



CLINICAL PRACTICE GUIDELINES

Management of early breast cancer

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NHMRC

National Health &
Medical Research Council

Clinical practice guidelines for the management of early breast cancer: Second edition

Prepared by the iSource National Breast Cancer Centre

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- fostering and supporting a high quality and internationally recognised research base;
- providing evidence based advice;
- applying research evidence to health issues thus translating research into better health practice and outcomes; and
- promoting informed debate on health and medical research, health ethics and related issues.

This document was prepared by the iSource National Breast Cancer Centre Early Breast Cancer Working Group.

This document is a general guide to appropriate practice, to be followed only subject to the clinician's judgement and the woman's preference in each individual case.

The guidelines are designed to provide information to assist decision-making and are based on the best information available at the time of publication.

This is the second edition of the Clinical Practice Guidelines for the Management of Early Breast Cancer and replaces the first edition released in 1995.

It is planned to review this Clinical Practice Guideline by 2006. For further information regarding the status of this document, please refer to the NHMRC web address: <http://www.nhmrc.gov.au>

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FOREWORD

In October 1995 the National Health and Medical Research Council released the *Clinical practice guidelines for the management of early breast cancer*. These guidelines were the first in the NHMRC's new program and they represented a landmark in evidence-based medicine in Australia.

The guidelines were based on a review of the available evidence about the management of breast cancer and were developed by a multidisciplinary team. In the six years since their launch, the guidelines were very well received by clinicians and were viewed by women as an important resource in understanding their treatment choices.

Commencing in December 1998, the iSource National Breast Cancer Centre undertook a revision of these guidelines. Ongoing review is vital if the guidelines are to remain a good summary of the most recent research. Our understanding of breast cancer management has moved forwards since 1995 and this is reflected in the revised guidelines.

Breast cancer remains a major health issue for Australian women, with 10,000 new cases diagnosed each year. I am confident that the guidelines will continue to make a significant contribution to ensuring that all women diagnosed with early breast cancer receive care based on the best available evidence.

Professor Christine Ewan
Chair
Board
iSource National Breast Cancer Centre

LIST OF ABBREVIATIONS

ADH	atypical ductal hyperplasia
AH	atypical hyperplasia
ALH	atypical lobular hyperplasia
BCSS	Breast Cancer Support Service
CA 15.3	breast cancer tumour marker
CEA	non-specific tumour markers
CLE	complete local excision
CMF	cyclophosphamide, methotrexate and 5-fluorouracil
CS	conservative surgery
CSF	colony stimulating factor
DCIS	ductal carcinoma in situ
EIC	extensive intraductal carcinoma
EORTC	European Organization for Research and Treatment of Cancer
ER	oestrogen receptor
FAC	5-fluorouracil, doxorubicin and cyclophosphamide
FNAB	fine-needle aspiration biopsy
G-CSF	granulocyte colony stimulating factor
GP	general practitioner
Gy	Gray
HRT	hormone replacement therapy
IBT	ipsilateral breast tumours
LCIS	lobular carcinoma in situ
LHRH	luteinizing hormone releasing hormone
NBCC/ the Centre	iSource National Breast Cancer Centre
NHMRC	National Health and Medical Research Council
NSABP	National Surgical Adjuvant Breast and Bowel Project
PgR	progesterone receptor
QALY	quality adjusted life year
QCHOC	Quality of Care and Health Outcomes Committee

RCT	randomised controlled trial
RR	relative risk
SD	standard deviation
TRAM	transverse rectus abdominis myocutaneous
UICC	Union Internationale Contre le Cancer (International Union Against Cancer)

IMPORTANT NOTICE

This document is a guide to appropriate practice, to be followed subject to the clinician's judgement and the woman's preference in each individual case.

The guidelines are designed to provide information to assist decision making and are based on the best evidence available at time of publication.

INTRODUCTION

DEFINITION OF EARLY BREAST CANCER

These guidelines refer to breast cancer in the early stages, as it commonly presents. Early breast cancer has been defined as tumours of not more than five centimetres diameter, with either impalpable or palpable but not fixed lymph nodes and with no evidence of distant metastases. This corresponds to tumours that are T1-2, N0-1, M0 as currently defined by the International Union Against Cancer (UICC).¹ Please refer to Appendix C for further details.

PURPOSE OF THE GUIDELINES

Clinical practice guidelines for the management of early breast cancer aims to be a document useful for both health professionals and consumers. It is designed to:

- assist women and their doctors in decision making
- educate all involved in the care of women with breast cancer
- assess and assure the quality of care
- reduce the risk of legal liability by improving care
- bring the issue of cost-effectiveness into the public arena.

This book presents guidelines; it does not pretend to be a textbook. Clinicians looking for further information on the biology and natural history of breast cancer should consult the relevant texts.

These guidelines are neither rigid procedural paths, nor prescriptive. They aim to provide information on which decisions can be made, rather than dictate what decisions should be.²

Clinical practice recommendations are boxed as 'Guidelines' throughout the text and are summarised at the beginning under 'Summary of Guidelines'. These are all evidence-based and the level of evidence is clearly denoted.

There are also boxed 'Key points' to draw the reader's attention to other issues of importance. These are not clinical practice recommendations. Some are based on evidence derived from different studies (not necessarily Level I), while others refer to areas for which there is no 'hard' evidence but which were considered by the working group as important for clinicians to note.

