

Implementing the NHS Cancer Plan:
Guidance on Cancer Services

Improving Outcomes in Breast Cancer

Draft

Update of the COG Guidance Manual

January 2002

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Foreword

The publication of the ‘Calman-Hine’ cancer policy¹ in 1995 marked the first broadly based cancer policy for England and Wales. It defined the principles and structural framework for the delivery of better care for patients with cancer, emphasising the central importance of meeting patients’ needs. A consequence of this approach was the recognition of the importance of inter-disciplinary and collaborative arrangements for the delivery of services. Probably the single most crucial recommendation was that hospital care should be provided by a range of specialists in the disease concerned, working together in site-specific multidisciplinary teams.

The National Cancer Guidance Group, as it is now called, was set up soon after the Calman-Hine report was published. It was charged with developing guidance for the implementation of the new policy in NHS services for the common cancers, starting with breast. There was no precedent for this type of document, and apart from the recognition that the guidance should complement existing clinical guidelines, no clear picture as to what the documents should be like, nor clarity about the ground they should cover. Only the aim was clear: to help those responsible for commissioning, organising and delivering good breast cancer care.

Cancer policy at that time was less well developed than it is today, but there had been both widespread concern and innovative thinking about the issues, particularly in relation to breast cancer. This was given an impetus by the implementation of the Breast Screening Programme in the late 80’s and early 1990’s, which challenged assumptions about the quality of care available for patients with symptomatic disease. Scientific papers and the popular media had revealed evidence of substantial variations in the management of patients with breast cancer, and there were constructive discussions between professional and concerned lay people about what was wrong with services at that time, as well as how to improve matters. Clinical bodies, including the British Association of Surgical Oncology² and the British Breast Group,³ had articulated their vision of improved breast cancer care.

The ‘*Improving Outcomes*’ breast guidance – widely known as the COG Guidance – built on that thinking. It was published by the Department of Health in 1996 and has been very influential in shaping service delivery and defining a detailed practical framework for modern breast cancer care. Inevitably, as the first of a new series of documents, it lacked the refinements of subsequent reports, such as a background section introducing the disease and the broad principles of its management to the non-expert reader. Nevertheless, the basic shape of these documents has remained substantially unaltered in all the subsequent guidance, suggesting that the original format was successful.

Progress, however, is continuous and all guidance needs updating. We welcome the opportunity that NICE has provided to review the original breast guidance in areas where science or practice has moved on. We have not rewritten the whole document since most of the original content remains valid, service guidance being less vulnerable to small clinical changes than clinical guidelines.

The context of this updated guidance is very different from that of six years ago. Mortality rates from breast cancer in women under the age of 70 have shown a sharp and sustained fall, well documented by Peto et al⁴ and Purushotham et al⁵. Although the cause is open to speculation, the observation by Richard Peto that it most probably reflects multiple influences, all of which have small individual effects but cumulatively result in a major impact on outcomes, is an attractive hypothesis. It emphasises the necessity of ensuring that optimal clinical decision-making takes place throughout a patient's experience of breast cancer, from the earliest diagnostic steps to the management of advanced disease. This extended and updated guidance makes revised recommendations for services to secure that objective.

There has been a great deal of progress since the original breast guidance was published, so much so that it may seem to some that implementation of that guidance is largely achieved, that modern multidisciplinary breast cancer care is 'a done deal'. But the challenges of rising numbers of new referrals, the need to respond within tight time-scales, and advances in diagnosis and treatment mean that teams must be very well organised and well supported to succeed.

Despite obvious progress, breast teams do not all work optimally. Breast teams need good internal systems and reliable support to ensure that all members meet regularly and operate effectively together and to ensure that agreed actions that should follow team decisions are implemented. Such support is frequently limited or absent. Some teams lack key staff and access to facilities.

Continuity and cover for key clinical roles is essential to maintain consistent standards of specialised care for all patients. This increasingly necessitates collaboration between those involved in breast services in neighbouring hospitals. The need for collaboration between breast teams and other services, such as screening, clinical genetics, and palliative care, has grown as these other services have developed. Ensuring that these clinical links work well for patients requires awareness of the potential benefits and efficient organisation.

This revised guidance comes at a time of modernisation and change. New NHS structures such as Primary Care Organisations and Strategic Health Authorities mean many of those concerned in these bodies will need to learn afresh what needs to be done and why. They need to appreciate how their organisation can contribute effectively to improving outcomes, including acting together for more centralised services such as radiotherapy.

An increasing range of cancer policies is now available, together with NICE appraisals. This guidance seeks to complement these other policies, so that initiatives are consistent with one another. Thus genetic issues in cancer are

subject to detailed recommendations in a report expected in Spring 2002. In a year's time there will be broadly based cancer guidance dealing with supportive care, also to be published by NICE. The appraisals of potential therapeutic advances, such as Herceptin and new generations of hormonal agents are important and need not be replicated in this guidance. The success of the Cancer Services Collaborative in improving specific aspects of service delivery at local level has been influential, and published evidence on good practice is an important new source of material.

One of the important ways in which this guidance is used reflects a greater concern with implementation. Recommendations from the original breast guidance were incorporated into the NHS cancer standards in both England⁶ and Wales⁷. These standards have in turn been used in help improve services in various ways (including national peer review in England), and have informed reviews of cancer services carried out by the Committee for Health Improvement and Audit Commission.

The task of producing the update has been greater than anticipated because of the scale of the evidence reviews required – although in reality, much of the updated evidence substantiated the validity of existing recommendations, rather than making the case for change. I would like to express appreciation for the work of the evidence review team at the Centre for Reviews and Dissemination at the University of York, who undertook these reviews.

In particular, I would like to acknowledge the role of one of the founder members of the National Cancer Guidance Group, Professor Robert Mansel from Cardiff University, who chaired the Editorial Board that oversaw the updating of this guidance.

Professor Bob Haward

Chair of the National Cancer Guidance Group

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2. Guidelines for surgeons in the Management of Symptomatic Disease in the United Kingdom. (1995) *European J of Surgical Oncology* 21 (Supp A): 1-13.
3. *Provision of breast services in the UK: The advantages of specialisation*. Report of a working party of the British Breast group, September 1994.

4. Peto R, Boreham J, Clarke M, Davies C, Beral V: Research Letter. *Lancet* 2000; **355**: 1822.
5. Purushotham AD, Pain SJ, Miles D, Harnett A , Variations in treatment and survival in breast cancer. *Lancet Oncol* 2001; **2**: 719-25
6. NHS Executive. *Manual of Cancer Service Standards* (Dec 2000). Department of Health.
7. Ditto Wales

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Key Recommendations

Multidisciplinary team working

All patients with breast cancer should be managed by multidisciplinary teams and all multidisciplinary teams should be actively involved in network-wide audit of processes and outcomes.

Multidisciplinary teams should consider how they might improve the effectiveness of the way they work. Some Units should consider working together to increase the number of patients managed by the team.

Minimising delay

No patient should have to wait more than four weeks for any form of treatment.

Follow-up

The primary aims of follow-up should be to identify and treat local recurrence and adverse effects of therapy, not to detect metastatic disease in asymptomatic women. Long-term routine hospital-based follow-up should cease, except in the context of clinical trials.

Review of services for screened and symptomatic patients

Each cancer network should review its arrangements for breast screening, with the goal of bringing services for screened and symptomatic patients into closer alignment. Networks should aim to achieve consistency in clinical policies, organisation and care, irrespective of the patient's point of entry into the system.

Note on the update format

This updated edition of *Improving Outcomes in Breast Cancer* is based on the Manual published by the Department of Health in 1996. Additional material, based on recent reviews of research evidence and discussions by a reconstituted Editorial Group, has been inserted in a larger font size (12 point as opposed to 10 point) so that it can be distinguished from earlier text.

The additional material includes a new Background section, intended to provide a broad overview of breast cancer for non-clinicians; a new Topic 1, *Primary care and the management of women at high risk*; and a new Topic 8, *Management of advanced, recurrent and metastatic disease*. The topic areas and numbers therefore differ from the previous Manual.

Material in the Evidence sections in the topic areas is based on systematic reviews of research evidence carried out by the NHS Centre for Reviews and Dissemination. These reviews will be available in full to accompany the final version of this update. Reference numbers in the current text refer to papers included in the reviews; other papers are also included and may be relevant, but for the sake of brevity are not mentioned in this update. The Background section is based on neither a systematic review nor comprehensive literature searches.

Some of the Evidence in smaller type may now be out of date. Where possible, information included in the previous Manual based on on-going reviews has been replaced by more recent material. Evidence is graded A (derived from randomised controlled trials - RCTs), B (observational studies) and C (professional consensus). These are broad categories and the quality of evidence within each category varies widely. Thus it should not be assumed that RCT evidence (grade A) is always more reliable than evidence from observational studies (grade B). Detailed information on the reliability of evidence will be given in the Review of Research Evidence.

Arabella Melville, writer, January 2002.

Background

Incidence, mortality and prevalence

Breast cancer is the most common female cancer, accounting for almost 30% of all cancers in women. In 1997, there were just under 33,500 new cases among women and 250 among men (Table 1). The likelihood of a diagnosis of breast cancer increases with age, doubling about every ten years until the menopause when the rate of increase slows dramatically (Figure 1). The lifetime risk for women is almost 11% (1 in 9).¹

Table 1. Breast Cancer (ICD10 50) – registrations, incidence and deaths, England and Wales.

Sources: Office for National Statistics; Welsh Cancer Intelligence and Surveillance Unit, data provided on request.

Country	No of registrations 1998		Incidence: crude rate per 100,000 1998		No of deaths 2000		Mortality: crude rate per 100,000 2000	
	Men	Women	Men	Women	Men	Women	Men	Women
England	269	32,908	1.1	131.0	67	10,609	0.3	41.9
Wales	18	1,914	1.25	128.05	3	731	0.2	48.7

Breast cancer is described as non-invasive and known as ductal carcinoma in situ, or DCIS, when the cancer remains localised in the ducts. In most cases, the cancer is invasive at the time of diagnosis. This means that malignant cells are liable to spread beyond the immediate area of the tumour.

There has been an overall increase in the incidence of both invasive and non-invasive breast cancer in England and Wales, the specific causes of which are unknown (Figure 1). Age-standardised incidence in the UK is among the highest in the world, but it has been increasing worldwide. In England and Wales, the increase is particularly apparent among women aged 50-64; this is believed to be primarily due to earlier detection through the breast screening programme, set up in 1988.

¹ Quinn MJ, Babb P, Brock A, Kirby L, Jones J. *Cancer Trends in England and Wales 1950-1999*. Studies on Medical and Population Subjects no.66. The Stationery Office: London 2001.

Figure 1. Age-specific incidence of breast cancer, England and Wales

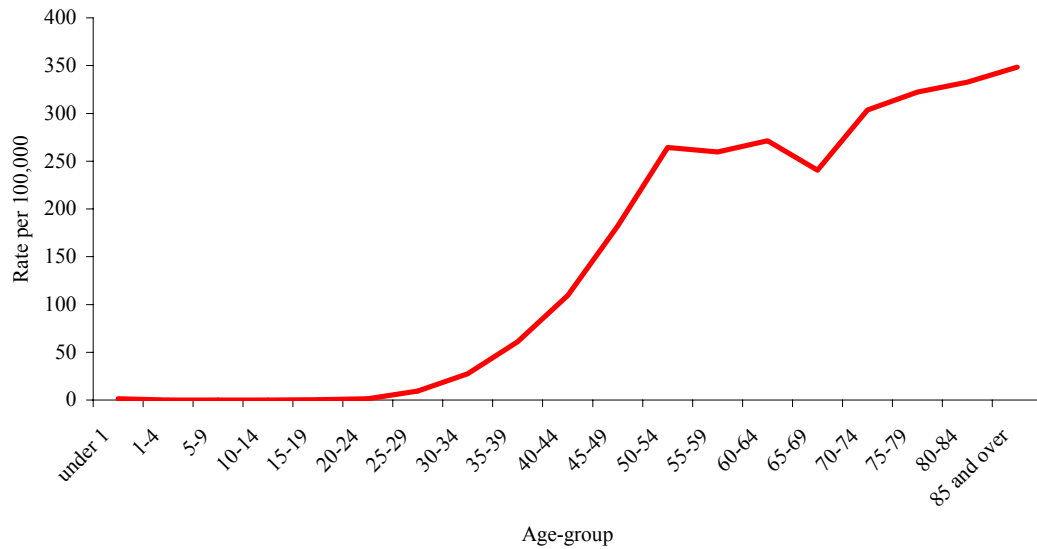
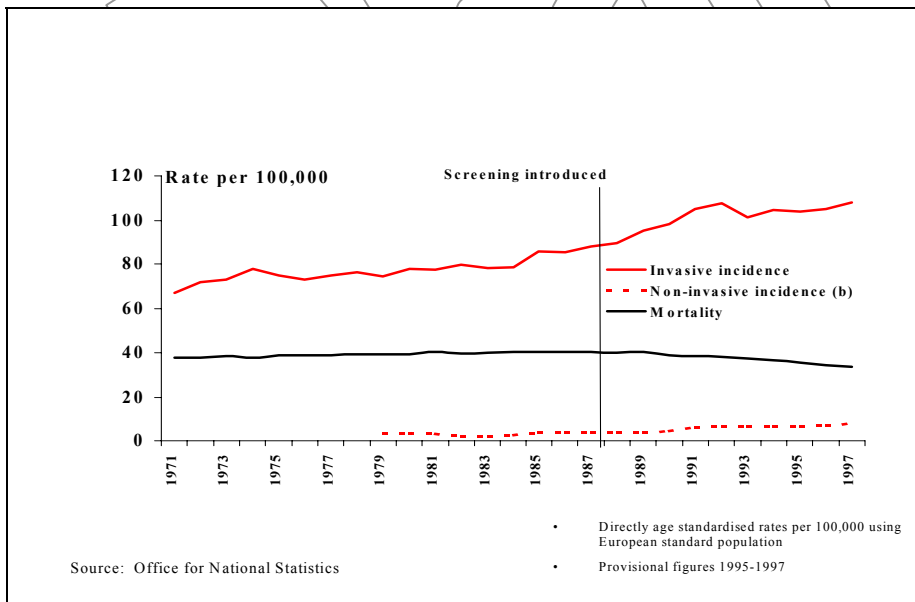


Figure 2. Breast cancer incidence and mortality, England and Wales, 1971-1997



In 2000, there were just over 10,600 deaths from breast cancer among women and 70 among men in England and Wales (Table 1). The survival rate for patients diagnosed between 1992-1994 was 92% at one year and 75% after five years (Table 2). Among women whose cancer was diagnosed by screening in 1994-95,

over 93% were still alive five years later.² Indeed, breast cancer survival rates are higher than those for any other major cancer in women except endometrium.

Table 2. Survival rates among women newly diagnosed with breast cancer in 1986-94, England.

Year of diagnosis	One year relative survival rate, %	Five year relative survival rate, %
1986-90	90.0	68.0
1991-93	92.1	73.9
1992-94	92.3	75.0

Source: Office for National Statistics

Mortality from breast cancer is falling in all age groups; in 1999, case-fatality rates were about one-fifth lower than in the mid-1980s. The reasons for this are not certain, but earlier diagnosis and improvements in treatment, particularly greater use of adjuvant therapies, undoubtedly contribute.³

Five year survival rates are highest among people aged 50-59 at diagnosis; both younger and older patients have a lower survival rate (Figure 2). However, better outcomes among women in this particular age-group could be an illusion created by lead-time and length biases associated with screening. Older people, who are generally less fit, tend to receive less aggressive treatment and this may account, at least in part, for lower cancer-specific survival rates in the elderly; but among younger people, it is possible that the higher case-fatality rate might be due to the nature of the cancer. A similar pattern can be seen with prostate cancer in men, which shares some features with breast cancer.

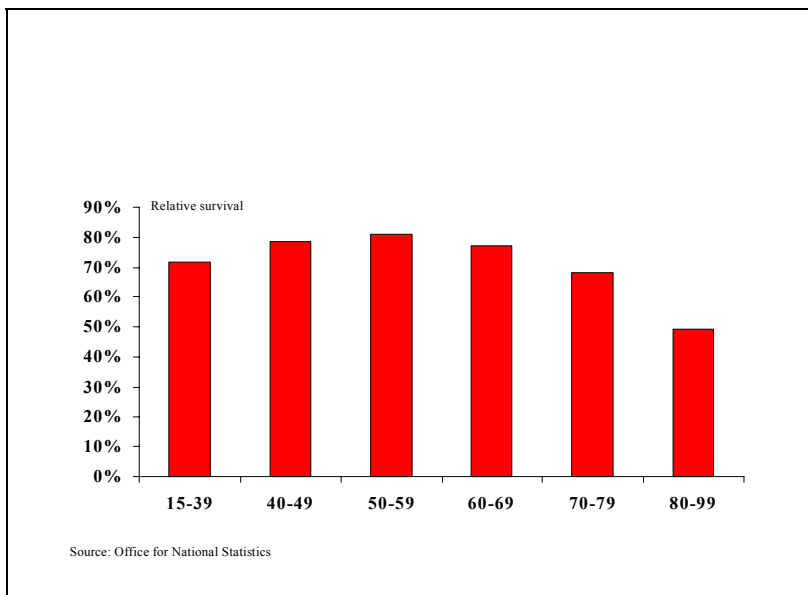
The relationship between mortality from breast cancer and economic status is complex. Incidence is almost one-third higher among the most affluent women than among the most deprived, but the lower incidence in deprived groups is balanced by poorer survival. The probability of survival was 6% greater for women from more affluent groups in the 1980s at one year after diagnosis, rising to 9% after five years.⁴ The reasons for these differences are unclear.⁵

² NHS Breast Screening Programme/British Association of Surgical Oncology Breast Group. *An Audit of Screen Detected Breast Cancers for the Year of Screening April 1999 to March 2000*. NHS Breast Screening Programme, April 2001.

³ Peto R, Boreham J, Clarke M, Davies C, Beral V. UK and USA breast cancer deaths down 25% in year 2000 at ages 20-69 years. *Lancet*; 2000; 355: 1822.

⁴ Quinn MJ, Babb P, Brock A, Kirby L, Jones J. *Cancer Trends in England and Wales 1950-1999*. Studies on Medical and Population Subjects no.66. The Stationery Office: London 2001.

Figure 3. Five year relative survival rates by age, England, 1992-94



Survival rates vary with the biological characteristics of the tumour and the stage of development at which it is detected. About 50% of patients have early disease at the time of initial diagnosis (stage I, T₁, N₀ – tumour confined to breast)⁶, for which the prognosis is excellent; fewer than 5% of patients have metastatic disease (stage IV) at this point, although the likelihood of an initial diagnosis of advanced breast cancer tends to increase with age and is higher among men. The average period of survival after identification of metastatic disease is 18-24 months, but this varies widely between individual patients.

A major pan-European study showed that survival rates in England and Scotland were lower than in other European countries in the 1980s.⁷ This was probably due, at least in part, to the fact that British patients tended to have more advanced disease at the time of diagnosis. It is not yet known whether the discrepancy in outcomes has been reduced in the period since this study was carried out.

⁵ Thomson CS, Hole DJ, Twelves CJ, Brewster DH, Black RJ; Scottish Cancer Therapy Network. Prognostic factors in women with breast cancer: distribution by socio-economic status and effect on differences in survival. *Journal of Epidemiology and Community Health*; 2001; 55(5): 308-315.

⁶ Figures derived from Goggedge J, Wiggins JE, Callam MJ, Effect of surgical subspecialisation on breast cancer outcome. *British Journal of Surgery*, 2000, 87, 1420-5.

⁷ Berrino F et al. *Survival of Cancer Patients in Europe: The EURO-CARE-2 Study*. IARC Scientific Publications No 151. Lyon. 1999.

Risk Factors

The causes of breast cancer are complex. It has been suggested that up to 10% of patients may have an inherited predisposition to the disease.⁸ This can arise from mutations in particular genes; two have been identified (BRCA1 and BRCA2), but there are believed to be others.^{9,10} A genetic disposition can be inherited from either parent, both of whom can transmit susceptibility without developing the disease themselves.

Established risk factors for breast cancer include older age, early onset of menstruation, late menopause and greater age at first completed pregnancy.¹¹ In addition, increased risk is associated with some forms of benign breast disease and with exposure of developing breast tissue to radiation.¹² Women who use products which contain oestrogen and progesterone – either oral contraceptives or hormone replacement therapy (HRT) – are at increased risk, but the effects are not large and disappear within a decade of giving up hormone use.¹³ Ten years' use of HRT appears to lead to six extra breast cancers per thousand women, increasing the individual risk over twenty years (age 50 to 70) from one in 22 to one in 19.¹⁴

The risk of breast cancer is affected by lifestyle. Obesity is associated with a two-fold increase in risk among post-menopausal women; this has been linked with high intake of meat and dairy fat, but the precise nature of these relationships are still unclear.^{15,16} *Add association with alcohol.*

⁸ McPherson K, Steel CM, Dixon JM. Breast Cancer – epidemiology, risk factors and genetics. *British Medical Journal*; 2000; 321: 624-628.

