ipsilateral lymph node(s) fixed to one another or to other structures, no distant metastasis.
- **Stage IIIB** Tumour of any size with direct extension to chest wall or skin, metastasis to ipsilateral lymph nodes, no distant metastasis; or any type of tumour, metastasis to ipsilateral mammary lymph node(s), no distant metastasis.
- **Stage IV** Tumour of any size, with or without lymph node(s) involvement, but with distant metastasis.

TNM staging

The TNM system, in which T defines primary tumour, N regional lymph nodes and M distant metastasis.

Primary tumour (T) is further sub-divided into:

T0	No evidence of primary tumour
Tis	Carcinoma *in situ*
T1	Tumour 2 cm or less in greatest dimension
T2	Tumour more than 2 cm but not more than 5 cm in greatest dimension
T3	Tumour more than 5 cm in greatest dimension
T4	Tumour of any size with direct extension to chest wall or skin

Regional lymph nodes (N) are sub-divided into:

N0	No regional lymph node metastasis
N1	Metastasis to movable ipsilateral axillary lymph node(s)
N2	Metastasis to ipsilateral axillary lymph node(s) fixed to one another or to other structures
N3	Metastasis to ipsilateral internal mammary lymph nodes

Distant metastases (M) are sub-divided into:

M0	No distant metastasis
M1	Distant metastasis (includes metastasis to ipsilateral supraclavicular lymph nodes)

Appendix III Age-specific incidence rates for breast cancer

Age group (years)	Rate per 100 000 population
Under 1	0.6
1–4	0.1
5–9	0.1
10–14	0.1
15–19	0.2
20–24	0.2
25–29	1.2
30–34	24.6
35–39	57.3
40–44	105.5
45–49	160.4
50–54	181.1
55–59	214.7
60–64	257.5
65–69	253.4
70–74	254.4
75–79	274.5
80–84	285.0
85 and over	356.0

Source: OPCS Cancer Registration (1989) Series MB1, No. 22

Appendix IV National Health Service Breast Screening Programme

Objective	Criteria	Acceptable standard	Achievable standard
To maximize the number of eligible women attending for screening	Proportion of eligible women who attend for screening	70% of women to be invited for screening	75%
To maximize the number of cancers detected	The rate of cancers detected in eligible women invited and screened (including CIS)	Greater than 50 in 10 000 (1st screen) Greater than 35 in 10 000 (routine re-screen)	60 per 10 000 (1st screen)
To maximize the number of small cancers	The proportion of invasive cancers equal to or less than 10 mm in diameter detected in eligible women invited and screened	15 in 10 000	
To achieve optimum image quality	a) High contrast spatial resolution b) Minimal detectable contrast (approx.) 5–6 mm detail, 0.5 mm detail	10 lp/mm 1% 5%	
To limit radiation dose	Average glandular dose per film to average breast using a grid	Less than 2 mGy	
To minimize the number of women undergoing repeat films	Number of repeated examinations	Less than 3% of total examinations	Less than 2%
To minimize the number of women referred for further tests	Onward referral assessment	Less than 7% of women screened	5% first screen 3% routine re-screen
To minimize the number of unnecessary invasive procedures	a) Malignant to benign biopsy ratio b) PPV c) Benign biopsy rate	1 : 1 50% Less than 50 per 10 000 (first screen) Less than 35 per 10 000 (routine re-screen)	1.5 : 1 60% Less than 40 per 10 000 (first screen)
To minimize the number of cancers in women screened between screening episodes	The proportion of cancers presenting in screened women in the subsequent 12 months after screening	Not more than three per 10 000 women screened	

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