LEVELS OF EVIDENCE RATINGS

The guidelines use a four-level rating system to enable the reader to identify the strength of the evidence base for key decision points. This rating system is recommended by CHOC² and has been adapted from the system developed by the US Preventive Services Task Force. The system is as follows:

- Level I** Evidence is obtained from a systematic review of all relevant randomised controlled trials.
- Level II** Evidence is obtained from at least one properly designed randomised controlled trial.
- Level III** Evidence is obtained from well designed controlled trials without randomisation; OR from well designed cohort or case control analytic studies, preferably from more than one centre of research group; OR from multiple time series with or without the intervention.
- Level IV** This represents the opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees.

The guidelines are based on reviews of the available evidence. They have also been informed by recommendations of expert groups. While Level I evidence represents the gold standard, it is not available for all areas of practice and for some recommendations the working party considered it appropriate to base recommendations on other levels of evidence.

These guidelines summarise areas of knowledge, but also highlight areas where knowledge is inadequate. This will provide guidance for research. The guidelines will continue to be evaluated to determine their degree of use by practitioners and their effects on patient outcomes.

Appendix B details the process for the development and evaluation of these guidelines.

NHMRC CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF EARLY BREAST CANCER

First edition (1995)

In 1993 the National Health and Medical Research Council (NHMRC), through its Standing Committee on Quality of Care (now the Standing Committee on Quality of Care and Health Outcomes (QCHOC)), established a working party to develop clinical practice guidelines for the management of breast cancer.

This was part of the national program to promote the development of evidence-based clinical practice guidelines, which was aimed at improving the quality of health care and patient health outcomes.

Breast cancer was chosen as a suitable topic because of concerns that knowledge of the treatment options was not well disseminated among health professionals, and that not all women with breast cancer were being presented with the range of appropriate treatment options. All women deserve access to advice and care of the best known standard.

QCHOC established a working party comprised of representatives from breast surgery, radiology, education, pathology, the consumer movement, medical oncology, radiation oncology, reconstructive surgery, counselling and support staff, nursing, general practice, research and psychiatry. The full list of members and the terms of reference of that working party are shown in Appendix A.

The guidelines were based on a number of reviews of the evidence. The outcomes of the Consensus Development Conference^{3,4,6}—conducted in June, 1994 under the sponsorship of the Clinical Oncological Society of Australia, the Australian New Zealand Breast Cancer Trials Group, the Medical Oncology Group of Australia and the Breast Section of the Royal Australasian College of Surgeons—also gave a sound basis on which to begin the development of the guidelines.

The report from the NHMRC women's sub-group was also important in drafting the guidelines.⁷ That report was commissioned by QCHOC at the request of the working party, which reviewed all available consumer literature regarding women's experiences of breast cancer.

The first edition (1995) of the guidelines was the result of the deliberations of the working party considering all of the available evidence. They were endorsed by the NHMRC and first released in October 1995.

The guidelines were well received by clinicians. For example, in a survey of 150 randomly selected surgeons, 97 per cent believed the guidelines were a good summary of the most recent evidence; 96 per cent reported that they were easy to understand; 86 per cent felt that they would assist in reaching agreement between clinicians and women; and 85 per cent believed that they would be useful in improving management.⁸ Many clinicians believed that their practice was already consistent with the guidelines.^{8,9}

Subsequent to the release of the guidelines, there has been considerable work by the iSource National Breast Cancer Centre, professional colleges and health authorities at the national, state and local level to foster their adoption. The guidelines have been the subject of much continuing medical education and are available on the Internet (www.nbcc.org.au). Current practice has been explored and the use of routine data audit fostered. Special initiatives have been directed at areas of concern, including the medico-legal consequences of the guidelines and multidisciplinary care in rural areas.¹⁰ A condensed guide (*The management of early breast cancer for general practitioners*)¹¹ has been produced for general practitioners, focusing on those aspects most relevant to primary care providers.

Second edition (2001)

In keeping with NHMRC recommendations, the guidelines have been reviewed and updated to provide a new edition for 2001 onwards.

The steps taken in reviewing the guidelines were as follows:

- A review of the scientific findings on which the original guidelines were based was completed by the Cochrane Collaborative Review Group in Breast Cancer. The update was conducted in December 1996 and repeated in December 1997. The accuracy of the statements in the guidelines, the supporting references and the levels of evidence were reviewed.
- Several new reviews of evidence have been completed by the iSource National Breast Cancer Centre and other agencies. The results of these analyses have been incorporated into the 2001 edition; a list of reviews conducted for the revision of the guidelines is included in Appendix B. In particular, detailed reviews about the psychosocial aspects of care^{12,13} enabled a more detailed discussion of these issues in this second edition of the guidelines.
- Feedback on the first edition of the guidelines was sought at the end of 1997 and the beginning of 1998 from a broad range of agencies involved in breast cancer control. A list of the organisations consulted is included in Appendix B. Comments from these organisations were reviewed by the working group which developed the 1995 edition of the guidelines.
- A sub-group of the original working group was established to provide a detailed review of the first edition of the guidelines. The sub-group comprised of Emeritus Professor Tom Reeve (Chair), Associate Professor Alan Coates, Mr Colin Furnival, Professor Allan Langlands (member until April 2000) and Ms Jayne Ross.

Further review and redrafting was undertaken in the particular areas detailed in Appendix B. Literature was included up until mid-2000.

For information on the management of advanced breast cancer, the reader is referred to the *Clinical practice guidelines on the management of advanced breast cancer, 2001*.