⁹ Evans DGR, Fentiman IS, McPherson K, Asbury D, Ponder BAJ, Howell A. Familial breast cancer. *British Medical Journal*; 1994; 308: 183-187.

¹⁰ Antoniou AC, Pharoah PD, McMullan G, Day NE, Ponder BA, Easton D. Evidence for further breast cancer susceptibility genes in addition to BRCA1 and BRCA2 in a population based study. *Genetic Epidemiology*; 2001; 21(1): 1-18.

¹¹ Longnecker MP, Bernstein L, Paganini-Hill A, Enger SM, Ross RK. Risk Factors for in situ breast cancer. *Cancer Epidemiological Biomarkers & Prevention*; 1996; 5 (12): 961-965.

¹² McPherson K, Steel CM, Dixon JM. Breast Cancer – epidemiology, risk factors and genetics. *British Medical Journal*; 2000; 321: 624-628.

¹³ Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 1000 239 without breast cancer from 54 epidemiological studies. *Lancet*; 1996; 347: 1713-27.

¹⁴ Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52 705 women with breast cancer and 108 411 without breast cancer. *Lancet*; 1997; 350: 1047-1059.

¹⁵ McPherson K, Steel CM, Dixon JM. Breast Cancer – epidemiology, risk factors and genetics. *British Medical Journal*; 2000; 321: 624-628.

¹⁶ Willett WC. Diet and Cancer: One View at the Start of the Millennium. *Cancer Epidemiology Biomarkers*

As with many other forms of cancer, eating fruit and vegetables can reduce risk,¹⁷ and physical activity also seems to reduce risk (in pre-menopausal women, at least); more intensive activity may produce greater benefits, although this is not yet certain.¹⁸ It seems, therefore, that there is scope for primary prevention, and intervention studies are in progress.

Screening, Diagnosis and Treatment

Screening for breast cancer began in the UK in 1988 and the prevalent screening round was completed in 1995. Currently, all women aged 50-64 are invited for mammograms every three years; the age range is to be expanded to women aged 70 by 2004.¹⁹ In 1999-2000, the NHS Breast Screening Programme detected 9,797 cancers by screening about 1,550,000 women.²⁰ The potential use of magnetic resonance imaging (MRI) for screening high risk women aged 35-50 is being evaluated.

Women with symptoms that could be due to breast cancer are referred by their GP to designated breast clinics in local hospitals. In a single year, the average GP, with a patient list of 2,000, could expect to see one or two new cases of breast cancer, but will see considerably more patients with benign breast problems. A hospital responsible for a population of 300,000 will deal with perhaps 40 new GP referrals each week, plus maybe two women referred after screening mammography. Breast cancer will be diagnosed in approximately 200 patients per year.

For the vast majority of cases, diagnosis is by triple assessment (clinical assessment, mammography and/or ultrasound imaging, and fine needle aspiration or core biopsy). Invasive cancers are classified on the basis of the nature of the cancerous cells (histological type and grade) and the size and spread of the tumour. Assessment of the lymph nodes in the armpit (axilla) is crucial to staging and prognosis; this requires surgical excision.

The treatment of primary breast cancer usually involves surgery, either breast conservation (wide local excision) or mastectomy. Normally, surgery is followed by adjuvant treatment such as radiotherapy, chemotherapy or hormone therapy or a combination of these, but these types of therapy may be given before surgery;

& *Prevention*; 2001; 10: 3-8.

¹⁷ Gandini S, et al. Meta-analysis of studies on breast cancer risk and diet: the role of fruit and vegetable consumption and the intake of associated micronutrients. *European J Cancer*, 2000, 36:636-646

¹⁸ Shephard RJ, Fitcher R. Physical activity and cancer: how may protection be maximised? *Critical Reviews in Oncogenesis*, 1997,8:219-272)

¹⁹ Department of Health. *The NHS Cancer Plan*. Department of Health, 2000.

²⁰ NHS Breast Screening Programme/British Association of Surgical Oncology Breast Group. *An Audit of Screen Detected Breast Cancers for the Year of Screening April 1999 to March 2000*. NHS Breast Screening Programme, April 2001.

this is described as neo-adjuvant treatment. The choice of adjuvant treatment depends on age, risk of relapse, potential benefits, oestrogen receptor status and acceptability to the patient. Tamoxifen is the most commonly used form of hormonal treatment. There is still some uncertainty about the optimum treatment for women with early breast cancer, particularly DCIS, because the potential benefits of adjuvant treatment may not outweigh its adverse effects when the risk of recurrence is low. Research is continuing into this and other aspects of therapy.

Psychosocial support is considered to be an integral part of the management of breast cancer, as up to one-third of women develop severe anxiety or a depressive illness within a year of diagnosis.²¹

Metastatic breast cancer can affect many parts of the body, particularly the bones, lungs, soft tissue and liver. It causes a wide variety of symptoms, particularly pain and fatigue, but also other problems as diverse as persistent coughing, paralysis due to spinal cord compression, and bone fractures. The intention of treatment at this stage is not curative – although some prolongation of life may be possible – but to relieve symptoms and improve quality of life. Patients may be offered radiotherapy, hormone treatment, chemotherapy and, possibly, immunotherapy.

The principles of treatment are generally similar for men and women.

Breast Cancer Services

Since the publication of the first edition of this Guidance Manual in 1996, there have been profound improvements in the provision of services for patients with breast cancer. Although there has not been an audit covering all the NHS, it appears that most of the recommendations have now been implemented in the majority of trusts in England and Wales.

A new report, jointly published by the Commission for Health Improvement and the Audit Commission (CHI/Audit), gives a snapshot of services in one cancer network in each of eight English regions, plus one in Wales. These networks dealt with 17% of the one and a quarter million hospital episodes for patients with a primary diagnosis of cancer in 1999/2000.

The CHI/Audit teams found that the concept of multi-disciplinary team (MDT) working is particularly well established in breast cancer. Almost all Trusts treating these patients now have weekly MDT meetings and all but one of the lead consultants felt that the benefits definitely outweighed the time invested in these meetings. There is evidence, too, of increased specialisation among surgeons. In 1995/6, when the COG guidance was being prepared, 39% of breast cancer operations in one network were carried out by surgeons with annual caseloads of

²¹ Maguire P. Psychological Aspects. In: Dixon M, ed. *ABC of Breast Diseases*. BMJ Books 2000.

50 or more patients with breast cancer; two years later, in 1997/8, this figure had doubled.

However, there are some problems with the way teams function. Some patients are still being treated by non-specialist surgeons who do not attend MDT meetings, and these patients may not be discussed by the MDT. Only about a third of MDTs have administrative support to list patients to be discussed and ensure that their notes are available at the meeting. In addition, record-keeping is not good, with minutes taken at just 56% of meetings.

Breast cancer services lead the field in patient-centred care. Two-thirds of lead consultants had made some attempt to assess patients' views of the services they provide – considerably more than for other cancer sites. All trusts had locally produced information for patients, although the quality of such information may not have been assessed. And 87% of Trusts had one-stop diagnostic clinics.

Even so, there are signs that services are not always as responsive to patients' views as they could be. For example, it appears that some surgeons may not give patients sufficient unbiased information to allow them to participate in the choice between mastectomy and breast conserving surgery. In some hospitals, breast conservation rates are as low as 20%, whilst in others, they are over 80% – and these rates remain consistent from year to year. The most probable explanation for this pattern is that lead clinicians in these hospitals have strong preferences for one or other particular type of operation, and this preference has an undue influence on the choice of surgical procedure.

There is much variation in service provision and treatment regimens. The introduction of a maximum two week waiting time to the first outpatient appointment for patients designated as 'urgent' has decreased waiting times for most patients but increased them for others. In a recent study in 15 breast units, however, approximately one-third of breast cancer cases were found to have been referred in the 'non-urgent' stream.²² There is also evidence of wide variation in waiting times for surgery.^{23,24}

Finally, although the evidence is scanty and largely anecdotal, it appears that the guidance suggesting that follow-up should be drastically curtailed is widely ignored. Scarce resources are still being used for this largely ineffective activity.

Any waste of time and facilities is particularly regrettable in view of the rising detection and prevalence of breast cancer, which produces increasing workloads for clinicians. It has been argued that improved services and treatments have

²² Sauven P on behalf of the BASO Breast Group. Letter, *BMJ*, 2001; 323:864-5.

²³ Cancer Services Co-ordinating Group, Cardiff. *The Management of Breast Cancer in Wales (1997) – a retrospective audit carried out on behalf of the Cancer Services Co-ordinating Group*. Cancer Services Co-ordinating Group 2000.

²⁴ Maguire P. Psychological Aspects. In: Dixon M, ed. *ABC of Breast Diseases*. BMJ Books 2000.

increased the workload of clinicians within designated breast units without a corresponding increase in staff.²⁵ There are personnel shortages in most of the key disciplines required for patients with breast cancer.

The Manual of Cancer Services Standards²⁶ outlines the framework intended to enable local cancer networks in England to assess the quality of services they provide. Breast cancer services are currently being assessed in the first round of peer review visits, which will be concluded by October 2001. *Information to be added on findings.*

Since 1999, the Cancer Services Collaborative has been developing practical ways of changing services to improve the experience and outcomes of care for people with breast cancer. This work has been summarised in a Service Improvement Guide which describes specific examples of new and effective initiatives in local hospitals across the country. Different clinical teams have tested and shared ideas and experiences and each is available to explain to others what worked – and what didn't work – for them. The Collaborative approach is now being rolled out to every cancer network in the country.

Where appropriate, information derived from the Cancer Services Collaborative *Breast Cancer Service Improvement Guide* (2001) is included in this Manual. Further information is available on the net at www.nhs.uk/npat.

²⁵ Dewar JA, Twelves CJ, Thomson CS for the Scottish Breast Cancer Focus Group and the Scottish Cancer Therapy Network. Breast Cancer in Scotland: Changes in Treatment and Workload. *Clinical Oncology*; 1999; 11:52-54.

²⁶ Department of Health. *The Manual of Cancer Services Standards*. Department of Health, Dec 2000.

1. Primary care and the management of women at high risk

Recommendations

Integration of screening and services for symptomatic patients

Patients with possible or suspected breast cancer are usually referred by GPs to breast services (around 80%) or identified through routine screening (20%). For historical reasons, breast screening has been organised separately from the network structure of the rest of cancer care, with different quality assurance arrangements.

Each cancer network should review arrangements for breast screening that exist in any part of the network, in conjunction with local service providers for symptomatic breast cancer, with the objective of better aligning these two forms of services. The review should aim to create greater consistency in clinical policies, organisation and care throughout the network, without reducing access to local services. The scope of the review should encompass the organisation of screening, the assessment of women with positive or suspicious mammograms, the clinical management of patients, and quality assurance/quality management arrangements across the whole service. Changes should be implemented without prejudicing the continuing breast screening programme.

Referral guidelines

All patients with possible or suspected breast cancer should be referred to a breast clinic without delay. Referral guidelines have been published by the Department of Health (see below).²⁷ The majority of patients present with lumps in the breast or axilla which can be detected by clinical examination; overall, about 10% of lumps assessed in breast clinics are found to be malignant. Less common signs and symptoms are also described in these guidelines; those which are usually caused by non-malignant conditions may not require urgent referral. Local referral guidelines should be agreed and disseminated by cancer networks; these should include guidance on dealing with asymptomatic patients with family histories of breast cancer (see below). GPs should be given feedback on their use of these guidelines, as reflected in the appropriateness of their referrals to breast clinics.

Urgent referral (within two weeks):

²⁷ Department of Health. *Referral Guidelines for Suspected Cancer*. Available on <http://www.doh.gov.uk/cancer>. The wording has been slightly altered in this document to improve clarity.

- Patients aged 30 or over (the precise age criterion to be agreed by each network) with a discrete lump in the breast.
- Patients with breast signs or symptoms which are highly suggestive of cancer. These include:
 - Ulceration
 - Skin nodule
 - Skin distortion
 - Nipple eczema
 - Recent nipple retraction or distortion (< 3 months)
 - Unilateral nipple discharge which stains clothes

Conditions that require referral, not necessarily urgent:

- Breast lumps in the following patients, or of the following types:
 - Discrete lump in a younger woman (age < 30 years)
 - Asymmetrical nodularity that persists at review after menstruation
 - Abscess (urgent referral required)
 - Persistently refilling or recurrent cyst
- Intractable pain which does not respond to simple measures such as wearing a well-fitting bra and using over-the-counter analgesics such as paracetamol.
- Nipple discharge:
 - Bilateral discharge sufficient to stain clothes in patients aged < 50 years.
 - Bloodstained discharge in patients aged < 50 years (urgent referral required if discharge is unilateral).
 - Any nipple discharge in patients over 50 years of age.

Clinical breast examination in primary care

Each primary care team should include at least one GP who has had specific training in carrying out clinical breast examination (CBE) in women with breast symptoms. Women with symptoms which could be due to breast cancer should be referred to the breast care team. Routine breast examination for asymptomatic women is not recommended.

Women with a family history of breast cancer

The level of risk for most women who have relatives with breast cancer will be only slightly higher than for others in the same age-group; such women should normally be reassured and managed by primary care teams. An information pack to facilitate risk assessment in primary care is available from the Cancer Research Campaign.²⁸ This pack includes referral guidelines, a management guide and information booklets for patients.

Women who are judged by their GP to have a moderate or strong family history, and who are anxious about the risk, should be referred to a breast cancer team at a local hospital or to a family history clinic for assessment, where those at high risk can be given information on the management options available. If regular surveillance is offered, the woman should be given a truthful description of the potential negative effects such as false positive results.

Accurate information on the advantages and disadvantages of genetic testing should be available to all who want it. At present, genetic testing is restricted to high-risk families after assessment by the regional clinical genetics service, but the Department of Health is planning to issue recommendations on services for people with a family history of cancer.

Prophylactic mastectomy should be available for women at high risk who request it. Such women should have counselling before any decision is made on surgery, and should be given opportunities to discuss all aspects of the operation, including reconstruction. No drug is licensed for prevention of breast cancer.

Treatment of menopausal symptoms in women at high risk

Although there is no evidence to show that high-risk women should not use hormone replacement therapy (HRT), it is known that forms of HRT which contain both oestrogen and progestogen can increase the risk of breast cancer. Women with strong family histories of breast cancer who request help with menopausal symptoms might therefore prefer to try non-hormonal interventions such as the serotonin re-uptake inhibitor venlafaxine as first-line treatment. Women who require treatment for osteoporosis and have a family history of breast cancer should be offered raloxifene.

Anticipated benefits

More appropriate referral for women with breast symptoms could be achieved if GPs followed referral guidelines more precisely. Clear information on risk and selective referral to a breast clinic can reduce the anxiety experienced by women with family histories of cancer, and is a cost-effective strategy for women at low

²⁸ CRC Primary Care Education Research Group, *Familial breast and ovarian cancer: an information pack for primary care*. Available on request from CRC Primary Care Education Research Group, University of Oxford; tel. 01865 226788, fax 01865 226784.

or moderate risk. For high risk women, prophylactic surgery can reduce the risk of developing breast cancer by as much as 90%.

Evidence

Appropriateness of referral

The number of patients referred to breast clinics varies widely between GPs.(B) A study in Wales reported that just over half of women who consulted with a new breast symptom were referred to a clinic. The median number of new presentations per GP was 6.5 per annum, with a range from 1.9 to 14.8.[The BRIDGE Study Group, 1999 #23242] A study of Sheffield GPs reported a slightly lower referral rate, but it appears that this under-estimated the target group.[Newton, 1999 #23293]

There is scope for improvement in selection of patients for referral. Surveys of consultants working in breast clinics reveal that about a quarter of GP referrals fall outside published guidelines – but also, a third of women who do have cancer are not referred urgently.[Patel, 2000 #23307; Laver, 1999 #23292; Sauven, 2001] There is wide variability between breast units in the overall proportion of urgent referrals (15% to 67%), the proportion of referrals outside guidelines (8% to 51%), and in the proportion of cancers diagnosed after non-urgent referral (6% to 60%).[Sauven, 2001] Careful adherence to NHS guidelines could substantially reduce the rate of inappropriate referral without increasing the risk of missing cases of cancer.(B)

Breast examination

A systematic review that included two very large RCTs, a controlled trial and five cohort or case-control studies concluded that regular breast self-examination has no effect on breast cancer mortality.[Baxter, 2001] There is in fact evidence of harm caused by significantly increased rates of biopsy for benign breast lesions. There is no reliable evidence of any benefit associated with breast self-examination in any group of women.(A)

Women with a family history of breast cancer

Although many GPs show an interest in cancer genetics, their knowledge of the subject is often limited.(B) GPs are 6.6 times more likely than their women patients to raise the issue of family history; only a minority of women consult with specific concerns about their risk of cancer.[Women's Concerns Study Group, 2001 #23255] A prospective study in the Netherlands concluded that the value of giving advice on genetic risk in primary care is questionable.[de Bock, 2001 #23254](B)

A computer programme designed to assess risk of breast and ovarian cancer associated with family history (RAGs) has been shown to produce appropriate management decisions when used by GPs. 33 of the 36 GPs in a study which

compared methods for assessing genetic risk produced more accurate pedigrees with RAGs than with Cyrillic or pen and paper, and also preferred using RAGs.[Emery, 1999 #23548; Emery, 2000 #23549](B)

Referral to a breast care team for counselling can reduce anxiety among high risk women,[Brain, 2000 #23079] and regular surveillance may improve the chance that breast cancer will be detected at an early stage.[Chart, 1997 #17908] However, adding individualised genetic assessment, genetic counselling, and gene testing to typical advice and surveillance from a hospital breast clinic does not improve psychological outcomes and the impact on other outcomes is not yet known. The cost of providing specialist services is greater than standard care and at present, appears to offer little benefit to women with family histories of breast cancer.[Brain, 2000 #23079](A)

Prophylactic mastectomy

There have been no randomised trials of prophylactic mastectomy, but prospective and retrospective studies are consistent in showing a very marked reduction in the incidence of breast cancer – probably around 90% – among women at moderate or high risk who undergo this form of surgery.[Meijers-Heijboer, 2001 #23572; Hartmann, 1999 #23185](B) Prophylactic mastectomy leads to a significant decrease in anxiety but some women's satisfaction with their appearance may be reduced despite breast reconstruction.[Bebbington Hatcher, 2001 #23268; Frøst, 2000 #22906] A US study suggests that, whilst few women regret having surgery, regret is less likely when discussion about prophylactic mastectomy is initiated by the woman herself.[Borgen, 1998 #23453]

Chemoprevention

Tamoxifen

Trials of chemoprevention using tamoxifen have not produced consistent results. A large US trial found a highly significant reduction in breast cancer incidence but European trials have yet to show any benefit.

The US trial (n=13,388) reported that tamoxifen reduced the incidence of breast cancer in high-risk women by 49% – a result so dramatic that the trial was stopped early.[Fisher, 1998 #23120] However, tamoxifen was associated with adverse effects including hot flushes, vaginal symptoms and sexual problems; and in women over 50, endometrial cancer, pulmonary embolisms and cataracts.[Day, 1999 #23230](A)

A UK trial recruited 2494 women with family histories of breast cancer. Interim analysis after a median period of almost six years shows no difference between tamoxifen and placebo in breast cancer rates (RR 1.1, 95% CI 0.7 to 1.7, P=0.8).[Powles, 1998 #23233] Follow-up is continuing.[Hutchings, 1998 #23231] An Italian trial in lower-risk women who had undergone hysterectomy also found no difference between tamoxifen and placebo in the incidence of breast cancer, but reported a significantly increased risk of vascular events in the tamoxifen group.[Veronesi, 1998 #19784]

Other potential chemoprevention agents

A study of raloxifene for postmenopausal women with osteoporosis found that it decreased the risk of invasive breast cancer by 76%, compared with placebo (RR 0.24 95% CI 0.13 to 0.44, $P < 0.001$), but the risk of thromboembolic disease increased (RR 3.1 95% CI 1.5 to 6.2). [Cummings, 1999 #23170] (A) Studies are in progress to assess whether the risk of breast cancer is reduced by fenretinide, either alone or in combination with low dose tamoxifen.

Measurement

Structure

- Availability of services for women whose family history leads them to be anxious about risk.
- Arrangements to deal with women at moderate or high risk of breast cancer.

Process

- Audit of appropriateness of GP referrals when assessed against NHS guidelines.
- Feedback to GPs on the appropriateness of referral to breast clinics.

Outcome

- Number of women at moderate or high risk referred for counselling and assessment.
- Correct identification and referral of urgent cases.
- Proportion of breast cancer rates in non-urgent referrals.

Resource Implications

The resource implications of these changes are not expected to be significant. More appropriate GP referral could reduce the number of women seen in breast clinics.

2. Patient-centred care

The welfare of patients - the *raison d'être* of health services - is multi-dimensional. While women with breast cancer are primarily concerned that their chances of survival are maximised through appropriate clinical treatment, it is important that their other needs are also met. In particular, they must always be treated as people and their dignity respected. The recommendations below refer to specific issues on which there is research evidence; there may be other areas where change may be required.

Recommendations

Minimising delay

There should be minimal delay between the referral from the GP and an outpatient appointment, and between the first consultation and communication of the diagnosis to the patient. The breast unit should have clear and unambiguous arrangements for rapid referral from GPs. Proposals on referral times are given in guidelines published by the British Association of Surgical Oncologists (BASO).¹

There should be pre-booking systems for appointments. This requires careful monitoring of clinic capacity and demand to ensure an appropriate balance between urgent and non-urgent clinics.

Whilst administrative delay and delays before treatment should be minimised, patients need adequate time to consider and discuss treatment options; this is one part of the patient journey at which some patients may appreciate a negotiated delay. Staff should be alert to the individual decision-making needs of different patients and appointment systems should be sufficiently flexible to accommodate them.

Clear information for patients

At every stage, patients should be offered clear, objective, full and prompt information in both verbal and written form. Each patient should receive information relevant to her case about the disease, diagnostic procedures, treatment options and effectiveness. The amount and timing of information should take each patient's preferences into account. When there is a genuine choice between treatments, the information given must be sufficiently clear and detailed to allow the woman to make a decision based on evidence of differences in outcome. For example, women for whom alternative surgical procedures are possible should be told about differing probabilities of local recurrence and the lack of significance of local recurrence in terms of survival, the effects of radiotherapy, possible adverse effects of treatment, and, as far as possible, given a realistic assessment of their predicted outcome. They should be offered well-produced information leaflets which are both accurate and comprehensible, and guidance from a member of the breast care team when required.

Patients should also be informed about sources of social and practical help, such as local support groups and disability and benefits helplines, both verbally and in written form. Information should be provided in appropriate languages for patients from ethnic minorities.

Patient records should include a checklist to show what information has been provided and a copy should be given to the patient.

Effective communication

Providers must be sensitive to potential problems with communication. Members of the breast care team - particularly those providing direct clinical care - should have special training in communication and counselling skills.

It is important that senior members of the breast care multidisciplinary team – specifically, surgeons and oncologists – should have formal training in communication skills.

They need to be aware that patients often find it difficult to take in information given during the consultation, especially just after receiving their diagnosis. Patients should be given adequate time to reflect before being expected to make any decisions about treatment.

There should be agreed procedures and protocols for breaking bad news at key transition points in the disease. Guidelines for giving the cancer diagnosis are available.²

The role of the breast care nurse (see topic area 8 Team) is especially important in facilitating continuing communication. The unit should ensure that there is a named person with whom each patient can communicate at any time. Patients should have the name and contact number for a particular nurse, and should, whenever possible, see and speak to the same nurse. The GP and the primary care team should be given the name of this nurse. Patients should have access via the nurse to specialists in the team if they become concerned about possible recurrence.

There should be a system for dealing with complaints by patients. Complaints should be taken seriously and answered promptly.

Psychosocial support

Psychosocial support should be available at every stage to help patients and their families cope with the effects of the disease. These issues should be considered in the design and provision of all aspects of treatment services. Health care personnel should have training to improve their ability to recognise the psychological needs of patients and to deal with them appropriately.

Social support should be available and there should be close liaison with local social services.

Anticipated Benefits

Minimising delay

Short delays reduce anxiety and may improve survival. During the period between initial suspicion of breast cancer and diagnosis most women are anxious, and delay may affect their subsequent relationship with breast cancer services. Patient surveys show that women are particularly concerned about delay between initial presentation to GPs and diagnosis.

Clear information

Women with breast cancer want to understand what is happening to them and may also want to know about their prognosis. Information is valued for its own sake and well informed women tend to suffer lower levels of anxiety. It is also crucial to effective involvement in decision-making about treatment. Most women do not suffer negative consequences and express satisfaction when

information is provided in a structured, understandable and comprehensive way. Good information may improve compliance with treatment, reduce complaints, and enhance outcomes valued by patients.

Effective communication

Good communication is likely to reduce anxiety and anger and give patients greater confidence. Discussion will increase the chance that each patient receives the treatment that is most appropriate for her, as well as reducing stress experienced by both clinician and patient. Health care workers may come to treat patients in detached or even dehumanised ways as a way of reducing their own emotional stress; training in counselling and communication skills can help professionals to recognise and overcome this problem. Supportive team working may also help.

Psychosocial support

Psychosocial support can reduce levels of psychological morbidity, reduce symptoms, and may improve survival. Some women may develop a significant anxiety disorder or depression; in many cases this is not recognised and these women may not receive appropriate treatment.

It should be noted that half the patient population is over 65; many older women live alone and may need practical help with their everyday lives. Women who have dependants are also likely to need assistance. The primary and palliative care teams have particularly important roles in ensuring that these needs are identified and met.

Evidence

Minimising delay

Although relatively short delays are unlikely to affect the clinical course of the disease, the importance of minimising delay is consistently reported by patients in surveys to be very important, and is recognised by professional consensus (C). Longer delays are usually due either to patient delay or the GP's failure to refer. Whilst there is evidence that delays of at least six months may reduce survival (B), there is debate about the effects of shorter delays.

Delays in diagnosis and treatment of breast cancer are generally short. Over a quarter of patients are referred urgently and 95% of these are seen within two weeks; the majority of non-urgent referrals are seen within a month, usually in one-stop clinics where all investigations necessary for a diagnosis are carried out in a single day.²⁹ Some hospitals have streamlined their systems so that all patients are now seen within two weeks; the Cancer Services Collaborative *Service Improvement Guide* for breast cancer explains how this was achieved in two particular hospitals.

About a third of operations for breast cancer take place within two weeks of diagnosis, 90% within a month. Overall, the average (median) waiting time from diagnosis to surgery is 17 days.³⁰ (B)

²⁹ CHI/Audit Commission report; hospital data from winter 2000/2001.

³⁰ CHI/Audit Commission report; hospital data from winter 2000/2001.

Clear information

Patients value accurate information and many women feel they are not given sufficient information. There is fairly strong evidence that breast cancer patients benefit from involvement in treatment decisions, but women vary considerably in the amount of responsibility they wish to take and clinicians need to be sensitive to the degree to which individual patients want to become involved in decision making (B). The evidence suggests that patients want to be confident that a certain treatment is really indicated, rather than necessarily to take responsibility for the ultimate decision.

Effective communication

There is considerable evidence of problems with communication between doctors and patients which cause unintended distress. Women report that they may be unable to take in information or to participate effectively in discussion immediately after receiving a diagnosis of breast cancer (B). A taped or written record of the consultation, which allows patients to consider the information during subsequent days, may be helpful.

Surveys of patients with cancer frequently highlight insensitive delivery of bad news as one of the most distressing aspects of their experience. (*References to NCA/charity reports to be added.*) An unpublished audit at a Plymouth hospital found that a quarter of patients with breast cancer felt that their diagnosis had been given in an insensitive manner, and that surgeons were the worst offenders. It was clear that some senior consultants needed training in breaking bad news.(B) A Dorset audit of women's experience of hearing that they had breast cancer reported improvements after a surgeon attended a communication skills course – a recommendation made in an earlier audit report.[Hughes, 1996 #23527](B)

Educational interventions for oncologists offer the additional benefit of improving their confidence in their ability to deliver bad news sensitively.[Fallowfield, 1998 #23117] In Plymouth, a short hospital-based training workshop produced an overall increase in confidence of 20% among senior doctors, nurses and other health professionals.[Abel, 2001 #23604](B)

Psychosocial support

There is fairly strong evidence that the current ability of many doctors and nurses to detect patients' needs is limited, but on-going contact with a trained and experienced breast care nurse can reduce patients' anxiety, depression and physical symptoms up to a year after treatment. A nurse who is involved in the patient's treatment appears to be able to offer more effective help than support organisations which do not have access to clinical information about the individual (A).

There is very strong evidence for cancer patients in general, that a variety of cognitive and behavioural interventions - including relaxation training, guided imagery, desensitisation, biofeedback, acupuncture/acupressure and standard information accompanied by counselling - can reduce side effects of therapy and alleviate psychological and functional disturbances. Some forms of psychological and psychosocial counselling have been shown to increase life expectancy and improve a range of psychological, quality of life and other functional outcomes (A).

The research on social support for patients is generally poor. There is a need for methodologically sound studies which focus on the effects of simple supporting strategies for breast cancer patients.

Measurement

Structure

- Availability of information in Cancer Units about breast cancer and its treatment.
- Availability of training courses for senior health professionals in communication skills.
- Provision for patients to give feedback on their experience of treatment, facilities and the service they receive.
- Availability of feedback from patients and carers to inform the need for, and nature of, action plans to improve services.
- Availability of appropriate and adequate verbal and written information about breast cancer in general and the patient's own situation and options, for every patient.
- Providers should demonstrate provision of services designed to meet the psychosocial needs of patients.
- There should be evidence that professionally produced written information is available for patients.

Process

- Audit of patients' views of how news of their diagnosis was broken.
- Audit of patients' experience of breast cancer services.
- Attendance at communication skills courses by senior clinicians who treat patients with breast cancer.
- Data on the average times and distributions of times for the following: between referral and first appointment; between first appointment and receipt of a diagnosis; between diagnosis and surgery. BASO guidelines' provide a standard.

Outcome

- Patients' views of information and services provided.
- Evidence that patients are given opportunities to discuss treatment options with both senior clinicians and their breast care nurse, and that they have adequate time to consider them.
- Proportion of women with newly-diagnosed cancer who undergo mastectomy (this should not be greater than 50%).
- Simple surveys of women or focus groups should be carried out by providers to assess the adequacy of each component of patient-centred care.

Resource Implications

- The organisational aspects of minimising delay are unlikely to have cost implications.
- Resources should be allocated for the purchase of information leaflets, for the production of leaflets on local services and support groups, and for patient surveys.
- Because good communication takes time, both for doctors and specialist nurses, arrangements for better communication have human resource implications. These are hard to quantify.
- The breast care nurse and lead clinicians may need additional training in identifying patients' psychosocial needs, counselling skills and communication skills.

Draft

3. Rapid and accurate diagnosis

Recommendations

All patients with suspected breast cancer should be treated in the same way, whether they are identified by screening or referred with symptoms. Ultrasound imaging should be available to increase diagnostic sensitivity when mammography fails to produce clear results. The role of MRI is being assessed in clinical trials.

Diagnostic services must be able to provide rapid and accurate information on imaging results and tissue samples. The combination of clinical examination, mammography/ ultrasound and image-guided core-biopsy or fine needle aspiration (FNA) - known together as triple assessment - should be available for women with suspected breast cancer at a single visit. Centres which predominantly use core biopsy should also maintain expertise in FNA cytology so that this method can be used when appropriate.

All facilities and staff needed to carry out these three types of test should be in close proximity. A breast care nurse should be available for support and counselling.

The results of tests should be given to the patient within five working days and within three days if possible. Thus women who do not have breast cancer can be reassured and treated if necessary, while those who do may proceed rapidly to treatment. (See Topic 2, *Patient-centred care*.)

The accuracy of triple assessment depends on the quality of each constituent test. There is wide variation in the adequacy of cytology samples taken by fine needle aspiration. Pathologists and cytologists should record the adequacy of samples; if they fall below the necessary standard for accurate diagnosis, surgeons and pathologists may require additional training in the technique and interpretation of samples, respectively.

Surgical biopsy is appropriate when triple assessment does not give a definitive result (see BASO guidelines).¹

After surgery, the pathologist should give detailed reports on excised cancers which include information on tumour type, pathological size, histological grade, vascular invasion, extent of ductal carcinoma in situ, tumour margins, and lymph node status when appropriate. This information should also be given to the cancer registry.

Assays to measure hormone receptor status should be carried out on all excised tumour samples; this information is crucial to decision-making on therapy. Oestrogen receptor status should be assessed first; if the tumour is oestrogen-receptor negative or poor, progesterone receptor status should be measured. Tissue blocks from individual patients should be retained for possible future use.

All laboratories which carry out hormone receptor status assays or other tests intended to predict response to therapy should participate in the national quality assessment scheme (UK NEQAS-ICC). Networks should ensure that these laboratories are able to demonstrate high levels of accuracy (in particular, low false negative rates for oestrogen receptor status); this should be confirmed by a high-volume reference laboratory.

Following primary treatment, regular mammography should be available (see Follow-up). Radiography facilities and imaging should be subject to the same quality assurance criteria as the NHS Breast Screening Programme.'

Anticipated Benefits

Routine use of triple assessment can increase the speed and accuracy and reduce the cost of diagnosis. When the three tests give consistent results, a definitive positive or negative diagnosis (predictive value) can be given 99% of the time. This minimises the need for open biopsy, thus preventing unnecessary surgery and reducing anxiety. Surgical biopsy rates can fall by over 50% when triple assessment is used.

Core biopsy samples can be processed within 48 hours, so the delay between investigation and the consultation at which women are informed of the results can be kept short. Greater use of ultrasound as part of the diagnostic strategy will reduce the risk that cancers will be missed, particularly in younger women. In addition, ultrasound is useful for predicting tumour size and planning surgery. More consistent and accurate assessment of hormone receptor status will permit better targeting of therapy.

Detailed diagnostic reports on tissue samples removed during surgery provide important information for decision making on subsequent management, and for cancer registry records. The survival and quality of life benefits associated with appropriate surgery and adjuvant therapy cannot be fully exploited if diagnosis is inadequate.

Evidence

There is fairly strong evidence that triple assessment increases the accuracy and reduces overall cost of diagnosis when compared with selective use of component tests (B).

Core biopsy or fine needle aspiration cytology (FNAC)?

Both core biopsy and fine needle aspiration (FNA) are effective methods for taking tissue samples from breasts, but there has been a widespread shift in the UK from FNA to core biopsy.(C) Audit evidence shows very wide variations between centres in both adequacy of sampling and false negative rates with both methods, which suggests that operator skill is crucial for determining outcome.[Britton, 1999 #23323]

Audit of UK screening centres found that core biopsy was more likely to give an unequivocal result (85% of core samples categorised as benign or malignant, compared with 62% of FNA samples) and inadequate sampling is less common

(core biopsy median inadequate sample rate 10.6%, range 0 to 40%, compared with 23.2% for FNA, range 4.7% to 75.8%); however, core biopsy false negative rates are higher (13% versus 6%).[Britton, 1999 #23323](B)

An audit from a single small centre (Princess Royal Hospital) shows that FNA cytology can produce excellent levels of accuracy and consistently adequate sampling when carried out by skilled clinicians.[Hinton, 1999 #23344] Core biopsy may be less effective than FNAC for small mobile lesions.[Ballo, 1996 #23458](B) Although the authors of these studies state that both core biopsy and FNA are well tolerated, they do not provide any information on patients' views.

Imaging

Ultrasound is particularly useful for guiding FNA or biopsy of small or non-palpable lesions.[Vielh, 1998 #23327; Okamoto, 1998 #23329; Saarela, 1996 #23326](B) It can also complement mammography in differentiating between malignant and benign disease. The combined sensitivity of these modalities is greater than either alone, but the specificity is reduced. Pathological processing and assessment of tissue samples is crucial if either mammography or ultrasound shows an abnormality, to increase specificity when imaging results are inconsistent.[Moss, 1999 #23313; Skaane, 1999 #23314; Reinikainen, 1999 #14722](B)

The evidence review included studies on the effectiveness of MRI but this research is not summarised here because no recommendations are made. A UK multi-centre randomised study, comparing triple assessment alone with triple assessment plus MRI, began recruiting in late 2001.

One-stop versus two-stop systems: psychological impact

A prospective audit of patients' views of a one-stop clinic reported high levels of satisfaction (mean score, 9.2; maximum 10). What aspects of the clinic contributed to patient satisfaction is not clear.[Berry, 1998 #23299]

Research on the effects of delay between diagnostic investigations and giving women the results shows that this period of waiting is equally distressing for those who have cancer and those who do not.[Poole, 1999 #23308](B) An RCT comparing one- and two-stop systems found – not surprisingly – that women with a benign result who had received their results at a one-stop clinic were significantly less anxious six days later than those in the two-stop system, who were still awaiting their results. No difference was detected in anxiety levels at this point between women with breast cancer who had been given their results and those who had not. After eight weeks, women with cancer in both groups showed comparable levels of psychological well-being, except for higher levels of depression among women in the one-stop group.[Harcourt, 1999 #23305; Harcourt, 1998 #23304](A)

A small non-randomised study also found no difference between immediate and delayed communication of results in the anxiety levels of women with breast

cancer. Immediate communication was, however, associated with a significant fall in anxiety among those with benign results.[Ubhi, 1996 #23248](B)

The Harcourt RCT described above is often quoted as demonstrating that a two-stop system produces superior psychological outcomes. Whilst it may be argued that a delay between undergoing diagnostic investigations and receiving the results may have little effect on the distress suffered by women with cancer, this is a period of severe anxiety for all those awaiting the outcome of tests, most of whom do not have cancer. In addition, 26% of women in the RCT were lost to follow-up and the remaining groups were small. The evidence that a two-stop system reduces the psychological impact of the diagnosis eight weeks later cannot therefore be regarded as reliable.

Quality of hormone receptor assays

Problems with assessment of hormone receptor status in breast tumour tissue were revealed by a recent postal survey of UK breast cancer units. All provided access to oestrogen receptor measurement but there were very wide variations in criteria used to judge whether a tumour was oestrogen-receptor positive; the cut-off point for a positive finding ranged from 5% to 80% of cells. {Wishart, 2001}

A national quality assessment scheme (UK NEQAS-ICC) has been established to minimise variability between laboratories in hormone receptor status measurement. The NEQAS-ICC centre's routine assay has been shown to be 90 to 100% efficient in achieving optimal demonstration of hormone receptor status in breast tumours from over 150 different laboratories.[Rhodes, 2000 #23561]

Measurement

Structure

- A single system providing diagnostic and assessment services for symptomatic patients and those identified by screening.
- Systems for quality assurance monitoring of pathology laboratory services.
- Availability of modern ultrasound equipment to improve diagnostic accuracy and guide biopsy.
- Mammography/ultrasound and fine needle aspiration/wide bore needle biopsy facilities available in close proximity.

Process

- Audit of adequacy of tissue samples produced by core biopsy and fine needle aspiration for histopathological assessment.

- Women's views on diagnostic investigations, including level of discomfort experienced.
- Involvement in the UK NEQAS-ICC scheme.
- Use of written protocols for diagnosis.
- Adherence to BASO guidelines and pathology^{3,4} and cytopathology⁵ guidelines from the UK National Breast Screening Programme. These are valuable aids to auditing and improving the consistency of diagnostic performance and inducing improvements in clinical practice.
- Proportion of breast cancer patients who underwent triple assessment on the first visit.
- Diagnostic surgical biopsy rate and outcome of biopsies should be audited to assess the adequacy of initial diagnostic procedures.
- Audit of completeness of pathology reporting.

Outcome

- Accuracy of diagnosis in terms of false positive and false negative rates, both for each individual modality used and for triple assessment.
- False negative rate for hormone receptor status assays.

Resource Implications

Setting up a dedicated diagnostic service which can offer triple assessment in a single visit is likely to involve capital and human resource costs.

This is likely to be offset by a reduction in unnecessary surgery, improved outcomes, fewer return visits by patients, and the use of more cost-effective treatment.

Triple assessment is highly cost-effective. The addition of fine-needle aspiration to routine clinical examination and mammography costs about £20. Using concordant results of cytology and one other test avoids the need for biopsy about 3 times out of 4, giving an average net saving per diagnosis of £240 (day case biopsy) or £470 (in-patient). If only concordant triple assessment results are relied upon, the saving would still be about £150 or £300 (1994-5 prices).

Provision of ultrasound machines to improve diagnostic accuracy has capital cost implications.

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Draft

4. Surgery

Recommendations

DCIS

In general, recommendations on surgery apply to all forms of breast cancer, including ductal carcinoma in situ (DCIS). As in invasive cancer, mastectomy for DCIS is associated with lower rates of local recurrence; but survival rates after breast conserving surgery with adjuvant radiotherapy are as high as after mastectomy. Treatment options and choice of surgical operation should be discussed with patients, whose views should be respected when decisions are made.

Surgical margins

Sufficient tissue should be removed to ensure that no tumour is found at the surgical margins, since positive or narrow (<2mm) margins are associated with high rates of local recurrence. The minimum pathology dataset³¹ should include information on the distance of the closest margin to the edge of the tumour, in order that this can be audited against outcome.

The pathologist should confirm that the margins of excised tissue are free of tumour cells. Patients who are found to have positive margins should be offered re-excision or mastectomy.

Management of the axilla

Axillary lymph node status is the single most powerful prognostic indicator for breast cancer. Management of the axilla is a controversial area. The possible adverse effects and anticipated benefits of axillary sampling or clearance should be discussed with patients. Each unit should have a clear policy on management of the axilla which takes account of the importance of prognostic information that may be derived from staging of the axilla and minimises the problem of axillary recurrence.