The consumer version

At the same time as the 1995 edition of the guidelines was released, NHMRC published a version of the guidelines for women with early breast cancer and their families (*A consumer's guide: early breast cancer*).¹⁴ The NHMRC recommends that doctors inform their patients of the availability of this book, and that they recommend it as a reference to be used in cooperation with their doctor and other health carers with whom they are involved.

Subsequently, the iSource National Breast Cancer Centre reproduced this document in a simpler format (*All about early breast cancer*).¹⁵ Both documents have been viewed very positively by women, and in a recent survey it was found that two-thirds of women diagnosed with early breast cancer now receive a copy of one of these documents.¹⁶

A revised version of these consumer resources, consistent with this second edition of the clinical practice guidelines, will be released.

Further information resources are available from the iSource National Breast Cancer Centre. *All about early breast cancer* is available on audiocassette and has been translated into Italian, Greek, Arabic and Chinese. A CD-ROM program based on these guidelines is also available so women can access this information interactively.

Clinicians are encouraged to promote the use of the consumer version of these guidelines and discuss them with the woman as required.

SUMMARY OF THE GUIDELINES

The following table provides a summary of the guideline recommendations presented in this document. All of the recommendations should be considered in the care and management of women with early breast cancer. Readers should turn to the appropriate chapters to understand each recommendation in context of the evidence.

Guidelines	Level of evidence	References	Chapter
COUNSELLING AND SUPPORT			
1. Providing women with support and detailed information about their diagnosis and treatment increases their emotional wellbeing and assists their physical and emotional recovery.	I	120–122	2.2
2. Strategies to improve recall of information are recommended, including: <ul style="list-style-type: none"> • the provision of a breast care nurse or counsellor • tape recording of the consultation • follow-up letter • psycho-educational programs 	II	116–119	2.2
3. Counselling is recommended for women with breast cancer, as it improves quality of life.	I	120	2.3
4. The involvement of a breast care nurse in the treatment team is recommended, as this reduces psychological morbidity.	II	79, 116, 123	2.3
PARTICIPATION IN CLINICAL TRIALS			
5. There is indirect evidence that women who participate in clinical trials have better outcomes than similar women given similar treatment outside trials.	III	136–138	2.7
MULTIDISCIPLINARY CARE			
6. The outcome of patients with breast and other cancers is better if they are treated by a clinician who has access to the full range of treatment options in a multidisciplinary setting.	III	134	3

Guidelines	Level of evidence	References	Chapter
SURGERY FOR INVASIVE BREAST CANCER			
7. In discussion of the choice between breast conserving surgery and mastectomy, women should be informed that body image is better preserved with conservation surgery.	I	207	4.3
8. Where appropriate, women should be offered a choice of either breast conserving surgery followed by radiotherapy or mastectomy, as there is no difference in the rate of survival or distant metastasis.	I	195	4.3
9. For most women with early breast cancer, a level I or level 2 axillary node dissection should be standard.	II	205, 217	4.4
RADIOTHERAPY			
10. Radiotherapy after complete local excision (CLE) is recommended as it significantly reduces the risk of local recurrence in the breast and the need for further surgery. It should not be omitted, even in selected patients.	I	195, 260, 266	5.1
11. Postmastectomy radiotherapy is recommended for women at high risk of local or regional relapse.	I	269, 228	5.2
SYSTEMIC ADJUVANT THERAPY			
12. Under the age of 50 years (pre-menopausal women), ovarian ablation reduces the risk of recurrence and death for women with breast cancer (see Chapter 6, Table 4).	I	299	6
13. Up to the age of 70 years, multi-agent chemotherapy reduces the risk of recurrence and death for women with breast cancer (See Chapter 6, Table 6).	I	298	6

Guidelines	Level of evidence	References	Chapter
SYSTEMIC ADJUVANT THERAPY <i>con't</i>			
14. Moderately prolonged (several months) combined chemotherapy is recommended as it is more effective than single agent therapy and than treatment lasting less than one month.	I	295	6.2
15. Anthracycline-containing regimes are superior to cyclophosphamide, methotrexate and 5-fluorouracil (CMF) for both recurrence-free survival and overall survival at the increased risk of alopecia, cardiac toxicity and febrile neutropenia.	I	298	6.2
16. Dose intensity is important to outcome in adjuvant cytotoxic therapy, at least in dose ranges achievable without colony stimulating factor (CSF) support.	II	311	6.2
17. Treatment with high-dose chemotherapy outside of clinical trials is not recommended.	II	314, 315	6.2
18. Women should be fully informed of the short- and long-term effects of cytotoxic chemotherapy on general functioning and on body image, sexuality and fertility.	III	333	6.2
19. Tamoxifen is recommended for most women with oestrogen receptor positive tumours, as it significantly improves recurrence-free and overall survival in women of all age groups.	I	297	6.3
20. Tamoxifen reduces the incidence of contralateral breast cancer.	I	297	6.3
21. Women should be informed of the potential side effects of tamoxifen, including endometrial cancer, stroke, pulmonary embolism, deep vein thrombosis, hot flushes and vaginal dryness and discharge, but not excess weight gain. For most women, the protective effect of tamoxifen against the recurrence of breast cancer will vastly outweigh the increased risk of side effects.	II	45–48	6.3

Guidelines	Level of evidence	References	Chapter
SYSTEMIC ADJUVANT THERAPY <i>con't</i>			
22. Ovarian ablation is more effective in women with oestrogen receptor positive tumours.	II	300	6.4
COMBINED MODALITIES			
23. Chemotherapy in combination with tamoxifen yields an increase in disease-free survival compared with tamoxifen alone.	I	352	6.5
24. Tamoxifen in combination with chemotherapy yields an increase in disease-free survival compared with chemotherapy alone.	I	297	6.5
FOLLOW-UP			
25. A minimal follow-up schedule is recommended, as there is no evidence that frequent intensive follow-up confers any survival benefit or increase in quality of life.	II	365, 366	7

Papers prepared by the iSource National Breast Cancer Centre are available from the Centre by contacting their publications voicemail service on (02) 9334 1882 or 1800 624 973.