Tumour is not likely to be found in the axilla in DCIS, but in invasive cancer, removal of lymph nodes affected by tumour is crucial to prevent recurrence in the axilla. Axillary clearance is likely to be appropriate for the 35-40% of patients with invasive cancer who have tumour in the axillary lymph nodes, but surgical dissection and complete clearance of these nodes represents over-treatment for most patients and is likely to increase morbidity without improving survival. Teams in centres which routinely carry out axillary clearance should consider

³¹ The minimum dataset for breast cancer pathology should correspond with the latest version available from the Royal College of Pathologists.

training in less invasive forms of surgery. When axillary sampling is used, at least four nodes should be removed.

Sentinel node biopsy is an alternative to axillary sampling or clearance which provides information on the probable tumour status of other axillary lymph nodes; when sentinel node histology is negative, further treatment to the axilla may not be necessary. This is a relatively new technique and still under study, but when carried out by skilled surgical teams, it can be as reliable as traditional axillary dissection. Teams which use sentinel node biopsy should have adequate training, should audit their results, and should be able to demonstrate false negative rates below 10%.

The optimum form of management for patients who have no clinical signs of tumour in their axillary nodes is uncertain. It is anticipated that ongoing multi-centre studies will provide further information on the effectiveness of sentinel node biopsy and these trials should be supported. Patients should be given realistic information about the balance of risks associated with alternative methods of axillary management and their views should be respected.

Breast reconstruction

Surgeons should aim to provide breast reconstruction at the time of initial surgery, rather than carrying out a cosmetic operation some time later. If breast reconstruction is not available within one month of diagnosis, women should be offered routine surgery but given the option of waiting a little longer for reconstruction. When women choose this option, the reason for the delay should be recorded.

Choice of operation

A range of primary operations should be available. If the cancer is not too large or diffuse, surgical options include mastectomy (removal of the whole breast) or breast conserving surgery (wide local excision or lumpectomy). In such cases, the choice should be made jointly by the surgeon and the patient, who should be fully informed of all the options and their potential risks, benefits and implications for further treatment. Breast reconstruction should be discussed with patients who are to undergo mastectomy.

The proportion of each type of operation done will reflect local differences in case-mix and women's preferences. Surgeons should have the technical skills to support a full range of choices. Suitable patients should be offered breast conserving surgery. Breast reconstruction should be available at the time of, or after, mastectomy, provided either by a plastic surgeon or a breast surgeon trained in the appropriate techniques.

Breast surgery, the management of excised specimens, and treatment decisions based on pathology and other prognostic information should follow locally written protocols based on BASO guidelines.' Surgical treatment should not be offered or withheld on grounds of age alone.

Post operative care

After surgery, women should be given information on wound care, advice on exercise, and information on dealing with the after-effects of surgery. Support and counselling should be

available and women should be given opportunities to talk over their feelings and fears with an experienced breast care nurse.

Anticipated Benefits

Improved surgical technique through training and audit should improve the overall standard of management of the axilla. At present, the axillary nodes are understaged in about 20% of patients; this could lead to inappropriate treatment and increased risk of recurrence. Increased use of sentinel node biopsy by trained surgical teams offers the advantage for patients of reduced morbidity and, depending on hospital discharge policy, it could reduce in-patient stay.

Immediate, rather than delayed, breast reconstruction is associated with better psychological outcomes for women and reduces the probability that surgery will be required more than once.

Surgery with associated radiotherapy and/or systemic adjuvant therapy where appropriate controls local disease and reduces recurrence. There appears to be no difference between surgical procedures in terms of overall survival. Clearance of surgical margins reduces local recurrence, which can cause great distress to patients.

Staging of the axilla by sampling or clearance of lymph nodes allows appropriate management of clinical disease. Staging can provide accurate prognostic information and provides essential information on case-mix for audit and outcome measures.

Women are likely to feel less anxious and depressed if they have opportunities to talk through the implications of their treatment and understand what is expected to happen next.

Evidence

Local recurrence in DCIS

A meta-analysis (n=2407) of 23 cohort studies and one RCT showed lower local recurrence rates at 5 years in women treated with mastectomy (4.6%, 95% CI 2.3 to 7.6), compared with breast conserving surgery with or without radiation (21.5%, 95% CI 14.0 to 30.7). Conserving surgery plus radiation had a similar risk of recurrence (10.6%, 95% CI 5.6 to 16.9) to mastectomy alone (7.3%, 95% CI 2.7 to 14.1). Five-year mortality rates were similar (around 4%) for both forms of surgery. Surgical margin involvement was associated with higher local recurrence rates. Radiotherapy reduced risk of local recurrence by 73-89%, but this was not associated with improved survival.[Cancer Care Ontario Practice Guidelines Initiative, 2001 #22955](B) The studies included in this meta-analysis were of weak design so these findings cannot be regarded as definitive.

Local recurrence in invasive cancer

Local recurrence is significantly more common when surgical margins contain tumour.

There is strong evidence from a review of 19 randomised controlled trials and retrospective series that local recurrence is more probable when cancer cells from tumour margins are left behind after

initial surgery. This holds true even after radiotherapy. The absolute magnitude of the risk varies from 5 to 20% at 10 years (A).

It is still not clear, however, what constitutes an adequate surgical margin. A retrospective analysis found no significant differences in outcomes between patients with negative and close margins (typically within 2mm), or between patients with positive and indeterminate margins. A US study of outcomes among women with invasive cancer found that breast-relapse-free survival at 10 years was 98% for patients with negative or close margins and 82% for positive or indeterminate margins ($p < 0.001$). [Obedian, 2000 #23334]

Management of the axilla

Effective axillary management is important both to reduce the risk of recurrence in the axilla, and for long-term survival. Different surgical techniques may be used to achieve this, and whilst the evidence is not yet robust, it appears that these methods can produce similar outcomes in terms of disease control.

There is strong evidence that axillary clearance reduces the rate of axillary recurrence (A). Clearance of the axilla is, however, associated with adverse effects in some cases, notably lymphoedema and limitation of arm movement, and is not indicated in in-situ cancer of the breast (C).

A randomised trial comparing level III axillary node clearance with axillary node sampling found no statistically significant differences in survival or time to recurrence. [Chetty, 2000 #22851] (A)

In 11 case-series of patients who had sentinel lymph node biopsy followed by standard axillary lymph node dissection, the sentinel node was identified in 83.6% of patients and its histology was the same as the axillary lymph dissection in 98% of cases. The false negative rate, where the sentinel node was negative but axillary dissection revealed malignancy, was 5.1%. In 52% of 281 cases in which the sentinel node was identified, malignancy was only found in this node. The authors of this meta-analysis suggest that surgeons should demonstrate a false negative rate no greater than 5% before they consider using sentinel node biopsy rather than axillary dissection. [Miltenburg, 1999 #19245] An additional primary study reported similar findings. [Jaderborg, 1999 #23125] (B)

In a study of women given a choice between sentinel node biopsy and routine axillary dissection, the sentinel node was negative in 285 of 379 biopsies and no dissection was performed. [Veronesi, 2001 #23511] After a total of 343 woman-years, there were no cases of clinically evident axillary node metastasis. The authors concluded that sentinel node biopsy should be the procedure of choice for staging the axilla in women with small tumours and clinically negative nodes. (B)

In a US study of 125 consecutive women with clinically negative nodes, 54% had negative sentinel nodes and no further axillary dissection was carried out. After a median of 39 months, there were no local or axillary recurrences. Complications (including seroma, wound infection, haematoma and chronic lymphoedema) were

ten times more common after axillary dissection – 34% compared with 3% after sentinel node removal only.[Giuliano, 2000 #23508](B)

Audit data suggest that trained British surgeons performing sentinel node biopsy procedure can achieve a success rate greater than 95% and a false negative rate as low as 5% (Robert Mansel, personal communication). Ongoing multi-centre studies (NSABP B-32 and ACSOG Z0010) are expected to show whether sentinel node dissection can replace axillary dissection.

Breast reconstruction

Retrospective reports suggest that women are more likely to require additional surgery if they have immediate, rather than delayed, breast reconstruction.[Francel, 1993 #23410; Walz, 1991 #23420] However, the majority of immediate reconstruction operations are successful, so there is a good chance that surgery will be required only once. In addition, women prefer immediate reconstruction and psychological outcomes are better.[Francel, 1993 #23410; Al Ghazal, 2000 #23085; Franchelli, 1995 #23417](B)

Post-operative care

A meta-analysis of six RCTs showed better wound drainage when physiotherapy was started 5 to 7 days after axillary dissection, rather than within 2 days.[Schinkelshoek, 1998 #19268](A) However, this appears to be a controversial area and there may be other benefits of earlier physiotherapy, such as improved shoulder mobility.(C)

Choice of operation for the primary tumour

Randomised controlled trials comparing mastectomy with breast conserving surgery plus radiotherapy show very similar five- and ten-year survival rates (A). If radiotherapy is not given as part of breast conserving therapy, local recurrence rates can be as high as 30% after five years - four times the rate found after radiotherapy (A).

Breast conserving therapy is associated with similar levels of anxiety and depression to mastectomy, but it is associated with better preservation of body image (A). Most women who choose breast reconstruction are satisfied with their choice but there is no evidence that they experience better psychological or psychosexual adjustment than other breast cancer patients. When compared with women who have breast conserving therapy, those who have immediate breast reconstruction report worse body image and less satisfaction. However, the studies on which these conclusions are based have been small and of poor quality (B).

There is no evidence that breast cancer is any less aggressive in older women, so there is no clinical basis for treating older women differently.

Measurement

Structure

- Availability of immediate breast reconstruction for all women who want reconstruction, and for whom this is possible.

- Availability of training for surgical/radiological teams in sentinel node biopsy technique.

Process

- Evidence that women are offered balanced information on advantages and risks of different options for surgical management of the breast and axilla.
- Audit of timing and outcomes of reconstruction.
- Where sentinel node biopsy is used, there should be evidence that surgeons and radiologists are appropriately trained and that they audit their results.
- False negative rate below 5% after sentinel node biopsy.
- Audit of surgical complications.
- Proportion of women who receive different types of operation.
- Proportion of breast cancers fully staged (including lymph node status) and reported to the cancer registry.
- Proportion of women with incomplete excision of the cancer at initial surgery.

Outcome

- Axillary recurrence rates in relation to tumour features and treatment.
- Lymphoedema rates, assessed by arm girth measurements one year after surgery.
- Arm and shoulder function.
- Rate of wound infection and flap necrosis.
- Local recurrence rate in the breast and axilla.
- Patients' reports of the physical consequences of surgery.

Resource Implications

High quality surgery which is appropriate to the stage of the cancer is cost-effective and likely to lead to long-term savings, although there may be training costs for provision of necessary levels of surgical expertise. Optimum initial therapy is associated with lower rates of local recurrence, which is expensive and difficult to treat. The costs of breast reconstruction are reduced when this procedure is performed at the same time as mastectomy.

Adequate resources need to be available for providers to audit the process and outcomes of care.

References

1. The Breast Surgeons Group of the British Association of Surgical Oncology. Guidelines for surgeons in the management of symptomatic breast disease in the United Kingdom. London: BASO, 1995.

Draft

5. Radiotherapy

Recommendations

Breast Cancer Site-Specific Groups should produce network-wide guidelines on the appropriate use of radiotherapy for patients with invasive or in-situ disease. Radiotherapy should be regarded as standard therapy for all women who have undergone breast conserving surgery, and should also be discussed with women who have had mastectomy. An additional boost dose of radiation to the tumour bed should be considered for younger women, particularly those below the age of 40. Radiotherapy may be given as adjuvant or neo-adjuvant treatment, or it may be used as the sole local treatment modality when surgery is inappropriate. The optimum fractionation level is currently unknown but the ongoing START trial is designed to answer this question.

Patients should be given clear information about both anticipated benefits and potential hazards of radiotherapy. In situations where there is uncertainty about the balance of risk and benefit – in particular, in low-risk DCIS when the potential improvement in disease control is slight and no survival benefit has been demonstrated – patients should be given precise information and enabled to participate in decision-making.

Radiotherapy centres should have sufficient staff and capacity to guarantee access to radiotherapy within four weeks of identification of need.

Imaging that shows the heart and major blood vessels should be used in planning radiotherapy so that the cardiovascular system can be adequately protected during treatment. Whenever possible, 3D computerised planning should be used.

Radiotherapy centres should have linac machines (linear accelerators) with electronic portal imaging and multileaf collimators.

A high quality radiotherapy service should be available for all patients. When one radiotherapy centre serves several cancer units, clinical oncologists should work between sites to assess and advise patients in one location and treat them in another.

The option of radiotherapy should be discussed with suitable patients before primary surgery, particularly those who are to have breast conserving surgery. Radiotherapy to the axillary area should not normally be given after surgical clearance of the axilla. Patients should be given clear information on the anticipated benefits and potential risks before decisions are made about treatment. Radiotherapy has an important role in the management of the symptoms associated with metastatic disease.

There is no evidence from controlled trials of the superiority of any one regimen over another in terms of benefit, but there is evidence of increased toxicity (nausea) with higher doses per fraction with some sites. However, in view of problems of transport to radiotherapy centres, some patients may prefer shorter courses of treatment with higher doses despite more severe side-effects. The issues involved in this trade-off should be discussed with patients.

There should be adequate facilities such as hospital and hotel beds, and access to radiology and pathology services. An experienced oncology nurse should be available for all patients who require help, information or support.

The radiotherapy service should conform with guidelines in Quality Assurance in Radiotherapy.'

Anticipated Benefits

Radiotherapy reduces local recurrence rates to about a third of what they would otherwise be, both in invasive breast cancer and DCIS. In patients with invasive disease, annual breast cancer mortality is reduced by 13% from two years after treatment, but this benefit has been counterbalanced by increased risk of death from other causes, particularly cardiovascular disease 10-15 years after treatment. Improved treatment delivery, designed to reduce cardiac exposure to radiation, should allow the reduction in breast cancer deaths to be reflected in improved overall survival rates.

Radiotherapy has been shown to reduce recurrence rates after surgery for primary breast cancer. However, complications such as nerve and skin damage may counterbalance benefits in some women. The complication rate may be minimised by following guidelines on good practice. In symptomatic metastatic disease, radiotherapy can help to control pain and symptoms and reduce disability.

Evidence

Effects of radiotherapy

Survival and local recurrence

Meta-analysis of individual patient data for 20,000 women shows 20-year survival rates of 37.1% with radiotherapy and 35.9% without, a non-significant difference of 1.2%. At ten years, the difference is 2.1%. [Early Breast Cancer Trialists' Collaborative Group, 2000 #22905] The risk of isolated local recurrence at 20 years is 10.4% with radiotherapy, versus 30.1% without. (A)

There was a significant reduction in breast cancer deaths. In the absence of other causes of death, the 20 year survival would have been 53.4% with radiotherapy and 48.6% without. Breast cancer mortality was not reduced by radiotherapy in the first two years, but after this period, radiotherapy reduced annual mortality rates from breast cancer by 13.2% (SE 2.5). However, deaths from other causes – mainly cardio-vascular disease – increased by 21.2% (SE 5.4).

The authors of this meta-analysis suggest that newer radiotherapy regimens might produce better long-term survival. The Danish national trials (3046 patients), in which special efforts were made to limit cardiac exposure, report 10% greater overall survival at 12 years with radiotherapy and no excess deaths from ischaemic heart disease. [Højris, 1999 #23546] The number of vascular deaths is small, however, and follow-up still too short to confirm long-term safety.

In DCIS, radiotherapy can halve the risk of local recurrence (RR 0.53, 95% CI, 0.37 to 0.75) after breast conserving surgery, but there is no evidence of any survival benefit.[Cancer Care Ontario Practice Guideline Initiative, 2001 #23077](A) When the risk of recurrence is low, radiotherapy may not offer any advantage.(B) Poor pathological features, large tumour size, and narrow surgical margins are associated with greater risk of local recurrence.

Women with invasive tumours and negative axillary nodes do not benefit from radiotherapy to the axilla.[Chetty, 2000 #22851]

Lymphoedema

Ten years after radiotherapy, 28% of women treated for breast cancer (but without tumour recurrence) report chronic arm swelling. There is a significant ($p=0.01$) increase in prevalence with time since treatment. Overall, radiotherapy is associated with more than double the incidence of arm oedema (OR 2.45, 95% CI 1.86 to 3.27).[Mortimer, 1996 #23264](B)

Radiotherapy in the NHS

Technical aspects of radiotherapy are improving with advances in computerised 3D planning.[Goodman, 2001 #23544] The accuracy of treatment delivery is also improving with the advent of linear accelerators, which can modulate field shape and beam intensity during therapy.[Evans, 2000 #23545]

However, the UK is lagging behind the US and mainland Europe in upgrading services. In 1999, 80% of radiotherapy departments in NHS hospitals planned curative treatment without access to 3D planning systems or CT imaging of the breast, heart or regional lymphatic pathways (START Trial Quality Assurance Survey 1999, unpublished).

The START trial has standardised radiotherapy practice in the delivery of treatment for women with early stage breast cancer in 35 participating departments in the UK (about 70% of the total number of radiotherapy departments). The definitions of target volume, patient position, field arrangements, beam quality, dosimetry, treatment delivery, verification, dose prescription and scheduling with other treatments are all prescribed in the protocol.[START Trial Management Group, 1998 #23165; START Trial Management Group, 1998 #23164] This trial is testing alternative radiotherapy dose fractionation schedules, an area of uncertainty in clinical practice.

Treatment for breast cancer is by far the largest component of demand on radiotherapy services, and the fractionation schedules used by a centre will have a marked influence on pressure on radiotherapy resources, and thus on waiting times. Other factors include the number of machines, the number of radiotherapy courses per machine, and staff available, and the way the radiotherapy department is run. Department of Health data, presented by CHI/AC, show wide variations between trusts in the number of radiographers per machine, threefold variation between the annual average number of RT courses per machine, and no relationship between therapeutic radiographer vacancy rates and the number of

fractions delivered per machine. It seems likely, therefore, that systems in some trusts could be improved to make better use of resources.

At least half of the radiotherapy machines in service at the end of 1998 were more than 12 years old, the RCR maximum recommended age. Older machines are more likely to break down and cannot perform more modern techniques such as beam-shaping. This situation has improved with new funding since 1998.

Morbidity due to radiotherapy

Radiotherapy can cause both short-term adverse effects and serious complications which usually develop within three years of treatment, but may occur up to ten years later (C). These include disabling arm problems, subcutaneous fibrosis and bone necrosis (B). A recent overview of randomised controlled trials indicates that some severe adverse effects may be associated with techniques which are no longer used (A).

The frequency and severity of complications appears to be related to variations in delivery of treatment. High dose techniques should be avoided, as should movement of the patient between treatment of the chest wall and treatment of lymph nodes. Complications are particularly common in women who undergo both surgical clearance of the axilla and radiotherapy (A).

Radiotherapy in metastatic disease

Radiotherapy is effective for pain control in patients with bone and brain metastases. It reduces neurological symptoms and improves function in those who have brain metastases.(A) There is no evidence of an effect on survival.

Measurement

Structure

- Availability of computerised CT for treatment planning.
- Availability of linear accelerators with multileaf collimators and portal imaging.

Process

- Evidence that patients are given full information on both risks and benefits of radiotherapy, with sufficient detail on outcomes to allow them to play an active part in decision-making if they so wish.
- Waiting times for radiotherapy.
- Use of protocols or guidelines for radiotherapy.

Outcome

- Short-term and long-term (≈ 10 years) adverse effects of radiotherapy.
- Proportion of patients who have breast conserving surgery who also receive radiotherapy.

- Quality assessment of radiotherapy services is being carried out by the Clinical Oncology Information Network.

Resource Implications

Additional resources will be required both to upgrade services with computerised 3D planning equipment and suitable linear accelerators. Resources may also be required to increase radiotherapy capacity.

The cost of radiotherapy treatment per patient varies with the patient throughput because of the large fixed capital costs of equipment. For patient numbers between 600 and 1000, each 10% increase in the number treated has been calculated to result in a unit cost reduction of approximately 10%.

This implies that centralisation of radiotherapy facilities will reduce health service costs; it also allows sub-specialisation by radiotherapists. However, centralisation may have significant costs for patients who may be seriously inconvenienced by the amount of time that may need to be spent travelling. It is especially likely to cause access problems in sparsely populated areas, since patients have to return repeatedly for treatment.

If this problem is solved through in-patient treatment, extra costs will be incurred. 'Hotel' accommodation provided by some centres is appreciated by patients and may be less costly.

DRAFT

6. Systemic therapy for early breast cancer

Recommendations

Systemic therapy for early disease

Networks should agree, and regularly revise, evidence-based protocols for the use of systemic treatments for breast cancer. The use of such treatments should be audited against these protocols to ensure that patients are receiving recognised forms of therapy with full doses of suitable drugs at appropriate times.

Neo-adjuvant treatment

Combination chemotherapy and hormone therapy, normally using the same drugs as would be given in an adjuvant setting, may be considered to downstage tumours before surgery.