CHAPTER 1 THE CLINICAL PICTURE

1.1 INCIDENCE AND MORTALITY

Incidence

In Australia in 1996, 9,556 women were diagnosed with breast cancer.¹⁷ The incidence of breast cancer has been increasing by between 1–2 per cent per annum for the past decade; however, there is some evidence that this increase may not continue.¹⁸ The incidence of breast cancer increases with age (see Figure 1).¹⁹

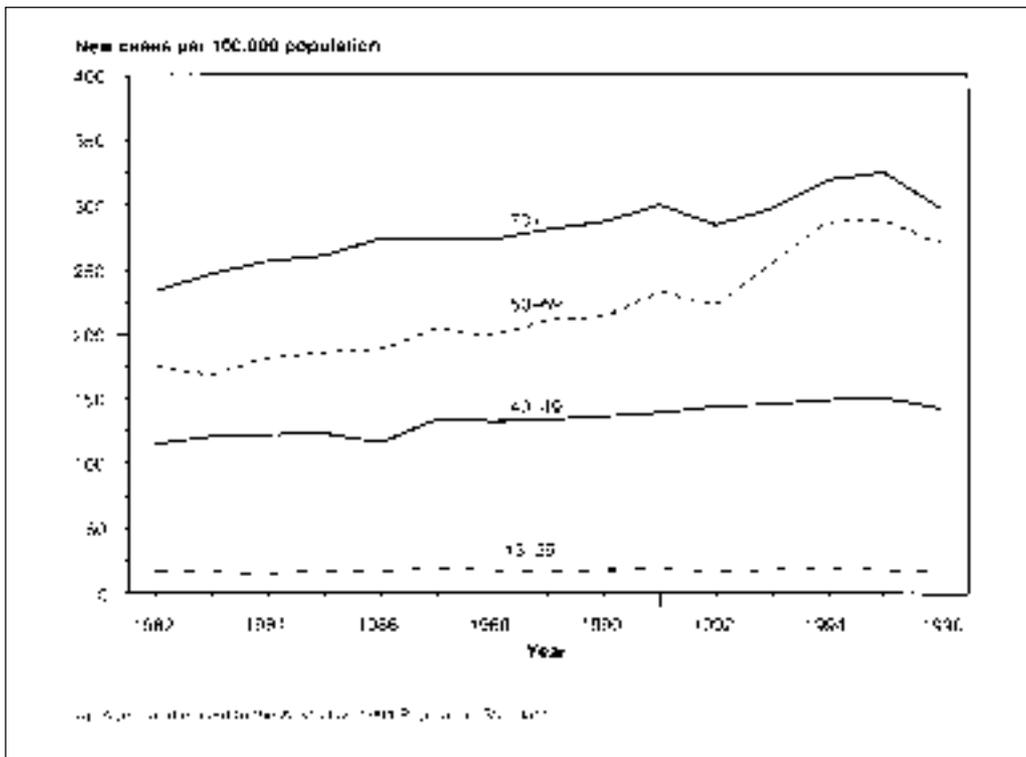


Figure 1: Age-standardised incidence rates of breast cancer by age in women in Australia, 1982–1996

Source: Australian Institute of Health and Welfare, Australasian Association of Cancer Registries and NHMRC National Breast Cancer Centre 1999. *Breast cancer in Australian women 1982–1996*. Canberra: AIHW (Cancer Series).

Mortality

Age-standardised rates have remained stable, at around 25–27 deaths per 100,000 woman-years between 1982 and 1996.²⁰

Survival

The report *Breast cancer survival in Australian women 1982–1994* showed that five-year relative survival in Australian women of all ages increased from 74.4 per cent in 1982–1987 to 78.9 per cent in 1988–1992.²¹ Survival was best in women aged in their 40s and poorer for women aged 80 years and over and under 30 years of age.²¹

1.2 RISK FACTORS IN WOMEN

The most important demographic risk factor for breast cancer is increasing age.²¹

A family history of breast cancer in first degree relatives, especially if the breast cancer was bilateral or diagnosed at an early age, strongly increases the risk of developing the disease, as discussed on the following pages.²²

The reproductive factors which most strongly influence a woman's risk of breast cancer are the determinants of her menstrual life and her childbirth history.^{23–25} These facts, combined with substantial evidence from experimental, clinical and epidemiological research, are taken to indicate that hormones play a major role in the aetiology of breast cancer.²⁵ The risk of breast cancer is increased while a woman is taking the oral contraceptive pill, although the effect of the pill on lifetime risk of breast cancer is small because risk of breast cancer is low at ages when women commonly take the pill.²⁶ Hormone replacement therapy (HRT) after the menopause also appears to increase risk by about 30 per cent.²⁷ The excess risk increases with increasing duration of use, but disappears within about 2 years of stopping use.

There is emerging evidence that a number of other factors may make a minor contribution to the aetiology of breast cancer. These include:

- high-energy intake and growth rate in childhood and adolescence (the risk may be reduced by high intake of fruit and vegetables at any age)²⁸
- a substantial increase in body size in post-menopausal women^{29,30}
- alcohol (a daily intake of more than two drinks)^{31,32}

Ductal carcinoma in situ, lobular carcinoma in situ and atypical hyperplasia

Some breast diseases, including ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS) and atypical hyperplasia (AH), are associated with an increased risk of invasive breast cancer.^{33,34}

DCIS is defined as an abnormal proliferative condition of epithelial cells in the mammary ducts. These cells display cytological features of malignancy, but unlike invasive cancer DCIS is confined within the ducts. The clinical significance of DCIS lies in the proportion of DCIS lesions which will eventually develop into invasive carcinoma. Historical data suggest that 20–30 per cent of untreated DCIS will progress to invasive cancer (**Level III**).^{35,37}

More recent studies also show a high frequency of invasive cancer after surgical excision of DCIS. In a report of mammographically-detected DCIS, invasive cancer occurred in 13 per cent of women within eight years of complete surgical excision of intermediate to high-grade DCIS.³⁸ This represents a ten-fold risk compared with recent incidence figures.

Although there are no reliable predictors for probability of progression to invasive carcinoma, the risk may be greater when DCIS displays features such as comedo necrosis or high nuclear grade.³⁹ On the other hand, in some cases invasion may never occur, presumably due to arrest of the genetic changes which lead to invasive cancer.⁴⁰

As the natural history is largely unknown, special consideration of the management of DCIS is required. As a general principle, small mammographically detected lesions should be treated by complete local excision, with preservation of the breast. In cases where the disease is extensive, total mastectomy may be a more reliable treatment. Randomised controlled trials demonstrate a reduction in DCIS recurrence and invasive breast cancer if radiotherapy is performed after local excision for DCIS (**Level II**).^{38,41,42} Axillary lymph node dissection is not necessary in the management of most patients with DCIS.⁴³ Chemotherapy has never been investigated or used in the treatment of DCIS. Recent evidence indicates that the use of tamoxifen in women with DCIS in the adjuvant setting reduces the risk of DCIS recurrence and invasive breast cancer (**Level II**).⁴⁴ Women should be informed of the potential side effects of tamoxifen.⁴⁵⁻⁴⁸

The natural history of lobular carcinoma in situ (LCIS) is unclear. However, even though little is known about the sequence of events leading from LCIS to invasive carcinoma of the breast, the clinical importance of LCIS is the increased risk of breast cancer associated with a diagnosis of LCIS. LCIS is a non-invasive multicentric proliferation of the epithelial cells in the lobules and terminal ducts of the breast. The relative risk of invasive breast cancer among women with a diagnosis of LCIS is estimated to be in the order of 7–9 over 15 years (**Level III**).⁴⁹⁻⁵² The absolute risk of developing invasive breast cancer among women

with a diagnosis of LCIS is approximately 17 per cent over 15 years, and applies to both the involved and uninvolved breast (**Level III**).⁴⁹

There is limited evidence available to determine the management of women diagnosed with LCIS as the only abnormality following a surgical breast biopsy. Close surveillance, including frequent clinical examination and bilateral mammography, supplemented by ultrasound if indicated, appears to be the best management option currently available.

Atypical hyperplasia (AH) refers to the proliferation of atypical cells in the breast epithelium. AH has been further sub-classified into atypical ductal hyperplasia (ADH) and atypical lobular hyperplasia (ALH). The cells in ADH are similar to those in DCIS, but the degree of involvement of the ducts and ductules is less extensive. Similarly, the cells composing ALH are similar to those that characterise LCIS, but the degree of involvement of the terminal ducts and lobules is less extensive. Ductal lesions (DCIS and ADH) and lobular lesions (LCIS and ALH) are usually regarded as representing continuums of abnormality which can eventually lead to invasive cancer. The relative risk of breast cancer for women with AH has been estimated to be three to four times that of the general population (**Level III**).^{53,54} The relative risk increases to approximately nine when AH is associated with a family history of breast cancer in a first-degree relative compared to women with non-proliferative benign breast disease and no family history (**Level III**).⁵³ Furthermore, the risk of invasive breast cancer seems to be greatest in the first ten years after diagnosis of AH.⁵⁵ Annual physical examination and annual bilateral mammography, supplemented by ultrasound if indicated, appears to be the best management option currently available to women who are diagnosed with AH as the sole abnormality following a breast biopsy.

(Clinical practice guidelines on the management of DCIS, LCIS and AH are currently being prepared by the iSource National Breast Cancer Centre.)

Key points

In some cases of DCIS, invasion may never occur. This may be the result of interruption of the genetic changes which lead to invasive carcinoma.

Radiotherapy should be considered for women with DCIS where conservation is desired.

Axillary lymph node dissection is not necessary in the management of most patients with DCIS.

For women with LCIS and AH, annual physical examination and annual bilateral mammography appears to be the best management option.

1.3 GENETICS

(Please refer to iSource National Breast Cancer Centre *Advice about familial aspects of breast cancer and ovarian cancer: a guide for health professionals* (2000) for more details on family history and risk of breast cancer.)

A history of breast cancer in other relatives may mean that a woman has an increased risk of breast cancer.²²

In the last few years several genes associated with a high risk for breast cancer, in particular *BRCA1* and *BRCA2*, have been discovered. In the general population, about 1 in 1000 women have inherited a mutation in one or other of these genes which increases their risk of breast cancer at least 8–9 fold. *BRCA1* and *BRCA2* mutations explain only 1–2 per cent of all breast cancer.⁵⁶ These mutations can be transmitted through either the maternal or paternal lines.