Adjuvant chemotherapy

Women at intermediate or high risk of recurrence, who have not had neo-adjuvant chemotherapy, should normally be offered four to eight cycles of multiple-agent chemotherapy which includes anthracyclines. CMF should also be available. High-dose chemotherapy is not recommended although it may be offered to selected patients in Cancer Centres in the context of well-designed multi-centre randomised controlled trials. Taxanes may be used for first-line treatment in the context of clinical trials.

Networks should establish clear protocols for the management of patients with chemotherapy complications, especially neutropenic sepsis, which enable these patients to be admitted rapidly to appropriate facilities. Inpatient support for chemotherapy complications should be available from a specialist MDT with expertise in chemotherapy.

Hormone therapy

All women with hormone receptor-positive tumours should be offered hormone treatment (normally tamoxifen) for five years after primary therapy. Ovarian ablation should be considered in place of, or in addition to, chemotherapy for selected women. It is not clear whether hormone treatment is appropriate for women at low risk of recurrence who have had conservative surgery for DCIS.

Facilities and systems for delivery of chemotherapy

Oncology wards should be available for patients who may not have adequate home support to cope with the adverse effects of chemotherapy. Access to such facilities is particularly important for elderly or vulnerable patients. Nursing staff

working in such units and staff in cancer wards should be trained to handle indwelling central venous catheters (Hickman lines) without exposing patients to the risk of infection. Systems are also required to provide support for patients in the community who may have problems associated with chemotherapy, and for those who have indwelling catheters.

Chemotherapy should only be prescribed by specialist non-surgical oncologists working with chemotherapy nurse specialists, expert pharmacy and laboratory support. It should be administered in designated day-care facilities or on an oncology ward. Patients, their carers, and primary care staff should be given specific written information about their treatment, its likely side-effects, contact details for help and advice if they should suspect a chemotherapy-related problem, and information on where patients would be admitted if necessary.

Networks should establish clear protocols for the management of patients with chemotherapy complications, especially neutropenic sepsis. These should enable patients to be admitted to appropriate facilities without delay. Inpatient support for chemotherapy complications should be available from a specialist MDT with expertise in chemotherapy.

Patients should be encouraged to participate in well-designed clinical trials whenever possible. Networks should provide support for clinicians working in local cancer units who might be in a position to increase recruitment of patients with breast cancer into multi-centre trials.

Almost all patients with invasive breast cancer should be offered adjuvant systemic therapy (hormone therapy and/or chemotherapy). Systemic therapy should not be offered or withheld on grounds of age alone.

The choice of systemic therapy for individual women should be guided by protocols based on up-to-date research knowledge and agreed by the breast care team. Risks and benefits of different options should be discussed with patients, who should have continuing access to a specialist nurse for support, practical advice and information.

Chemotherapy involves a wide range of agents, many of which are toxic and require special care in delivery and dealing with adverse effects. Chemotherapy should only be given in units or centres where close supervision by oncologists and chemotherapy nurse specialists is available, plus expert pharmacy and 24 hour laboratory support. Chemotherapy should be given in a designated daycase area.

Patients receiving chemotherapy and their GPs should have access to emergency care, information and advice from oncology trained staff on a 24 hour basis. They should be given written information on appropriate action for dealing with side-effects of chemotherapy. There should be written protocols on the management of complications and toxicities.

Anticipated Benefits

Systemic therapy aims to treat undetectable cancer and thus improve survival prospects. There are marked variations in practice between clinicians and hospitals in the extent to which such therapy is used, variations which cannot be explained by differences in case-mix. Ensuring that adjuvant therapy is always offered to women with primary breast cancer when appropriate may be expected to reduce recurrence and improve survival rates.

Neo-adjuvant chemotherapy and/or hormone treatment can reduce tumour size so that less extensive surgery is required. For women who would have required mastectomy, a good response to neo-adjuvant chemotherapy can mean that breast-conserving surgery becomes possible; in addition, it can reduce the probability of tumour in axillary lymph nodes, permitting less invasive surgery to the axilla.

Improved support and facilities for patients who are undergoing chemotherapy, plus better training for staff who manage such patients, is likely to reduce the risk of death from infection.

Evidence

Neo-adjuvant treatment

Neo-adjuvant treatment for early breast cancer has been evaluated in four RCTs, all of which reported that significantly fewer women required mastectomy when systemic therapy was given before, rather than after, surgery.[Fisher, 1998 #19720; Makris, 1998 #19670; Mauriac, 1999 #14890; Scholl, 1995 #23564] Recurrence and survival rates do not seem to be affected by the sequence of treatment modalities.(A)

Adjuvant treatment

Chemotherapy

A meta-analysis of individual patient data from 11 RCTs shows that adjuvant chemotherapy that includes an anthracycline such as adriamycin (also known as doxorubicin) or epirubicin is more effective than CMF (cyclophosphamide, methotrexate and 5-fluorouracil).[Early Breast Cancer Trialists' Collaborative Group, 1998 #16660] Compared with CMF, anthracycline-containing regimens reduced recurrence by 12% ($p=0.006$) and increased 5-year absolute survival rates from 69% to 72% ($p=0.02$). (A)

This meta-analysis did not consider adverse effects or quality of life, but one form of anthracycline chemotherapy (adriamycin/cyclophosphamide/5-fluorouracil – FAC) is better tolerated than CMF and fewer cycles are necessary to produce an equivalent level of benefit.[Fisher, 1990 #23171](A)

Despite many trials of chemotherapy for breast cancer, the optimum regimen remains unclear and there are wide variations between UK oncologists in prescribing habits. A 1999 survey identified 36 regimens and 33 different dose-intensities for CMF alone.[Brown, 2000 #23348] In the US, standard adjuvant therapy is four cycles of AC. Six cycles are normally given in most of Europe.

Five RCTs of high dose chemotherapy with bone marrow transplant/stem cell rescue in high-risk patients, and three in patients with advanced breast cancer, have failed to produce consistent or convincing evidence that high-dose treatment leads to better outcomes.[Coleman, 2000 #23386; Peters, 2000 #23392](A)

It is not yet clear which patients with early breast cancer may benefit from adjuvant treatment with taxanes; this is being assessed in the UK in the TACT and TANGO trials. These trials should be supported.

Hormone therapy

Hormone treatment produces significantly better outcomes in women with oestrogen receptor-positive tumours than in those whose tumours are oestrogen receptor-negative.[Miles, 1999 #23338; Coradini, 1999 #23336; Nomura, 1998 #23339](A) Recent results from a large trial (n=907) suggest that letrozole produces better outcomes than tamoxifen in women with locally advanced, recurrent or metastatic breast cancer (median survival 42 months with letrozole, 95% CI 38 to 56, versus 30 months with tamoxifen, 95% CI 27 to 36 months).[Mouridsen, 2001]

Treatment with tamoxifen reduces the rate of breast cancer recurrence from 13.4% to 8.2% over five years (p=0.0009) in women who have been treated for DCIS. The absolute benefit is small when the risk of recurrence is low, and is balanced by adverse effects including increased risk of endometrial cancer.(A)[Cancer Care Ontario Practice Guidelines Initiative, 2001 #22955; Fisher, 1999 #19625]

Hormone manipulation by ovarian suppression can be achieved in various ways: by treatment with drugs (LHRH agonists) such as goserelin, surgical removal of the ovaries or ovarian irradiation. All seem equally effective.[Boccardo, 2000 #23502] No comparative studies were found which assess the effectiveness of LHRH agonist treatment for women with ER-positive tumours who maintain ovarian function despite chemotherapy and tamoxifen. This is an important gap in the research literature.

Primary Disease

While chemotherapy and hormone therapy both improve outcome independently, less is known about their effects when used together or in sequence.

Hormone therapy

Tamoxifen, a drug which blocks the action of oestrogens (oestrogen receptor antagonist), is generally well tolerated and requires no special precautions or facilities for use. However, tamoxifen can have short and long term side-effects such as early menopause and endometrial cancer. The benefits of tamoxifen are greatest when the primary tumour is oestrogen-receptor rich (A). There is no evidence of benefit in women under 50 whose tumours are oestrogen receptor negative.

Very strong evidence for the effectiveness of tamoxifen in the treatment of early breast cancer is derived from a systematic review of randomised controlled trials involving 30,000 women. Highly significant reductions in the risk of death and recurrence have been demonstrated; overall, tamoxifen reduces the annual death-rate by 17% and reduces the annual recurrence rate by 25%. Absolute improvements in recurrence-free survival at 10 years were 8.8% for node-positive and 5.1% for node negative women (A).

Treatment with tamoxifen for two years or more has been found to reduce the risk of death by 38% and is more effective than treatment for one year. There is no evidence suggesting additional benefit from continued

tamoxifen treatment for more than five years, and no evidence that higher doses are more effective than the standard dose of 20mg (A).

In Britain, 40% of all breast cancers occur in women over 70, yet only 10% of women in tamoxifen trials were in this age-group. The evidence suggests that tamoxifen is as effective in this group as in younger women. There is therefore no justification for withholding tamoxifen treatment from older women (A).

Ovarian ablation

There is very strong evidence from systematic reviews of randomised controlled trials that ovarian ablation (the destruction or removal of the ovaries by means of surgery, radiotherapy or drugs) is of the same order of effectiveness as chemotherapy for pre-menopausal women with breast cancer. Among women below 50 years old, ovarian ablation reduces annual recurrence rates and annual death rates by 26% and 25%, respectively. After 15 years, 52.9% of ovarian ablation patients and 42.3% of controls were alive and free of recurrence. Although ovarian ablation has not been found to significantly affect non-breast cancer mortality (A), adverse effects are those of a sudden early menopause compounded by the fact that doctors may be reluctant to give hormone replacement therapy.

A randomised controlled trial comparing ovarian ablation with chemotherapy showed equivalent effects on survival (A). Further comparative studies are in progress.

Chemotherapy

There is very strong evidence from systematic reviews of randomised controlled trials involving 75,000 women that multiple-agent chemotherapy reduces annual recurrence rates and overall death rates by 28% and 17%, respectively. Absolute reductions in mortality risk after 10 years range from about 2% for women with stage 1 cancer and good prognosis to about 6% for women with stage 11 cancer. Although the effect is greatest among younger women, recurrence rates among women aged 60-69 are reduced by 20%. Chemotherapy has no apparent effect on non-cancer deaths (A).

The survival benefit of an initial course of polychemotherapy increases with time; even after ten years, the survival difference between treated and untreated women continues to grow larger. The benefits are greatest for node-positive women (47% vs. 40% alive at 10 years), but node-negative women also show improved 10 year survival rates (67% vs. 63% alive) (A).

Most trials involved CMF (cyclophosphamide, methotrexate and 5-fluorouracil), usually for about 12 months; however, there is no evidence of difference in survival rates between CMF and other multiple-agent regimens, nor is there evidence that shorter treatment regimens (median 6 months) are less effective than longer courses of treatment (A).

Measurement

Structure

- Availability of appropriate facilities (including inpatient beds and adequately trained nurses) for the safe delivery of chemotherapy.
- Protocols, agreed by breast cancer MDTs across the network, to guide the choice of systemic therapy and management of complications.
- Protocols and systems for management of emergencies related to chemotherapy.

Process

- Evidence that patients are given full information on both risks and benefits of treatment, with sufficient detail on outcomes to allow them to play an active part in decision-making if they so wish.
- Evidence that patients and their carers are given clear information on what they should do if they suspect a chemotherapy-related problem.
- Audit of chemotherapy regimens used, doses given, and timing of treatment.
- Audit of adverse effects of systemic therapy (both hormone treatment and chemotherapy).
- Evidence that patients with hormone-receptor positive tumours are offered appropriate hormone therapy.
- When women with primary breast cancer are not given adjuvant therapy, the reasons for this decision should be recorded.
- Documentation of individual therapy should be adequate and reported to the cancer registry.
- Proportion of patients in clinical trials.

Outcome

- Short-term and long-term complications of chemotherapy.
- Long-term, stage-specific age-adjusted survival.

Resource Implications

There is likely to be some increase in the use of tamoxifen and a substantial increase in the use of polychemotherapy in primary therapy. The additional costs of adjuvant treatments for primary breast cancer are likely to be reflected in improved survival rates and may be balanced by a reduction in treatment costs for recurrence and for advanced disease, which places far heavier demands on resources than early breast cancer.

The devolution of chemotherapy from centres to units (a key Calman and Hine recommendation) will carry personnel and resource implications.

Systemic therapy for primary breast cancer is highly cost-effective, since both tamoxifen and polychemotherapy using CMF are relatively cheap. Even in women whose prognosis is good (and who could therefore expect the smallest benefit), adjuvant therapy is cost-effective. Cost-effectiveness is particularly high for tamoxifen in node-positive women over age 50, and CMF in node-positive women under 50.

7. Follow-up after treatment for early breast cancer

Recommendations

Follow-up for asymptomatic women

Protocols for limited (two or three years) follow-up should be agreed by each network. The aims of follow-up should be to detect and treat local recurrence and adverse effects of therapy, particularly lymphoedema. Intensive follow-up, designed to detect metastatic disease before symptoms develop, is not beneficial and should not be provided.

All patients who have undergone treatment for breast cancer should have continuing access for an indefinite period to a breast care nurse, who should provide a telephone advice service and arrange appointments at a breast clinic if there seems to be cause for concern. Breast care nurses should also be available to offer support and counselling for patients – including those who have been released from follow-up – who develop psychological problems linked with their experience of cancer.

It should be acknowledged that recurrent breast cancer does cause symptoms and that these are almost always first noticed by the patient herself. Patients should be encouraged to contact the breast care nurse if they have any problems that could be linked with their cancer or treatment, and given specific information about symptoms – for example, persistent backache of increasing intensity – that should be brought to the attention of the breast care nurse.

Routine long-term follow-up has not been shown to be effective and should cease. Networks should agree the period of time after which patients will be released from routine follow-up; this should not normally be more than three years except for women in clinical trials, for whom the trial protocol is likely to require long-term follow-up. Networks should agree evidence-based policy on the frequency of mammography for women who have been treated for breast cancer.

GPs should take responsibility for looking after women on long-term treatment with tamoxifen or other hormone-modifying drugs, and for stopping such treatment after five years. There should be an open access policy to enable GPs or other healthcare professionals to refer patients back to the breast care team without delay if they suspect recurrent cancer or problems related to treatment for breast cancer.

At the end of primary treatment, the patient and specialist should agree a written care plan. Intensive follow-up of women who have been treated for primary breast cancer should not be offered by the breast unit as a matter of routine. Women and their GPs should be reassured that routine tests to detect metastatic cancer are not necessary because they do not improve quality of life or survival. However, regular mammography is important to detect local recurrence or a second primary in the other breast.

Locally agreed measures should be developed to support the woman's transition from treatment by the unit. This should be designed to minimise anxiety and should include both verbal and written information on signs and symptoms which should be reported. Each woman should have a contact number for her breast care nurse and should be aware of other ways of accessing the specialist breast care team.

General practitioners should be involved in shaping local arrangements for follow-up whenever routine breast unit follow-up is to be discontinued or reduced in scale. They will need information on new arrangements and may need access to training in relevant aspects of breast cancer. Health Authorities should work with Postgraduate Deans to ensure that such training is available.

Under the protocols for some clinical trials, there will be a continuing need for follow-up by the breast unit team.

Hormone replacement therapy

The question of the safety of hormone replacement therapy for women who have been treated for breast cancer has not been resolved. Until the results of current trials become available, there is no reliable research evidence on which to base judgements on the risk of precipitating recurrence. Non-hormonal therapies for hot flushes (such as clonidine, beta blockers, SSRIs such as venlafaxine, physical exercise, acupuncture and other complementary therapies) can be helpful and should be discussed with patients.

Management of lymphoedema

Networks should agree protocols for identification and management of lymphoedema. A lymphoedema service, staffed by nurses and physiotherapists who have experience in dealing with this problem, should be available for all patients who experience arm swelling or discomfort. Patients should be warned that lymphoedema may develop some years after treatment. They should be given information on how they can contact the local lymphoedema service and encouraged to do so if their arm begins to swell. Those affected should be given specific advice on caring for the limb and contact details for the Lymphoedema Support Network.³²

It is not yet clear what physical therapies should be recommended for women with lymphoedema.

Anticipated Benefits

³² <http://www.lymphoedema.org/lsn>

Reducing intensity of routine follow-up and ending long-term follow-up will release resources – notably clinic and consultant time – which then become available for more productive use. It has been found in some hospitals that reducing follow-up can make it possible for all women with breast symptoms to be seen within two weeks.

More than a quarter of women who undergo treatment for breast cancer develop lymphoedema in the arm next to the treated breast. This can cause considerable distress and disability. A good lymphoedema service should be able to reduce the distress experienced by these patients.

Continued care by suitably trained GPs and/or access to trained specialist nurses is likely to be convenient for patients and will reduce demand on the time and resources of the specialist breast team.

Evidence

Effectiveness of different follow-up strategies

There is very strong evidence from two Italian randomised controlled trials that intensive follow-up (regular examination by specialists, mammography, plus an array of other diagnostic procedures such as liver and bone scans) is not associated with better survival than minimal follow-up (mammography plus clinical examination when necessary by the patient's GP) (A). A British randomised controlled trial has shown that this approach is acceptable to patients and GPs (A). While the diagnosis of metastatic disease may be made a few weeks earlier with frequent and intensive monitoring, there is no evidence that this affects survival rates or patients' quality of life (A). Local recurrence is most often detected by the woman herself, between follow-up consultations.

Patients' preferences

Qualitative findings from focus groups show that women wish to be fully informed and to participate in decisions about follow-up care in the context of a close relationship with the specialist breast team (B). There is no evidence of a general preference for intensive or minimalist follow-up among well-informed women (A). Doctors do show preferences: the majority of hospital-based clinicians support routine follow-up by the clinic, whilst most general practitioners believe GP follow-up (with referral to specialists when necessary) to be more appropriate.

Patients do, however, need to know how to get care when necessary. They appear to prefer to ask their breast care nurse for advice when they feel there may be cause for concern (A).

The research described in the previous edition of this Guidance is supported by additional studies which confirm the lack of evidence for the effectiveness of routine follow-up of asymptomatic women.(A)[Gulliford, 1997; Grunfeld, 1998] Many clinicians have, however, been reluctant to implement this aspect of the Guidance.(C)

A recent retrospective study from a Humberside breast clinic described how recurrent disease was discovered in patients who relapsed after treatment for operable breast cancer between 1992 and 1998.[Donnelly, 2001] 108 of 643 consecutive patients had recurrences after a median disease-free period of 18 months; three-quarters (74%) were seen at expedited (interval) appointments and most of the remainder drew attention to symptoms at a routine visit. The median

duration of symptoms before attending clinic was a week longer when recurrence was diagnosed at routine appointments than among interval referrals. Unsuspected locoregional disease was diagnosed in seven patients – 1% of the total group – at a routine follow-up appointment, and recurrent disease was detected by imaging in just two cases.

This study shows, as have previous studies investigating follow-up, that recurrence is usually symptomatic and first noticed by the patient herself. It also shows that the yield of mammography in this population is very low. Finally, it suggests that routine follow-up, far from detecting recurrence early, could be counter-productive, leading some patients to defer consultation for symptoms until their next appointment.(B)

The Frenchay Hospital in Bristol has adopted a policy of discharging patients from routine follow-up after five years, after which patients have open access to the breast clinic when required. It has been estimated that, over a year, the time saved will permit 204 new patient appointments and the financial saving will be almost £50,000.

Lymphoedema

Lymphoedema results from damage to the axilla, which may be unavoidable when tumour is found in the lymph nodes. This makes it difficult to use the affected arm, causing swelling, pain, weakness, and problems with clothing, and is associated with diminished quality of life.[Tobin, 1993 #23246](B) The prevalence rate of lymphoedema among women treated for breast cancer is in the region of 25 to 28%. This means that approximately 30 000 women in England and Wales could be affected,[Logan, 1995 #23238] but the numbers seem to be increasing.(C)

Surgical axillary clearance is associated with significantly more lymphoedema than node sampling.[Chetty, 2000 #22851] An RCT of different surgical approaches to the axilla found that arm volume increased by 4% after axillary clearance. After three years, arm circumference was significantly greater in women who underwent clearance than in those who had sampling alone (P=0.005)(A) or sampling and radiotherapy (P=0.04).(B) Radiotherapy to the axilla resulted in a significant reduction in range of shoulder movement.(A)

In a study from Worthing, 28% of 1077 women experienced arm swelling after treatment for breast cancer. Lymphoedema was twice as common among women treated with mastectomy than lumpectomy, or who had radiotherapy. The prevalence of lymphoedema increased with time after radiotherapy.[Mortimer, 1996 #23264](B)

It is not clear whether effective long-term treatment of lymphoedema is possible. Several agencies, including The UK Lymphoedema Support Network, produce fact sheets for breast cancer patients which suggest precautions that women should take to reduce their risk of developing arm lymphoedema. These precautions, although logical, are not based on research.[Hull, 2000 #23383]

A systematic review of physical therapies concluded that some combination modalities show promise but the primary research lacks rigour.[Megens, 1998 #15514] The only RCT included in the review found that compression garments can reduce arm size over six months. Complex physical therapy is supported by two cohort studies, one of which advocates the use of compression garments. There is no evidence that elevation alone is effective.