It is now technically possible to determine whether a person has inherited some *BRCA1* or *BRCA2* mutations. With current technology, it is not possible to detect every mutation and only a few Australian laboratories can conduct this specialised testing. Genetic testing raises complex medical and ethical issues, and should only be offered with pre- and post-test counselling in conjunction with a specialist genetics service for breast cancer. These issues are discussed in the Australian Cancer Network's *Familial aspects of cancer. A guide to clinical practice*.⁵⁷

Evidence-based recommendations about categorising risk based on family history are outlined in the National Breast Cancer Centre's *Advice about familial aspects of breast cancer and ovarian cancer: a guide for health professionals* (2000),⁵⁸ along with recommendations about the appropriate management of women in different risk groups.

This guide categorises women into three risk levels: women at or slightly above the average risk; women at a moderately increased risk; and women at a potentially high risk.

Women fall into the moderately increased risk category if:

- one or two first degree relatives were diagnosed with breast cancer before the age of 50 (without the additional features of women at potentially high risk described below)

OR

- two first or second degree relatives on the same side of the family, diagnosed with breast or ovarian cancer (without the additional features of women at potentially high risk described below)

Fewer than 4 per cent of women are in the moderately increased risk category, and their lifetime risk of developing breast cancer is 12–25 per cent. They should be advised to discuss any concerns with their general practitioner (GP).

Women at a potentially high risk due to their family history have about a 1 in 3 chance of belonging to a family in which a high risk mutation is causing cancer. This includes those women who have:⁵⁸

- three or more first or second degree relatives on the same side of the family with breast or ovarian cancer

OR

- two or more first or second degree relatives on the same side of the family with breast or ovarian cancer including any of the following high risk features:
 - diagnosis at age 40 or younger
 - bilateral disease
 - breast and ovarian cancer in one individual
 - breast cancer in a male
 - Jewish people of Ashkenazi origin.

Fewer than 1 per cent of women will be categorised as at high risk. Even in this high risk group, 50–75 per cent of women will not develop breast cancer. The lifetime risk on average of women in this category is between 25 per cent and 50 per cent but may be as high as 80 per cent in those women who have a high-risk mutation. Women in this category should be offered appropriate clinical surveillance.

If a woman with the above characteristics wishes to clarify her genetic risk or that of her family, health professionals should discuss referral to specialist genetic services for advice, appropriate counselling and management. A list of specialist genetic services for breast cancer is available from the iSource National Breast Cancer Centre, and can also be accessed through its website, <http://www.nbcc.org.au>

If a major intervention such as a bilateral mastectomy is planned—because of a very strong family history or when a woman is found by genetic testing to have inherited a mutated copy of a high risk gene, such as *BRCA1* or *BRCA2*—a second opinion is recommended before any final therapeutic decisions are made.

Information is available for women about these issues from the iSource National Breast Cancer Centre in the booklet *Breast cancer and family history: what you need to know*⁵⁹ and also from state and territory cancer organisations.

In most major Australian cities, family cancer clinics have been established with the aim of providing individuals with information about familial aspects of cancer and their risk of developing breast cancer associated with family history, and they may also offer genetic testing where appropriate. Guidelines for national best practice for family cancer clinics are available from the iSource National Breast Cancer Centre.⁶⁰

1.4 PROGNOSTIC INDICATORS IN BREAST CANCER

Factors generally associated with a less favourable prognosis are:

- increasing tumour size^{61,62}
- higher grade⁶²⁻⁶⁵
- the presence and number of lymph node metastases⁶¹

Factors associated with less favourable prognosis among node negative disease are:⁶⁶⁻⁶⁸

- increasing tumour size
- increasing histological grade
- oestrogen-receptor negative
- progesterone-receptor negative

1.5 THE IMPACT OF DIAGNOSIS AND TREATMENT ON THE WOMAN

The diagnosis of breast cancer and its subsequent treatment may have a significant impact on a woman's body image, self-esteem, sexuality and relationships.^{12,69-71} The impact may be greater with more intensive management,⁷² although there is not always a correlation between the emotional impact of cancer and the severity of the disease and treatment. The psychological impact of breast cancer may last long after the diagnosis is made.⁷³

Many women who have breast cancer, like many people with any form of cancer, feel helpless and powerless in the face of the disease.⁷² In addition to the threat to their life, the diagnosis may:

- threaten their femininity
- be seen as a threat to their family
- cause worry over whether the cancer has spread
- lead to ongoing uncertainty over the future, which has an impact on relationships, children, employment and many other parts of life
- lead to ongoing uncertainty over a whole range of issues, including what to do about treatment
- produce a fear of being stigmatised and rejected once the diagnosis is known⁷⁴

The diagnosis and treatment of breast cancer may have a substantial impact on the ability of the woman to continue with her normal daily life. The cancer and/or the treatment may interfere with aspects of her life including work, sports, sexual relationships, housework and caring for children.⁷

The treatment of breast cancer may have a significant financial impact on the woman and her family, due to time off paid work and medical and other expenses.⁷

Women will have different concerns at different times during diagnosis, treatment and after the active treatment phase. They face important and often complex decisions at each stage.⁷⁵ They may wish to make decisions after discussion with their doctor and nurses, or with their families.