Hormone replacement therapy (HRT)

It is widely feared that using HRT could activate occult tumours but there is no reliable evidence to show whether this actually occurs. It is to be hoped that ongoing RCTs will clarify the balance of risks and benefits. One of these, IBCSG-17-98, EU-98077, compares HRT with non-hormonal treatments (clonidine, beta blockers, psychological support, physical exercise, acupuncture) and measures quality of life and breast cancer recurrence in women previously treated for early breast cancer. There is also a Nordic trial (SBG 9701) in which women are randomised to HRT or symptomatic treatment with clonidine or beta blockers. Venlafaxine, a serotonin re-uptake inhibitor antidepressant, may also be capable of reducing hot flushes.[Loprinzi, 2000 #23457] As with any medical treatment for unpleasant, though not life-threatening symptoms, benefits have to be balanced against side effects.

Mammography

The risk of local recurrence is considerably higher in treated breast cancer patients than is the risk of breast cancer in the general population. Similarly the risk of primary breast cancer in the other breast is higher in women diagnosed with breast cancer than in women who have not had breast cancer. These risks are greatest in the first few years after initial surgery, and diminish slowly.

It is therefore appropriate that all women who have been treated for breast cancer should undergo mammography yearly during the first five years after surgery, and every two years thereafter (C).

Measurement

Structure

- Written care plans for women who have completed cytotoxic treatment.
- Continuing access for patients to a breast care nurse: this should be available indefinitely.
- Availability of advice and treatment for lymphoedema.
- Evidence-based network-wide protocols for minimal routine follow-up of asymptomatic patients.
- Training in breast cancer follow-up should be available for GPs.

- There should be evidence of the existence of an information package for patients which explains clearly signs and symptoms which should be reported. There should also be evidence that patients have access to appropriate members of the team after initial treatment is complete.

Process

- Evidence that non-hormonal treatments for hot flushes (including non-drug methods such as relaxation and exercise) are discussed with sufferers.
- Evidence that women are given written details of signs and symptoms that should be discussed with their breast care nurse.
- Purchasers should ensure that women are offered regular mammography at appropriate intervals after initial treatment for breast cancer.
- The percentage of patients with written care plans regarding follow-up should be monitored.
- The use of tests such as scans and assays for tumour markers for metastatic disease should be audited, and the reasons for their use monitored.

Outcome

- Lymphoedema rates one and three years after treatment.
- Avoidable late-diagnosed recurrences (pathological fractures, spinal cord compression) should be monitored, to be used as “sentinel events”.

Resource Implications

Resources will be conserved by reduction of routine follow-up.

Currently, significant time is locked up in follow-up of treated patients. There is the potential for real resource savings through reduced follow-up, but this must be part of a managed process. Arrangements must be made for patients to receive all the information they need both to minimise anxiety and to be aware of signs and symptoms that should lead them to contact the breast care team. In addition, general practitioners and/or nurse specialists must have adequate training in follow-up of treated breast cancer patients. Only when these steps have been taken is it appropriate to transfer resources away from hospital-based follow-up.

A minimal routine follow-up strategy reduces pressure on breast clinics, allowing specialists to concentrate on those who need their care, and avoids unjustified use of resources for diagnostic procedures which do not influence outcome.

GPs should receive training in follow-up of breast cancer patients. Such training has resource implications but it is likely to be more cost-effective than investment in hospital based follow-up. If nurse specialists are to undertake follow-up, they will require appropriate training.

Resources should be allocated to the provision of professionally-produced written information for patients to prepare them for the post-treatment period.

For the secondary and tertiary sectors, reduction in the routine follow-up of women will result in major savings. An economic analysis of intensive vs. minimalist follow-up strategies in Italy found that intensive follow-up cost three to five times more than the minimum regime.

Draft

8. Management of advanced, recurrent and metastatic disease

Recommendations

Every patient with advanced, recurrent or metastatic disease should be treated by a breast cancer multi-disciplinary team which includes a specialist oncologist. The team should have close links with a pain specialist and orthopaedic services. (See Topic 9, *The Specialist Breast Care Team*.)

Locally advanced breast cancer

Patients with locally advanced (T4) tumours are likely to have metastatic disease, so pre-treatment staging should include a bone scan, liver function tests and a chest x-ray as well as clinical evaluation. Local treatment should follow systemic therapy with chemotherapy, hormone treatment, or, in most cases, both.

Patients who respond well to systemic therapy should be offered surgery and radiotherapy to control local disease. Those with a poor response should normally be treated with radiotherapy.

Recurrent disease

Breast cancer must be regarded as a long term condition. At least one third of patients develop recurrent disease, sometimes many years after initial treatment; this usually produces symptoms which prompt the patient to consult a doctor or breast care nurse. Treatment of local recurrence aims to increase survival time and eliminate symptoms.

The management of each patient with local recurrence should be discussed by the breast cancer MDT. Any combination of the major therapeutic modalities – surgery, radiotherapy and systemic treatment – may be appropriate, the optimum treatment depending on various factors including previous treatment, the patient's general fitness, the site and extent of the recurrence, and tumour characteristics.

Metastatic breast cancer

Systemic treatment

Metastatic breast cancer is incurable. Systemic treatment with chemotherapeutic and/or hormone-modifying agents may produce modest improvements in survival time, but the primary aim of any form of treatment at this stage should be to relieve symptoms and optimise quality of life.

Hormone therapy is usually appropriate for women with hormone-receptor positive tumours. This is likely to mean tamoxifen or an aromatase inhibitor, plus ovarian suppression by radiotherapy, surgery, or an LHRH analogue for

premenopausal women. A range of hormone-modifying agents, including aromatase inhibitors and progestogens, should be available for second line therapy.

Immunotherapy, using the monoclonal antibody trastuzumab, may be considered for selected patients – *if NICE review, not yet published, recommends this.*

Chemotherapy can give useful palliation, particularly for patients with rapidly-progressing disease, or who do not, or would not be likely to, respond to hormone treatment. A variety of agents, including taxanes and vinorelbine, should be available. The choice of regimen will depend on the extent of the disease, previous treatment experience, and the patient's fitness and wishes. A course of chemotherapy should involve no more than six cycles, and treatment should be stopped if the disease continues to progress or side-effects cannot be adequately controlled. Participation in clinical trials should be encouraged.

Chemotherapy should only be prescribed by specialist non-surgical oncologists, working with chemotherapy nurse specialists, expert pharmacy and laboratory support. It should be administered in designated day-care facilities or on an oncology ward. Patients, their carers, and primary care staff should be given specific written information about their treatment, its likely side-effects, contact details for help and advice if they should suspect a chemotherapy-related problem, and information on where patients would be admitted if necessary.

Networks should establish clear protocols for the management of patients with chemotherapy complications, especially neutropenic sepsis. These should enable patients to be admitted to appropriate facilities without delay. Inpatient support for chemotherapy complications should be available from a specialist MDT with expertise in chemotherapy.

Management of bone metastases

Bone metastases usually cause pain and may result in long bone fractures, vertebral collapse and metabolic imbalances (hypercalcaemia). Non-steroidal anti-inflammatory drugs (NSAIDs) are particularly effective for pain relief and short courses of radiotherapy (1-5 fractions) can relieve localised pain. Wide-field irradiation or radioisotope treatment may occasionally be appropriate for bone pain at multiple sites.

The symptoms of bone metastases may respond to systemic interventions, particularly hormone therapy and treatment with bisphosphonates; chemotherapy may also be effective but is more hazardous. Bisphosphonates reduce skeletal complications significantly, diminishing need for radiotherapy and orthopaedic interventions, and they should be given for as long as skeletal disease remains an important clinical problem.

Whilst these forms of treatment reduce the risk of disabling problems such as fractures and spinal cord compression, they are not always sufficient to prevent them. Each Breast Cancer MDT should therefore have systems in place to ensure that patients can be assessed without delay by professionals with specific

expertise in dealing with problems due to bone metastases. These should include radiologists, radiotherapists, specialist orthopaedic surgeons and neurosurgeons.

Any patient with suspected spinal cord compression should be referred as an emergency to an appropriate MDT for combined radiological, surgical and oncological assessment. There must be emergency access to MRI, spinal surgery and radiotherapy services at any time, including weekends.

Management of metastases to other organs

Metastatic breast cancer can affect many organs and tissues and patients may require a wide range of different forms of treatment to control local symptoms. These patients should be managed by the specialist breast cancer MDT, working closely with palliative care teams.

Anticipated benefits

Appropriate treatment of recurrent and metastatic breast cancer can improve survival, sometimes producing periods of complete remission when patients are free from symptoms of cancer. This can be achieved with systemic therapy even when the patient has metastatic disease affecting many body systems. Treatment of bone pain with bisphosphonates can reduce the need for radiotherapy and reduce the risk of fractures.

Evidence

Hormone treatment for metastatic disease

A variety of drugs can be beneficial as first-line therapy for metastatic breast cancer.[Fossati, 1998 #15774; Stockler, 2000 #19454; Stockler, 1997 #23558](A) Aromatase inhibitors (anastrozole, letrozole, formestane and exemestane), which have previously been reserved for second-line treatment, may be more effective than tamoxifen for first-line therapy. *Further evidence to be added from recent trials.*

Choice of treatment depends, at least in part, on the hormone receptor status of the tumour. This may not be the same in recurrent tumours as in the primary tumour, but appears to remain stable in secondary and metastatic tumours.[Balleine, 1999 #23562] The status of both oestrogen and progesterone receptors (ER and PR status) affects the response of metastatic breast cancer to tamoxifen; in patients with ER-positive cancer, elevated PR levels significantly and independently correlate with better outcomes.[Ravdin, 1992 #23563](B)

Chemotherapy

Cytotoxic drugs used for adjuvant treatment of early breast cancer (see Topic 6, *Systemic therapy for early breast cancer*) may also be used in advanced or metastatic disease. Drugs used for second-line chemotherapy or initial treatment of metastatic disease include the cytotoxic antibiotics (e.g. anthracyclines, mitomycin, mitoxantrone), vinorelbine, and the taxanes; these drugs may be combined in various ways.

The taxanes, paclitaxel and docetaxel, are basically similar drugs but the range of indications and the toxicity pattern for each differs in detail. The evidence for their effectiveness has been systematically reviewed for NICE.³³ This review shows that the quality of trials has been relatively poor but there is substantial consistency between them. Taxanes appear to be more effective than longer-established forms of chemotherapy such as FAC or single agent doxorubicin for progressive or metastatic breast cancer, offering better response rates, longer remission and an increase in survival time of perhaps 20-25%.(A)

Evidence on vinorelbine to be added.

Immunotherapy

A novel immunotherapeutic agent, the monoclonal antibody trastuzumab, has been developed to treat patients whose tumours produce relatively large amounts of a protein known as HER2/neu. A Canadian systematic review looked at trials of trastuzumab, both as a single agent and in combination with chemotherapy. Reported response rates in women with progressive disease after previous chemotherapy for metastatic breast cancer range from 12% to 27%, and significant improvements in response rate, time to disease progression and one-year survival were found in an RCT that compared trastuzumab plus chemotherapy with chemotherapy alone in women who had not previously had chemotherapy for metastatic disease. Some studies, however, have found a high incidence of cardiac dysfunction, especially among women who received trastuzumab with chemotherapy (28% cardiac dysfunction with adriamycin/cyclophosphamide plus trastuzumab; 4.8% with chemotherapy alone).[Crump, 2001 #23333](A)

The benefits of trastuzumab are largely confined to women whose tumours produce the highest levels of the HER2/neu protein. These tumours can be reliably identified using immunohistochemistry and other specialist laboratory techniques.[Crump, 2001 #23333](B) A consensus statement has been published which gives recommendations on HER2/neu status testing in the UK, and laboratories have been established in London, Nottingham and Glasgow.[Ellis, 2000 #23556]

Management of bone metastases

³³ Available on the NICE website (<http://www.nice.org.uk/>)

Bisphosphonates can reduce the incidence of pathological fractures in patients with metastatic breast cancer, reduce bone pain and the need for palliative radiotherapy, and improve quality of life.[Cancer Care Ontario Practice Guidelines Initiative, 2001 #22970](A) They do not affect survival time. Meta-analysis of RCTs comparing the bisphosphonates pamidronate or clodronate with placebo or observation reveals that these drugs reduce pathological fractures by 28% (risk ratio 0.72, 95%CI 0.6 to 0.87) and reduce the need for radiotherapy for bone pain by 39% (risk ratio 0.61, 95%CI 0.51 to 0.73). Serious adverse effects are uncommon. The optimum times for starting and stopping bisphosphonate treatment are not, however, well defined (Rob Coleman, personal communication).[Diel, 2000 #23270]

It is not clear whether bisphosphonates can delay the development of bone metastases or related skeletal events in women with breast cancer.[Cancer Care Ontario Practice Guidelines Initiative, 2001 #22970] There might be some delay in bone metastasis development with clodronate, but relevant trials are only just beginning and will not report for some years. The use of bisphosphonates in the adjuvant setting should, therefore, be confined to the treatment and prevention of osteoporosis, which falls within their existing licence (Rob Coleman, personal communication). They may be particularly appropriate for premenopausal women with breast cancer, among whom chemotherapy-induced ovarian failure causes rapid bone loss which can be significantly reduced by clodronate.[Saarto, 1997 #19904](A)

Metastatic Disease (material from 1996 edition)

A wide variety of chemotherapeutic and hormonal agents are used in metastatic disease. A review of randomised controlled trials does not reveal any clearly superior regimen, although toxicity and side-effect patterns vary. However, there is strong evidence that polychemotherapy produces a greater decrease in mortality over three years' follow-up than single agent therapy, without appreciable increase in toxicity (A).

There is evidence from single arm before-and-after studies to suggest that a proportion of patients benefit from systemic therapy for metastatic disease; benefits may include tumour regression, relief of symptoms and improved quality of life (B). However, because there have been no randomised controlled trials comparing any of these drugs with placebo or support care only, no reliable research evidence is available on any overall benefit in terms of quality or length of life. Nevertheless, many breast cancer specialists believe that the use of chemotherapy can prolong life in some patients (C).

Measurement

Structure

- Rapid access systems for bone scanning and other imaging, including MRI.
- Rapid access to orthopaedics, neurology and other specialities which may be required for patients at risk of spinal cord compression or other catastrophic complications of metastatic disease.

- Availability of a wide range of chemotherapeutic agents and staff with the necessary expertise to use them safely in vulnerable patients.
- Access to short courses of palliative radiotherapy.

Process

- Evidence that patients are given full information on both risks and benefits of treatment, with sufficient detail on outcomes to allow them to play an active part in decision-making if they so wish.
- Proportion of patients who receive systemic treatment for advanced or metastatic disease, agents used and number of chemotherapy cycles given.
- Evidence that the effects of systemic treatment are appropriately monitored.
- When individual patients do not receive taxanes, the reasons for this should be recorded.
- Time-period between the decision to give radiotherapy and delivery of treatment.
- Use of pain scoring systems.
- Proportion of patients entered into clinical trials.
- Audit of outcomes of treatment.

Outcome

- Proportion of patients who suffer catastrophic fractures or spinal cord compression.
- Proportion of patients with uncontrolled pain.

Resource Implications

Costs for systemic treatment are likely to increase.

9. Palliative care

Recommendations

New guidance on palliative and supportive care is due to be published by NICE in 2002. This section has not, therefore, been updated.

Although palliative care is particularly important in the later stages of illness, a palliative approach, involving both symptom control and attention to the psychological, social and spiritual well-being of the patient and her family/carers, should be provided throughout the course of the illness. Palliative care is frequently provided by generalists, but all patients and health care professionals should have access to specialists in palliative care. In some circumstances, these specialists will take a leading role. At any one time, it must be clear who is taking overall charge of the patient.

Women with breast cancer should have access to a range of services based in hospitals, hospices and in the community to ensure the delivery of effective palliative treatments and care. Palliative care should be integrated between services provided by the breast care unit, the primary health care team, and specialist palliative care services, including the voluntary sector.

Multidisciplinary specialist palliative care teams should be available to provide optimal relief of pain and other symptoms and psychological, social and spiritual support for patients and their relatives and carers. The palliative care team should include the following members:

- Consultant in palliative medicine
- Nurses trained in palliative care
- Social worker or other person trained in counselling patients who are dying and/or in pain.

The team should have ready access to the following services:

- Physiotherapy
- Occupational therapy
- Counselling for both patients and relatives/carers.

All members of the palliative care team should participate in regular meetings to discuss patient care. A specialist pain relief team should be available, as should access to spiritual support for women of different religions and those with no religious faith.

Women and their GPs should have access to the palliative care team on a 24-hour basis, and should have continuity of contact with a named member of the team. Mechanisms to ensure effective collaboration between services and personnel must be established and implemented. Appointment of a key worker to co-ordinate the care provided by different teams for each patient should be considered.

Patients should be helped to remain in the place they prefer, whether this is their home, a nursing home or hospice, and should choose where they wish to die.

Anticipated Benefits

Provision of effective palliative treatments, including a range of anticancer treatments (Topics 4 and 5), combined with high quality care services, may be expected to lead to improved quality of life for women with breast cancer and reduce the burden on informal carers. Effective palliative care by home care teams allows patients to stay at home longer. This is generally preferred by women, and is likely to be the least expensive option.

Evidence

The needs of patients and carers

More than 50% of women diagnosed with breast cancer will at some time develop symptomatic metastases; median survival is then about two years. Physical and psychological problems are common among patients with metastatic cancer and there is fairly strong evidence of high levels of unmet need for social support. Cancer in a family member puts a burden on carers which can result in morbidity and increased mortality after bereavement (B).

Women with breast cancer spend, on average, 90% of their final year of life in the community. There is strong evidence that palliative home care teams and hospices are effective and cost-effective providers of holistic palliative care (A). Day care has not been adequately evaluated.

There is fairly strong evidence of under-treatment of pain; failure to assess pain appears to be the critical factor involved. Lack of recognition of the severity of pain experienced by patients and under-use of appropriate drugs leads to poor pain relief (B). Cancer pain can be well controlled in 75-85% of patients treated according to World Health Organisation recommendations (A).

Adding a multi-disciplinary support team to conventional care can result in a higher quality service (A). There is fairly strong evidence that referral to specialist palliative care services leads to improvements in pain control and reductions in the severity of other symptoms. There is weak evidence of greater satisfaction with specialist palliative care services than with services provided by general practitioners or hospitals; patients and their carers report high levels of satisfaction with the effectiveness of palliative care teams (B).

Continuity of care

No evidence was identified showing an association between any specific organisational model and better continuity of care, but good communication between the palliative care team and the patient's GP may improve continuity of care (C). There is weak evidence that patients may be distressed by seeing many different doctors during hospital visits, and that this is associated with reduced quality of life (B).

Measurement

Structure

- There should be evidence that adequately resourced and staffed specialist palliative care services are available in hospitals, community and hospices.
- Providers should demonstrate clear mechanisms for referral to, and communication between, services required to deliver both general and specialist palliative care.
- There should be evidence that specialist pain relief services are available when required.
- There should be protocols to guide symptom assessment and treatment.

Process

- The proportion of patients referred to palliative care services should be monitored.

Outcome

- Results of symptom control audits.
- Surveys of satisfaction with care.

Resource Implications

The establishment of specialised multidisciplinary palliative care teams within hospitals and the community may require some restructuring of existing resources, for example the development of more effective partnerships between small providers.

The availability of specialised palliative care staff varies across the country. Increased resources will be required in some regions to create multidisciplinary teams.

Care at home by multidisciplinary teams is appropriate for the majority of patients for the final stage of their illness. Comparative studies in the UK have estimated that home care costs only one-quarter to one-eighth as much as hospice care.

Hospice care generally involves lower costs to the NHS than in-patient hospital care. Many hospices are currently largely financed by charitable donations with additional funding from the NHS. Changes in the pattern of charitable funding could have major resource implications.

10. The Breast Care Team

The defining features of the breast care team are its composition, the way it works, and the co-ordinated care it offers. Such a team functions in the context of a cancer unit or centre, which may consist of one or more sites using shared facilities.

When the previous Breast Cancer Guidance Manual was published, there were few established MDTs and specialist breast care clinicians were uncommon, but the position has improved dramatically in the intervening period. This update is therefore intended to build on a structure which generally appears to be working well, but which would benefit from some adjustments.

Recommendations

The aim of the service is, in principle, simple: that expert care should be available locally for all patients with breast cancer. How this is achieved will vary from place to place, but it is anticipated that some smaller teams will merge so that the level of commitment to breast cancer care by each individual in these teams can increase. Within each network, the Breast Cancer Site Specific Group ensure consistency throughout the network by establishing local guidelines for referral and treatment, ensuring equity of access for all patients, and agreeing minimum data sets that can be used for network-wide audit.

Networks should re-assess local team structures in the light of audit and other information to ensure that sufficient expertise is available at all times. There should be at least two specialists for each role in the core breast care team and each of these individuals should dedicate at least 50% of his or her time to breast care. Smaller units and Trusts should consider combining resources so that clinicians who provide cover see at least 50 new patients with breast cancer each year.

Multidisciplinary teamwork

Optimal delivery of the services described in previous sections requires co-ordinated work by a multidisciplinary team of people with particular expertise in breast cancer care. The team would include clinicians who have specialised knowledge of each aspect of diagnosis and treatment, and specialised nursing and staff who give support to patients. A lead clinician should be designated who will take responsibility for the work of the team as a whole, communication with patients, implementation of change, and audit.

Personnel

The breast care team should be made up of individuals who have experience with breast cancer patients, substantial fixed time commitment to breast cancer patients, and where appropriate, specialist qualifications in breast cancer work. Details of what a consensus group considers to be

appropriate expertise, qualifications, and time commitment for members of the breast team, are given in the British Breast Group report, Provision of Breast Services in the UK.¹

The core breast team should include the following:

- *Designated breast surgeon(s).*

Surgeons should devote at least three sessions a week to breast work. Specialist training should be in accordance with the policy document published by the Breast Surgeons Group of BASO². Breast surgeons and others who talk to patients should also receive training in communications skills.

Breast cancer treatment should not be seen as a normal part of the work of the general surgeon.

- *Breast care nurse(s).*

Breast care nurses should work only in breast care and should have completed the ENB All Advanced Breast Care Nursing course. They should be trained in counselling and communication.

- *Pathologist*

A named pathologist with a special interest and training in breast care should attend team meetings. This pathologist should be skilled in breast cancer histology and cytology, or work closely with a cytologist who has particular expertise in this area. The pathologist is likely to have to commit at least three sessions a week to breast work. There must be adequate cover for the absence of the named pathologist.

- *Radiologist*

The radiologist should be trained and experienced in interpreting mammograms.

- *Oncologist*

Oncologists should devote at least three sessions per week to breast oncology. Newly appointed oncologists should have at least one year's experience in an established breast unit. Where the oncologist is a medical oncologist (qualified to use chemotherapy but not radiotherapy), a firm link must be established between the core team and the clinical oncologist from the centre to which patients are referred for radiotherapy.

- **Co-ordinator.** The co-ordinator should take responsibility for organising MDT meetings (see below) and should have the authority to ensure that extended team members such as social workers and psychologists are available when required.
- **Team secretary** who will provide clerical support for the MDT, recording all decisions made by the team and communicating appropriate information promptly to all those (such as GPs) who may require it. In smaller teams, the co-ordinator may take the role of team secretary.

The role of the breast care team

The team as a whole should be responsible for planning care in a seamless way so that each patient receives prompt and appropriate care throughout the process of diagnosis and treatment, up to and including the period when palliation may be needed. The team must maintain close contact with all other professionals who are actively involved in supporting the patient or carrying out the treatment strategy decided by the core team. These include the following:

- GPs/primary care teams
- Palliative care specialist/team
- Breast radiographer
- Psychiatrist/clinical psychologist
- Social worker
- Plastic surgeon
- Clinical geneticist/genetics counsellor
- Physiotherapist/lymphoedema specialist
- Nominated orthopaedic surgeon with expertise in management of bone metastases
- Neurosurgeon

Each network should ensure that nominated individuals are available not only to fill each role in every extended team, but also that they do, in fact, fulfil the function associated with that role when required. Trusts may pool resources so that individuals with specific expertise work with more than one breast care team.

Teams based in cancer units must have close liaison with the associated cancer centre.

At any one time, a named member of the team should be the principal clinician to whom the patient relates, e.g. the surgeon in the early stages of the disease, the oncologist during the phase of adjuvant treatment, and the palliative care physician at a late stage. It is important that such arrangements should be explicit and properly understood by patients. Patients should be given information about the members of the team involved in their management.

Organisation of MDT meetings

Whilst each MDT needs an administrative head (usually the Lead Clinician, who should work closely with the co-ordinator), teams should seek to achieve pluralistic or distributed leadership for decision-making. A democratic ethos should be encouraged.

Meetings should be arranged weekly by the team co-ordinator, who should ensure that information necessary for effective team functioning and clinical decision-making is available at each meeting. This information will include a list of patients to be discussed and copies of their case notes, along with diagnostic,

staging, and pathology information. Team members should be adequately prepared for the meeting, so that they can discuss each case without delay; such preparation and attendance at meetings should be recognised as clinical commitments and time should be allocated accordingly.

All new patients should be discussed, as well as any other patients whose cases are thought to require discussion as their condition or treatment progresses. Audit, clinical trials, and other issues of relevance to the network should also be discussed at these meetings.

There should be an operational policy meeting at least once a year at which the breast care team discusses and reviews its policies. This meeting should be organised around an open agenda to which all members of the team may contribute.

Achieving consistency within networks

Network-wide guidelines should be agreed, with joint protocols for clinical management, referral and audit. There should be network-wide audit, not only of clinical issues and outcomes, but also of patients' and carers' satisfaction with the service and of the availability and quality of information for patients. Information derived from audit should be used to identify and reduce variations within networks.

The core team should work closely together and meet on a regular basis (normally weekly) to discuss each patient with confirmed breast cancer both after initial diagnosis and after surgery to plan and monitor treatment. Decisions about future treatment should be discussed at these meetings in relation to clinical practice guidelines and protocols agreed by the team (see Topic 10). The team itself should also work according to a written protocol which specifies how quickly decisions should normally be made about diagnosis and treatment.

The team must have adequate support to ensure that all decisions are recorded and communicated to patients and all those outside the core team - for example, GPs and other professionals - who require, or may benefit from, information about decisions made by the team about the care of particular patients.

The team should allocate adequate time to audit the activities and outcomes of the unit.

Patient throughput

All breast referrals should be to specialist breast teams working in units which deal with at least 100 new cases of breast cancer per year (a level which may be anticipated from a population of around 200,000 people). This throughput figure should apply to the breast team as a whole (which may operate across more than one hospital), rather than to individual members or the whole institution.

In areas which are both sparsely populated and geographically remote, this level of throughput may be impracticable. Under these circumstances, there may be a trade-off between the quality of care offered by the team and ease of access. There should be a defined arrangement with a properly constituted team whereby specialists or patients are moved to agreed locations for breast cancer care.

Anticipated Benefits

Of multidisciplinary teamwork and specialist care

Teamwork allows for all aspects of care to be given due weight, and enables decisions to be discussed and questioned from a broad base of expert knowledge. In addition, discussion of patient management at multidisciplinary team meetings should ensure that each patient receives consistent information and co-ordinated treatment from all those involved in her care. This will tend to reduce the variation in management and outcomes around the country and in particular, avoid individual “outliers” who may provide sub-optimal care. It will thus increase the chances that each patient will be offered the most effective treatments.

Specialists in the management of breast cancer are likely to have higher levels of the expertise and skills. Benefits associated with optimal provision of surgery, radiotherapy and chemotherapy are more likely to be realised by this form of organisation.

If general surgeons for whom breast care is not a specialist interest pass this work to specialist teams, reductions in morbidity and mortality among patients may be anticipated.

Of adequate patient volume

Higher patient volumes are believed to be associated with:

- Greater accuracy of diagnosis
- Better quality, more up-to-date surgical treatment
- Better non-surgical treatment
- Better survival rates.

Evidence

The effectiveness of breast cancer teams varies with the mix of members in the team, the team’s joint workload, and the way they work together.[Haward, 2001, unpublished]. A questionnaire-based study of a random sample of breast care teams in England found that higher team workload and a larger proportion of breast care nurses were associated with better clinical performance. Teams in which leadership was shared between members were most effective, but lack of clarity and conflict over leadership reduced effectiveness.(B)

No research evidence was found on the optimum MDT membership or structure for dealing with bone metastases; the recommendations above are based on professional consensus and the BASO guidelines.(C)

The justification for the throughput figure of 100 new breast cancer patients per team per year rests on five strands of argument:

- Research evidence of benefit from specialised multi-disciplinary care (B)
- Research evidence of benefit from a case-load above 30 per surgeon (B)
- The belief that this level of workload is operationally cost-effective for the deployment of a suitable group of specialists which functions as a team. It is likely to be neither feasible nor cost-effective for a group of specialists to meet weekly and invest time and resources co-ordinating care if the number of new breast cancer patients falls below two per week (C)

- The belief that this level of workload is necessary to sustain the collective expertise of the team (C)
- Professional consensus in BASO and British Breast Group clinical guidelines of the desirability of such a figure (C).

Nevertheless it is acknowledged that the figure of 100 is arbitrary. The research evidence behind these strands of argument is summarised below.

Multidisciplinary teams and specialist care

There is fairly strong evidence that multidisciplinary services are likely to provide better care, and that multidisciplinary care is associated with better five year survival (B).

Specialist centres are more likely to provide up-to-date treatment and have better five year outcomes (B). A review of observational studies suggests that specialisation (however defined) is associated with a reduction in 5 year mortality among breast cancer patients (B). There is also some evidence to support the view that specialisation is associated with better diagnostic work-up (B).

There is fairly strong evidence demonstrating the value of specialist nurses (B). They play a variety of important roles and their work produces lasting beneficial outcomes. Findings from a range of studies reveal the following benefits accruing from the nurse's role in providing information and psychosocial support:

- Improved understanding by the patient of her condition (B)
- Enhanced patient involvement in decision-making (B)
- Reduced anxiety and depression and increased levels of self-esteem among patients (A)
- Improved general health and reduced somatic symptoms (A)

Linking better outcomes with higher patient volume

The evidence supporting an association between better diagnosis and non-surgical treatment and higher patient volumes is weak (C). A review of observational studies provides fairly strong evidence supporting an association between higher case volume and better surgical care (B). At the hospital level, the lowest threshold at which a relationship between case volume and process of surgical care was visible was twenty patients per year.

The evidence linking higher case volume with better long term outcome is also fairly strong (B). Surgeons who treat over thirty new breast cancer patients per year achieve lower 5-year mortality rates. In a recent Yorkshire study, 64% of women were managed by such surgeons, but the treatment of the remaining 36%, managed by surgeons with a lower case-load of breast cancer patients, must be a cause for concern.

There have been several overviews of research evidence linking between patient throughput and improved outcomes in cancer generally, and breast cancer in particular. (*Add references*) These have consistently concluded that higher volumes tend to be associated with better outcomes, however measured. No study has found an inverse relationship between patient volume and quality of service.

Measurement

Structure

- Availability of designated orthopaedic and neurological surgeons.
- Systems for network-wide audit.
- Adequate facilities and support staff for MDT meetings.
- Purchasers should look for evidence that the unit has, or has access to, a suitable range of named specialists, with adequate cover for absence for each core team member.
- The team should use a written protocol as a benchmark to manage co-ordinated care.

Process

- Development and use of network-wide protocols.
- Evidence that all members of MDTs feel that they can contribute effectively to discussion about patients.
- Evidence that every patient has access to a named breast care nurse, and that cover arrangements exist to ensure that a breast care nurse is always available during normal working hours to provide support and information for patients and carers.
- There should be evidence that all members of the breast care team meet regularly as a team, plan treatment as a team, and record their decisions.
- The number and percentage of new breast cancer patients treated per year by the specialist breast care team, and by the hospital as a whole.

Outcome

- Involvement of MDTs in clinical trials.
- The results of audit of the team's activities and breast unit outcomes should be published and made accessible to purchasers.

Resource Implications

Some Trusts will need to employ additional staff to co-ordinate and support MDT meetings.

It is assumed that breast teams will be established as part of cancer centres or cancer units which may involve more than one hospital site. The main costs will be in re-organisation of existing services and recruiting and training specialist staff. The groups most likely to be affected are clinical and medical oncologists.

The costs required to train staff to a high standard appropriate for breast care may be counterbalanced in the long term by more efficient and effective use of resources and improved outcomes.

Time must be allocated for all team members to attend each meeting.

This is an explicit recommendation in the Calman/Hine Report.

References

1. Provision of breast services in the UK: the advantages of specialist breast units. Report of a working party of the British Breast Group. Edinburgh: Churchill Livingstone, 1995
2. The Breast Surgeons Group of the British Association of Surgical Oncology. Guidelines for surgeons in the management of symptomatic breast disease in the United Kingdom. London: BASO, 1995.

Draft

11. Interprofessional communication

Recommendations

Effective communication between professionals, and between primary, secondary and tertiary sectors of care, is extremely important. The breast care team must develop and implement systems that ensure rapid and effective communication between all healthcare professionals involved in each patient's management. There should be adequate means for communicating information on referral, diagnosis and treatment, follow-up and supportive/palliative care. District Nurses and Practice Nurses in primary care must be linked into the communication network and aware of referral criteria and routes to the breast care team for women who have been treated for breast cancer.

There should be sufficient administrative support, and the unit should be equipped with up-to-date facilities to aid communication. Rapid communication with each patient's GP of diagnosis, treatment plans and treatment given, and with hospices and palliative care teams, is particularly important. The need for confidentiality should be recognised in all communication.

Some patients will be diagnosed in assessment centres after breast screening. When the assessment centre is not part of the breast cancer unit, there should be an agreed system for referral to the specialist breast team.

Anticipated Benefits

Breast cancer diagnosis and treatment is a co-operative activity involving a range of professionals, both within and outside the unit. Good interprofessional communication is essential to co-ordinate the activities of all those involved.

Evidence

There is both audit and anecdotal evidence of problems in interprofessional communication; such problems have been linked with complaints and litigation (C).

Measurement

There should be audit of speed and adequacy of communication between the breast unit and primary care team, between the breast unit and the cancer centre, and between the unit and the palliative care team.

12. Clinical guidelines, up-to-date practice and continuing professional development

Recommendations

Guidelines and protocols

Breast care units should adhere to explicit protocols in the management of breast cancer patients, so that patients are treated according to pre-defined evidence-based courses of action. These should be adapted from nationally recognised documents to fit local requirements and updated periodically to reflect new evidence. The guidelines should be disseminated to all relevant members of the health care team and management and used to guide treatment for individual patients. The entry of patients into appropriate clinical trials in which management is governed by protocols can be a valuable means of improving standards of care, as well as contributing to knowledge.

Up-to-date practice and continuing professional development

As evidence defining the effectiveness of interventions for breast cancer accumulates, it should be reflected in changing practice. Providers should be alert to new information and should use it to update protocols and guidelines. They should have access to databases of high quality systematic reviews.

It is important that members of the breast care team should continue their education in order that proven advances in treatment may be adopted. Educational strategies need to be tailored to local circumstances and clinicians' needs, and to include more than provision of scientific information.

Team members should also be trained in non-clinical aspects of their work, particularly counselling and communication. Training for GPs - particularly in cancer detection and follow-up after surgery - is necessary to ensure that they can adequately fulfil their role in these areas.

Anticipated Benefits

Of implementing guidelines and protocols

There is substantial variation between different centres in both treatment and outcome, which would be reduced if appropriate guidelines were followed. The implementation of 'evidence-based' guidelines would ensure that the most effective treatments would be used more frequently, resulting in increased survival and improved quality of life.

Of up-to-date practice and continuing professional development

Established practice tends to change slowly in the face of new knowledge; this reduces the potential effectiveness of treatment. Continuing education can help to keep all team members in touch with new developments in the field and new ways of accessing the latest information.

Training for GPs in the management of breast cancer allows the GP to play a larger role, particularly in follow-up. This is likely to be convenient for the patient and is not associated with any reduction in effectiveness (See Topic 7, Follow-up).

Evidence

There is very strong general evidence that use of clinical guidelines can improve the process and outcome of care. Local adoption of guidelines of good quality, incorporating the best up-to-date evidence and addressing relevant aspects of care, can lead to better outcomes for patients (A).

Educational interventions designed to meet clinicians' needs can be effective in promoting up-to-date practice (A).

Measurement

Structure

- Purchasers should ask to see guidelines and protocols, and evidence that they are regularly updated and adhered to.
- When breast cancer reviews become available on the Cochrane Library, there should be evidence that clinicians have access to it and are trained in its use.

Process

- Attendance on education programmes by all team members should be monitored.
- Number of patients entered into clinical trials and number of trials in which the unit is involved.

Resource Implications

Time for education and to discuss policy.

Costs of databases and on-line searching.

13. Environment and facilities

Recommendations

Breast cancer treatment should be offered in a pleasant and appropriate physical environment. There should be private areas where patients and staff can discuss the diagnosis and treatment, where patients can be counselled without being overheard, and sufficient space for each woman to be accompanied by a friend or relative. Attention should be paid to matters such as privacy in changing facilities, arrangements for the fitting of prostheses, availability of refreshments, and proximity and privacy of toilets, which are important to patients.

Hospitals may wish to set up breast care clinics and wards in such a way that early breast cancer patients are separated from women with advanced disease, in order to be sensitive to the feelings of the two groups of patients.

Single-sex wards or bays should be available.

All units ideally should be equipped to offer dedicated diagnosis and treatment of all stages of breast cancer (other than radiotherapy facilities, which will be based in cancer centres).

Providers should also ensure that adequate transport facilities are available for patients. These should recognise and meet the needs of sick and vulnerable patients who may have to travel long distances for repeated episodes of treatment which may make them feel very unwell (radiotherapy and chemotherapy), and may compromise their employment and reduce compliance. Car or minicab services should be arranged for such patients.

Anticipated Benefits

The provision of suitable facilities is likely to enhance morale and improve satisfaction with care among both patients and staff.

Evidence

There is patient survey evidence showing concerns about the physical environment (C). Physical and aural privacy is particularly important; both patients and clinicians express unhappiness about hospitals with such poor facilities that they are forced to discuss distressing issues in corridors. Patients also express distress about poor changing facilities and poor facilities in toilets.

Patient surveys reveal that contact between women whose cancers are at different stages can be distressing, and that most women prefer to be separated from men on wards. Transport is a very important issue in some areas; long, roundabout journeys in minibuses, which wait for every patient to complete treatment before being returned home, can cause particular problems (C).

There appears to be no research evidence linking these issues with longer term health outcomes.

Measurement

Providers should be required to elicit validated patient feedback on facilities.

Resource Implications

The cost of implementing these recommendations will vary widely from unit to unit. For example, the cost of re-organising transport arrangements will depend largely on the local population density.

Draft

Appendix I:

Production of the guidance

This update of the 1996 Guidance Manual is based on a partial re-iteration of the process described below.

Areas in which there were recent research developments, or which were believed to be important for good outcomes in breast cancer and not adequately covered in the 1996 documents were identified. Reviews of research evidence were carried out by the NHS Centre for Reviews and Dissemination. Both the evidence and new material for the update were discussed extensively by an Editorial Group and a specially convened “focus group” of NHS professionals who are likely to be involved in implementing the guidance. The draft update was then scrutinized by stakeholders identified by NICE and a variety of other referees.

Production of the 1996 Guidance

The initial stage is a residential event at which people from a range of disciplines and organisations identify what they believe to be the most important attributes of a breast (or other site of cancer) service necessary to deliver good outcomes. These are set out in a common format and constitute a set of 'proposals'. Each proposal includes key elements such as the evidence on which it is based, implications for the NHS, and relationships to outcome.

These proposals are then subject to 'refereeing', involving a spectrum of clinical opinion, those likely to use the eventual guidance, and organisations representing the concerns of cancer patients. The comments of referees are collated for use in committee, but the full comments, together with the original proposals, go into the evidence review stage.

Evidence reviews are commissioned through the NHS Centre for Reviews and Dissemination at York University and separately funded by the Research and Development Directorate. The task of the reviewers is to prepare a systematic assessment of the nature and strength of the evidence underlying the proposals and arising from comments by referees. This work is summarised in the supporting Evidence document to this manual and in the August 1996 *Effective Health Care* bulletin.

The synthesis of the three strands of work into a coherent report is overseen by the whole Cancer Guidance Subcommittee, most of whom are not involved in the earlier stages of any one site-specific report. The shaping of the document is assisted by feedback from Purchasers on issues of style and content. Draft reports are submitted to the full Clinical Outcomes Group for comment and approval.