Stressful times will vary with different circumstances for different women. They occur most commonly at:

- the time of diagnosis
- awaiting biopsy results
- the period after diagnosis while waiting for treatment
- any prolonged wait for treatment
- the period following discharge from hospital—both immediately after, then four to six weeks later
- the period following completion of treatment

All women react differently and deal with their cancer and its treatment differently. All will find their mood and ability to deal with the situation fluctuates with time.

Some women will experience more emotional difficulties than others. Women may be more vulnerable to adverse outcomes, including anxiety and depression, if they are younger, single, separated, divorced, widowed, economically disadvantaged or have poor social support or poor marital/defacto/partner relationships. Also included in the high risk group are women who have a past history of psychiatric illness, cumulative stressful life events or poorer physical health.⁷⁶⁻⁷⁸ Sexual, social and cultural factors will also modify morbidity.

A proportion of women will become clinically depressed following a diagnosis of breast cancer. It is estimated that at three months post diagnosis 10–17 per cent of women will be clinically depressed.^{79,80}

The patient's ethnic background and level of understanding of the English language is critical. Referral to a professional medical interpreter is recommended as appropriate.

1.6 THE EFFECT ON THE FAMILY

The impact of breast cancer may be profound not only for the woman affected, but also for her family.⁸¹ Family members of newly diagnosed cancer patients report high levels of concern and psychological distress (**Level IV**),⁸² and for spouses of women with breast cancer the level of distress are comparable to the

woman's (**Level IV**).⁸³ The impact on children depends on their developmental stage, and there is a need for each member of the family to have information appropriate to their level of understanding (**Level III**).⁸⁴

Family reactions play a key role in the coping of the woman, and promotion of more open communication and expression of feelings is generally helpful in adjustment (**Level III**).⁸¹ Lack of support from family and friends may be associated with poorer emotional adjustment (**Level III; Level IV**).⁸⁵⁻⁹⁰ Furthermore, not all women are members of a traditional family unit. For these reasons, it is important that key supportive relationships are identified for these women.⁹¹⁻⁹³ In some instances, the family or individual members may benefit from referral for counselling.

(For further information refer to: NHMRC iSource National Breast Cancer Centre *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer*, 2000).⁹⁴

CHAPTER 2 GENERAL PRINCIPLES OF CARE

2.1 AIMS OF TREATMENT

The primary goal in the treatment of early breast cancer is to control disease with the aim of achieving cure.

There are various other desirable outcomes for treatment, including:

- to improve survival
- to minimise the risk of distant recurrence
- cosmesis
- the return to a quality of life as close as possible to the life before diagnosis
- relief of symptoms

When contemplating the aims of treatment, the woman and her doctor—and, if desired, the woman's family—should discuss the options in the realisation that the initial management of breast cancer offers the best hope of cure. There is no evidence that cure is possible after recurrence of breast cancer.

Key point

As there is no evidence to suggest that recurrent breast cancer can be cured, (with the exception of in-breast recurrence after breast conservation surgery), it is important to select the most effective treatment from the outset.

Health professionals should be aware of which forms of management of breast cancer have been shown to be effective and which ones have not. That knowledge should be made available to women with breast cancer in a form appropriate to each woman's educational level and culture.^{95,96}

The choice to proceed with treatment, and the choice of which form of treatment, should be made by the woman after discussion with her doctor and any others she may care to consult.⁹⁷ The doctor is only entitled to decide which form of treatment to pursue if the woman expressly delegates her decision to the doctor. The doctor is not obliged to undertake a form of treatment with which he or she does not agree.

Key point

There are significant individual differences in women's views about, and needs for, information, choice and support. In the absence of research assisting health professionals to predict the needs of individual women, these differences are best accommodated by creating an environment in which each woman can secure a level of information, autonomy and support that suits her needs (**Level III**).^{98,99}

As well as correct surgical or medical treatment, good management requires attention to all factors that play some part in the management plan, such as:

- respecting dignity, privacy and confidentiality
- treating the woman as a whole person rather than as a host for a cancer
- acknowledging and accommodating if possible, a woman's work and family responsibilities
- minimising waiting times for appointments, treatments and results
- giving attention to amenities such as waiting areas⁷

2.2 ESTABLISHING GOOD COMMUNICATION PRACTICES

The way a clinician relates and communicates with a woman with breast cancer will have an impact on her wellbeing.

Women need to be accurately and fully informed about their disease and treatment options, so that they can understand both the nature of the threats to be faced and the available support and treatment for breast cancer. Effective communication involves more than the provision of information; it involves explanation, problem solving and acknowledgment of feelings. Improved psychological adjustment, decision-making, treatment compliance and satisfaction with care are potential benefits of effective communication practices. These are documented in detail in the iSource National Breast Cancer Centre's *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer*.⁹⁴

Women report a preference for communication styles and patterns that:

- acknowledge the emotional aspects of breast cancer and its treatment
- convey messages in a positive but accurate fashion
- convey friendly interest in the woman as a person
- cultivate a positive attitude⁷

Positive communication between women and their doctors in an atmosphere of reassurance is important to allow the assimilation of information and to assist in

women's psychosocial adjustment.⁷ In one study, 84 per cent of women reported difficulty in communicating with the medical team and difficulty comprehending information.¹⁰⁰ Communication problems were strongly positively associated with mood disturbance.¹⁰⁰

Outlined below are a number of general interactional skills to help establish and maintain effective communication at all stages of treatment.⁹⁴

General interactional skills

- Express empathy and listen effectively.
 - Avoid medical jargon and explain difficult terms.
 - Use explicit categorisation.
 - Actively encourage questions.
 - Actively seek understanding.
 - Repeat important information.
 - Summarise important information.
 - Write down relevant information.
 - Tape the consultation as needed and if wanted.
 - Send a summary letter as follow-up.
-