Appendix II:

People and organisations involved in production of the 1996 guidance

1. COG Cancer Sub-group
2. Members of the proposal generating group
3. People/organisations invited to comment on original proposals
4. Researchers carrying out literature reviews
5. Members of purchaser focus groups

Guidance synthesis and writing

Dr. A Melville Research Fellow
Professor T A Sheldon Director
NHS Centre for Reviews and Dissemination, University of York

People/organisations invited to comment on drafts of the guidance

Members of COG

COG Cancer Sub-group

Various professional organisations

DoH

Dr K Dickersin, Director, Baltimore Cochrane Centre, Dept of Epidemiology & Preventive Medicine, University of Maryland, USA

Appendix II.1

Membership of the COG Cancer Sub-group

Chairman

Professor R A Haward Professor of Cancer Studies, University of Leeds

Members

Dr S Atkinson Regional Director of Public Health, NHS Executive - South Thames

Dr J Austoker University of Oxford, Department of Public Health and Primary Care

Dr J Barrett Consultant Clinical Oncologist, Royal Berkshire Hospital

Mr M Bellamy Chief Executive, Ealing, Hammersmith and Hounslow Health Authority

Professor J Hardcastle Chair, Royal College of Surgeons Cancer Committee

Mrs S Hawkett Nursing Officer, Department of Health, Eileen House

Professor R Mansel Chair, Royal College of Surgeons working group on Guidelines for Cancer

Mrs R Miles Regional Cancer Adviser, NHS Executive - West Midlands and Chairman of National Cancer Alliance

Mrs G Oliver Director of Nursing, Clatterbridge Centre for Oncology

Professor M Richards Sainsbury Professor of Palliative Medicine, St Thomas's Hospital

Mr H Ross Chief Executive, United Bristol Healthcare Trust

Professor P Selby Professor of Cancer Medicine, University of Leeds

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Professor J Sloane Professor of Pathology, University of Liverpool

Mr E Waterhouse Assistant Secretary, Department of Health, Eileen House

Professor I Williams Professor of General Practice, Kendal

Dr E Wilson Senior Medical Officer, Department of Health, Eileen House

Appendix II.2

Participants in the Breast Cancer Proposal Generating Event

Dr M Armitage	Patient, Bournemouth
Professor M Baker	Medical Director, North Yorkshire Health Authority
Mr H M Bishop	Consultant Surgeon, George Eliot Hospital NHS Trust, Nuneaton
Professor R Blarney	Professor of Surgical Science, City Hospital, Nottingham
Ms S Denton	Clinical Nurse Specialist, St Bartholomew's Hospital, London
Dr L Fallowfield	Reader in Psycho-Oncology, CRC Communication and Counselling Research Centre, University College London Medical School
Professor A Faulkner	Education Consultant, Trent Palliative Care Centre
Ms K Gerard	Lecturer in Health Economics, Department of Epidemiology/Public Health, University of Newcastle-upon-Tyne
Dr P Harvey	Consultant Clinical Psychologist, Birmingham Oncology Centre
Mr K Horgan	Consultant Surgeon, The General Infirmary at Leeds
Dr A Howell	Consultant Medical Oncologist, Christie CRC Research Centre, Christie Hospital NHS Trust, Manchester
Dr T Hughes	General Practitioner, Kirbymoorside, North Yorkshire
Dr C Keen	Consultant Clinical Oncologist, Mid-Kent Oncology Centre, Kent
Dr S Kelly	General Practitioner, Chichester, West Sussex
Ms M King	Patient, London
Dr R C F Leonard	Consultant Medical Oncologist, Western General Hospital, Edinburgh
Dr P Littlejohns	Director, Healthcare Evaluation Unit, St George's Hospital Medical School, London
Dr I Maher	Consultant Clinical Oncologist, Mount Vernon Hospital, Middlesex
Professor R Mansel	Professor of Surgery, University of Wales College of Medicine
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Mr N Offen	Chief Executive, Essex Rivers Healthcare

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Dr A R Timothy	Consultant Clinical Oncologist, St Thomas' Hospital, London
Dr C Wells	Consultant Pathologist, St Bartholomew's Hospital
Dr R Wilson	Clinical Director, Nottingham National Breast Screening Training Centre

Facilitated by.

Professor D Eddy	Senior Adviser for Health Policy and Management, California, USA
Professor R Haward	Professor of Cancer Studies, University of Leeds
Professor T A Sheldon	Director, NHS Centre for Reviews and Dissemination, University of York

Draft

Appendix II. 3

Referees of the Breast Cancer Proposals

Invited to comment

Mr B Aisbitt	Chief Executive, South Tyneside Health Care
Mr W Allum	Consultant Surgeon, Epsom General Hospital, Surrey
Dr C Anderson	GP and part-time lecturer at Nottingham Medical School
Dr T Anderson	Consultant Pathologist, University Medical School, Edinburgh
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Dr D Ash	Consultant Clinical Oncologist, Cookridge Hospital, Leeds
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Ms C Badger	Macmillan Nurse Consultant in Lymphoedema, St Catherine's Hospice, Surrey
Professor M Baker	Medical Director, North Yorkshire Health Authority
Mr G Barnes	Chief Executive, East Riding Health Authority, Hull
Dr P Barret-Lee	Chair, Breast Group for COIN
Mr T Bates	Consultant Surgeon, William Harvey Hospital, Ashford
Professor M Baurin	Professor of Surgery, University College London Medical School
Mr M Bellamy	Chief Executive, Ealing, Hammersmith and Hounslow Health Authority
Professor AJ Bellingham	President, Royal College of Pathologists
Mr D Bennett	Regional Cancer Co-ordinator, NHS Exec - Trent
Mr H Bishop	Consultant Surgeon, George Eliot Hospital, Nuneaton
Professor N Black	Professor of Health Service Research, London School of Hygiene and Tropical Medicine
Professor R W Blamey	Professor of Surgical Science, City Hospital, Nottingham
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Mr T Brennan	Consultant Surgeon, St James's Hospital, Leeds
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Dr J Bullimore	Member of the Expert Advisory Group on Cancer
Professor M Buxton	Director, Health Economics Research Group, University of West London

Sir K C Calman	Chief Medical Officer, DoH
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Ms J Clark	Consultant Surgeon, Radcliffe Infirmary, Oxford
Dr A Clover	Consultant Homeopathic Physician, Royal London Homeopathic Hospital
Dr R Coleman	Hon.Consultant Medical Oncologist, Western Park Hospital, Sheffield
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Professor C Coombes	Professor of Medical Oncology, Charing Cross Hospital, London
Dr B Cottier	Chief Executive, Clatterbridge Centre for Oncology
Dr I G Cox	GP, Birmingham
Ms D Crowther	Wirral Holistic Care Services
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Dr R Daniels	The Cancer Help Centre, Bristol
Dr T Davies	Member of the Expert Advisory Group on Cancer
Miss B Dick	Director, Patient Services, Royal Marsden Hospital
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Professor A Dixon	Consultant Radiologist, Addenbrooke's Hospital, Cambridge
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Dr F Dudley	GP, Peckham Rye, London
Dr A Dunbar	GP, Craven
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Mr S Ebbs	Consultant Surgeon, Mayday University Hospital, Surrey
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Dr G Evans	Consultant Geneticist, Christie Hospital, Manchester
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Mrs E Gough	Breast Cancer Care Association, Arundel
Mr R Gray	Senior Scientist, ICRF Cancer Studies Unit, Oxford
Mr M Greenal	BASO representative
Lady S Greengross	Age Concern
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Dr A Jones	Consultant Medical Oncologist, Royal Free Hospital, London
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Dr C Keen	Clinical Director, Mid-Kent Oncology Centre, Maidstone
Dr S Kelly	GP, Chichester, West Sussex
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Mr R Kingston	Consultant Surgeon, Trafford General Hospital
Mr M Kissin	Consultant Surgeon, Guildford
Mr T Lennard	Consultant Surgeon, Royal Victoria Infirmary, Newcastle upon Tyne
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Miss J Lord	Health Economist, St George's Hospital Medical School
Dr M McIlmurray	Consultant Medical Oncologist, Royal Lancaster Infirmary
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Dr P Maguire	Honorary Consultant Psychiatrist, Christie CRC Research Centre
Dr J Maher	Consultant Clinical Oncologist, Mount Vernon Hospital, Middlesex
Dr W Makin	Executive Committee Member of the Association for Palliative Medicine, Christie Hospital, Manchester
Professor R Mansel	Professor of Surgery, University of Wales College of Medicine
Dr H Marsh	Member of the Expert Advisory Group on Cancer
Ms A Maslin	Manager of the Breast Group, Royal Marsden Hospital

Dr M Michell	Consultant Radiologist, King's College Hospital, London
Mrs R Miles	Regional Cancer Adviser, NHS Exec - West Midlands
Ms K Money	Director of Commissioning and Primary Care, East Sussex Health Authority
Dr D Morgan	Clinical Oncologist, City Hospital, Nottingham
Ms J Mossman	BACUP
Dr V Murday	Geneticist, St George's Hospital Medical School
Dr L Newman	President, Royal College of General Practitioners
Mr N Offen	Chief Executive, Essex Rivers Healthcare
Mrs G Oliver	Director of Patient Services, Clatterbridge Centre for Oncology
Dr G Park	GP, Cleveland
Mr M C O Parker	Consultant Surgeon, Joyce Green Hospital, Kent
Dr T Perren	Consultant Cancer Physician, St James's Hospital, Leeds
Dr M Pitman	Regional Cancer Co-ordinator, NHS Exec - South West
Dr T Powles	Consultant Medical Oncologist, Royal Marsden Hospital, Surrey
Mr C Quick	Consultant Surgeon, Hinchingsbrooke Hospital, Cambs
Ms J Raiman	Head of Medical Services, Cancer Relief Macmillan Fund
Dr A Ramirez	Senior Lecturer & Honorary Consultant in Liaison Psychiatry, Guy's Hospital, London
Ms R Rawson	Clinical Nurse Specialist, Farnborough Hospital, Kent
Professor M Richards	Sainsbury Professor of Palliative Medicine, St Thomas's Hospital, London
Dr S Richards	GP, Woodcote, Berkshire
Professor R Rubens	Professor of Clinical Oncology, Guy's Hospital, London
Mr R Sainsbury	Consultant Surgeon, Huddersfield Royal Infirmary
Mr K Salsbury	Chief Executive, Wakefield Health Authority
Dr H Sapper	GP, Acton Health Centre, London
Mr G Saunders	Chief Executive, Harrogate Health Care
Dr E Scott	Regional Cancer Co-ordinator, NHS Exec - Northern & Yorkshire
Professor P J Selby	Member of the Expert Advisory Group on Cancer
Mrs A M Seymour	Patient, North Yorkshire
Professor K Sikora	Member of the Expert Advisory Group on Cancer
Dr K Simpson	Executive Committee Member of the Association for Palliative Medicine, Leeds

Professor J Sloane	Professor of Pathology, University of Liverpool
Dr I Smith	Consultant Medical Oncologist, Royal Marsden Hospital, London
Dr H Smedley	Consultant Clinical Oncologist, Kent & Canterbury Hospital
Dr J Spiby	Director of Public Health, Bromley Health Authority
Dr M F Spittle	Dean, Faculty of Clinical Oncology, Royal College of Radiologists
Miss M A Stebbing	Consultant Surgeon, North Hampshire Hospital, Basingstoke
Dr N S A Stuart	Welsh Cancer Services Expert Group
Sir R Sweetnam	President, Royal College of Surgeons of England
Dr N Sykes	Consultant in Palliative Care, St Christopher's Hospice, London
Professor I Taylor	Professor of Surgery, University of London Medical School
Dr C Thompson	GP, Cardiff
Ms L Thomson	Chair, Breast Care Nursing Society, Royal College of Nursing
Dr A R Timothy	Consultant Clinical Oncologist, St Thomas's Hospital, London
Ms J Todd	Clinical Nurse Specialist, Marie Curie Centre, Ilkley
Dr A Tucker	Consultant Radiologist, The Princess Grace Hospital, London
Ms K Turner	Regional Cancer Co-ordinator, North Thames
Professor Sir L Turnberg	President, Royal College of Physicians
Dame M Tumer-Warwick	Chairman, United Kingdom Co-ordinating Committee on Cancer Research
Dr B Walker	GP, Seascale, Cumbria
Dr M Watson	Consultant Clinical Psychologist, Royal Marsden NHS Trust
Dr I Watt	Dean of the Faculty of Clinical Radiology, Royal College of Radiologists
Dr C Wells	Consultant Pathologist, St Bartholomew's Hospital, London
Dr J Whiteman	GP, Twickenham, Middlesex
Dr R Wilson	Clinical Director, Nottingham National Breast Screening Training Centre
Professor C Woodman	Professor of Epidemiology, Christie Hospital, Manchester
Ms M Woods	Clinical Nurse Specialist, Lymphoedema Services, Royal Marsden Hospital
Dr J Yarnold	Hon. Consultant Academic Radiotherapy Unit, Royal Marsden Hospital
Ms J Young	Cancer Support Services Manager, Linda Jackson Cancer Information Centre, Mount Vernon Hospital, Middlesex
Ms T Younger	Regional Cancer Co-ordinator, NHS Exec - South Thames

170 people were asked to act as referees, of whom 64% responded.

Appendix II.4

Reviews of the Research Literature:

Composition of the Appraisal Team from the Mario Negri Institute, Milan

Overall Co-ordinators:

Dr A Liberati	Clinical Epidemiologist
Dr R Grilli	Health Services Researcher

Appraisal Team.

Professor C Confalonieri	Medical Oncologist
Mrs B D'Avanzo	Epidemiologist
Ms R Ferrario	Oncology Nurse
Dr R Fossati	Statistician, General Practitioner
Ms P di Giulio	Registered Nurse
Dr M Maistrello	Statistician
Dr S Minozzi	Epidemiologist
Dr A Penna	Epidemiologist, Specialist in Obstetrics & Gynaecology
Mrs V Pistotti	Librarian Specialist
Mrs E Sternai	Epidemiologist
Mr A Tinazzi	Computer Scientist
Dr V Torri	Medical Oncologist/Statistician

In collaboration with

Professor T A Sheldon	Director
Dr A Melville	Research Fellow

NHS Centre for Reviews and Dissemination, University of York, Heslington, York

Appendix II.5

Focus Groups: Purchaser Membership

Professor M Baker	Medical Director, North Yorkshire Health Authority
Mr G Barnes	Chief Executive, East Riding Health Authority
Mr M Bellamy	Chief Executive, Ealing, Hammersmith and Hounslow Health Authority
Mr G Bennett	Director of Finance, Birmingham Health Authority
Dr P Bevan	Director of Public Health, Merton, Sutton and Wandsworth Health Authority
Mr D Campbell	Director of Finance, Liverpool Health Authority
Dr A Charlesworth	Consultant in Public Health, North Derbyshire Health Authority
Dr V Hempsall	Deputy Director of Public Health, Dorset Health Authority
Mr J Henly	Director of Health Care Commissioning, Portsmouth and South East Hampshire Health Authority
Dr S Oliver	Senior Registrar in Public Health, Sunderland Health Authority
Dr S Pearson	Director of Public Health, Gloucester Health Authority
Dr F Pitt	Consultant in Public Health, Sheffield Health Authority
Mr R Priestley	Chief Executive, North Staffordshire Health Authority
Dr J Spiby	Director of Public Health, Bromley Health Authority
Dr J Verne	Consultant in Public Health, Barnet Health Authority
Dr P Watson	Director of Acute Services, Cambridgeshire and Huntingdon Health Authority
Dr S Will	Consultant in Public Health, Bury and Rochdale Health Authority

Facilitated by:

Ms S O'Toole Consultant in Health Policy and Management

Glossary

Adjuvant chemotherapy/hormone therapy

The use of either chemotherapy or hormone therapy after initial treatment by surgery or radiotherapy. The aim of adjuvant therapy is to destroy any cancer that has spread.

Axilla

The armpit.

Axillary clearance/dissection

Surgery to remove fat and lymph nodes from the armpit. It can be done either at the same time as a mastectomy or as a separate operation, and it can be partial or complete.

BCS

See breast conserving surgery

Biopsy

Removal of a sample of tissue or cells from the body to assist in diagnosis of a disease.

Breast conserving surgery (BCS)

Surgery in which the cancer is removed, together with a margin of normal breast tissue. The whole breast is not removed.

Breast reconstruction

The formation of a breast shape after a total mastectomy, using a synthetic implant or tissue from the woman's body.

Chemotherapy

The use of medications (drugs) that are toxic to cancer cells. These drugs kill the cells, or prevent or slow their growth.

Clinical Oncologist

A cancer specialist who is trained in the use of radiotherapy, and who may also use chemotherapy and hormone therapy.

CMF

The combination of cyclophosphamide, methotrexate and 5-fluorouracil.

Cycle

Chemotherapy is usually administered at regular (normally monthly) intervals. A cycle is a course of chemotherapy followed by a period in which the body recovers.

Cytology

Examination of cells, usually obtained by fine needle aspiration (FNA)

Ductal carcinoma in situ (DCIS)

A malignant tumour which has not yet become invasive but is confined to the layer of cells from which it arose. A form of pre-invasive cancer.

Fine needle aspiration (FNA)

The sampling of cells from breast tissue for examination by a pathologist.

Fraction

Radiotherapy is usually given over several weeks. The dose delivered each day is known as a fraction.

Halstead mastectomy

Total mastectomy with removal of underlying muscles of chest wall and complete clearance of axillary lymph nodes. This operation is now considered obsolete.

Histological grade

The degree of similarity of the cancer cells to normal cells. A grade 1 carcinoma is well differentiated and is associated with a good prognosis. A grade 2 carcinoma is moderately

differentiated and is associated with an intermediate prognosis. A grade 3 carcinoma is poorly differentiated and is associated with a poor prognosis. Grade is assessed by a pathologist.

Histology

An examination of the cellular characteristics of a tissue.

Hormone therapy

The use of drugs, or hormones which specifically inhibit the growth of hormone responsive cancer cells.

Immediate reconstruction

The reconstruction of the breast at the time of mastectomy.

Immunotherapy

The use of interventions intended to stimulate the immune system.

Local recurrence

Return of the cancer in the affected breast.

Lumpectomy

Surgical removal of a lump from the breast. See wide local excision.

Lymph node

A small collection of tissue along the lymphatic system which acts as a filter. White cells and cancer cells, in particular, collect in lymph nodes. They are found in the neck, the armpit, the groin and many other places. Lymph nodes are also known as glands.

Lymphodema

Swelling in the arm or breast because of a collection of lymphatic fluid.

Mammogram

A soft tissue X-ray of the breast which may be used to evaluate a lump or which may be used as a screening test in women with no signs or symptoms of breast cancer.

Mammography

The process of taking a mammogram.

Margins of resection: surgical margin

The edge of the tissue removed. See wide local excision.

Mastectomy

Surgical removal of the breast. May be total (all of the breast) or partial.

Medical oncologist

A cancer specialist with special expertise in the use of chemotherapy and hormone therapy.

Meta-analysis

A statistical technique used to pool the results from research on a particular issue.

Metastasis

The spread of a cancer from the primary site to somewhere else via the bloodstream or the lymphatic system.

Metastatic cancer

Cancer which has spread to a site distant from the original site.

Necrosis

The death of an individual cell or groups of cells in living tissue.

Nodal status

The presence or absence of cancer in the lymph nodes of the armpit. A woman with cancer in one or more nodes is node positive, or node +ve. A woman with no cancer in her nodes is node negative, or node -ve.

Oestrogen receptor(ER)

A protein on breast cancer cells that binds oestrogens. It indicates that the tumour may respond to hormonal therapies. Tumours rich in oestrogen receptors have a better prognosis than those which are not.

Oncologist

A doctor who specialises in treating cancer.

Oncology

The study of the biology and physical and chemical features of cancers. Also the study of the cause and treatment of cancers.

Ovarian ablation

Treatment which destroys ovarian function.

Palliation

The alleviation of symptoms due to the underlying cancer, without prospect of cure.

Polychemotherapy

The use of more than one drug to kill cancer cells. The most frequently used regime in breast cancer is the combination of cyclophosphamide, methotrexate and 5-fluorouracil (CMF).

Primary breast tumour

Tumour arising in the breast.

Protocol

A well defined program of treatment.

Quality of life

The individual's overall appraisal of her situation and subjective sense of well-being.

Radiotherapy

The use of radiation, usually X-rays or gamma rays, to kill tumour cells.

Reconstruction

See breast reconstruction.

Recurrence/disease free survival

The time from the primary treatment of the breast cancer to the first evidence of cancer recurrence.

Staging

Refers to the allocation of categories (0, I, II, III, IV) to groupings of tumours defined by internationally agreed criteria. Staging helps determine treatment and indicates prognosis.

Subcutaneous fibrosis

Thickening of tissue under the skin.

Surgical biopsy

Surgery performed under local or general anaesthetic in which a sample of breast tissue is removed so it can be examined by a pathologist.

Systemic

Involving the whole body.

Triple assessment

The use of three separate procedures (clinical examination, mammography, and needle biopsy - usually fine needle aspiration) in the diagnosis of primary breast cancer. When all three tests give the same result, the diagnosis is almost always correct.

Ultrasound

The use of sound waves to form a picture of internal tissues.

Vascular infiltration

Invasion of veins or lymphatic vessels by carcinoma cells, indicating a propensity for distant spread.

Wide local excision

The complete removal of a tumour with a surrounding margin of normal breast tissue. Also known as breast conserving surgery.

Acknowledgement

This information in this glossary is mainly derived from the Australian National Health and Medical Research Council Clinical Practice Guidelines: The Management of Early Breast Cancer and A Consumer's Guide: Early Breast Cancer (Canberra: Australian Government Publishing Service, 1995). Some entries have been added and others edited for inclusion in this document.

Draft