Adapted from iSource National Breast Cancer Centre Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer.⁹⁴

2.2.1 Telling a woman that she has breast cancer

No doctor ever gets used to telling people they have a life-threatening disease, and nobody has ever developed a formula that will make it easy on either the doctor or the woman. It requires time, patience, sensitivity and compassion. The manner in which the diagnosis of cancer is revealed may have important consequences for the woman's ability to cope with the diagnosis and treatment (**Level III**).¹⁰¹

Telling a woman that she has breast cancer is the responsibility of the senior clinician involved, and should not be delegated to junior and less experienced staff. It should not be delayed. Women should be dressed and fully alert when such discussions are held.¹⁰²

Non-verbal communication—eye contact, facing the woman, allowing her to speak without interruption, nodding encouragingly, giving her your full attention—can be just as important as the actual words spoken when telling a woman she has breast cancer. If the woman does not understand English well, a qualified and appropriate interpreter is essential.

Telling a woman she has breast cancer, a recurrence or metastasis

Prior to discussing diagnosis

- Ensure news of a diagnosis is given in person and in a quiet, private place.
- Encourage a second person to be present if appropriate.
- Allow enough uninterrupted time in the initial meeting.
- Arrange to provide other methods to convey the information (eg written materials, video tapes, tapes of consultations, etc).

Providing information

- Use the general interactional skills suggested on previous page.
- Assess the woman's understanding of her condition.
- Briefly explain the process by which the diagnosis was reached.
- Provide information simply and honestly.
- Use lay terms, without using euphemisms.
- Avoid the notion that 'nothing can be done'.
- Adhere to the patient's preference for information.
- Clearly indicate that the woman will have the final decision regarding her care.

Emotional and supportive role

- Encourage the woman to express her feelings (eg crying freely, talking about concerns, fears, anger, anxieties, etc).
- Respond to her feelings with empathy.
- Address disturbing or embarrassing topics directly and with sensitivity.
- Be sensitive to the woman's feelings and concerns and communicate this understanding.
- Offer assistance to tell others.
- Provide information about support services.

After discussing a diagnosis

- Summarise the main points of the consultation.
- Assess the woman's understanding.
- Arrange a further appointment to review the situation within a stated time period (eg within 24 hours–two weeks).
- Indicate your availability for contact in the interim to address any questions or concerns.
- Ask if there is anything further the woman would like to discuss.
- Document information given to the woman and family members.
- Let others, particularly the woman's GP, know the extent of information given and your perception of her understanding.

Adapted from *How to break bad news*, by the NSW Cancer Council (1994).¹⁰² Source: NHMRC (Source National Breast Cancer Centre Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer.⁹⁴

The words used in discussing the diagnosis and prognosis must be chosen judiciously. One hundred women newly diagnosed with early breast cancer were surveyed to determine whether they understood the prognostic information communicated by clinicians after diagnosis. Many women misunderstood the language used by doctors to describe prognosis: 73 per cent did not understand the term 'median' survival and 33 per cent believed a cancer specialist could predict an individual patient's outcome. The information that women most wanted was that relating to probability of cure, staging of their cancer, chances of treatment being successful and 10-year survival figures with and without adjuvant therapy.¹⁰³

(Appendix E lists some questions women may ask of their clinicians in relation to diagnosis, treatment and prognosis.)

2.2.2 Providing information and involving the woman in decision-making

The attitudes of health care consumers towards their role in decision-making has changed dramatically in the past three decades, with a trend toward health care being perceived as a partnership between the health care consumer and the provider.

A consistent finding is that women want to make a collaborative decision involving their doctor, family and close friends,¹⁰⁴⁻¹⁰⁸ for the following reasons:

- women have little control over breast cancer and many of its treatments
- some women may not entrust treatment decisions entirely to health professionals¹⁰⁹
- the choice between breast conservation and mastectomy is dependent on clinical imperatives, including the tumour characteristics and breast size, and on factors that only the woman can assess—personal preference, lifestyle, the impact on her life of availability of resources and so on.

It is important to discuss with a woman the level at which she wants to be involved in decision-making. The National Health and Medical Research Council (NHMRC) says that women are entitled to make their own decisions about treatments or procedures and should be given adequate information on which to base those decisions.¹¹⁰ It says:

- information should be provided in a form and manner which helps patients understand the problem and treatment options available, and which is appropriate to the patient's circumstances, personality, expectations, fears, beliefs, values and cultural background
- doctors should give advice, but should not coerce
- patients should be encouraged to make their own decisions
- patients should be frank and honest in giving information about their health, and doctors should encourage them to be so¹¹⁰

Explanation of her diagnosis, prognosis and treatment options, accurate clinical information and information about the likely impact of treatment on the individual woman's life should be provided, so that the woman can be fully informed and encouraged to participate in the selection of surgical and subsequent treatment.^{111,112}

The information that women may need and request includes:

- the causes of breast cancer
- the extent of the disease
- the proposed approach to investigation and treatment, including information on expected benefits, the process involved, common side effects and material risks, whether the intervention is conventional or experimental, and who will undertake the intervention
- other options for investigation and treatment
- the likely consequences of choosing either another form of treatment, or no treatment
- the degree of uncertainty involved in all facets of the management
- the time involved
- the costs* involved
- the effect of cancer on interpersonal and sexual relationships
- typical emotional reactions
- any significant long-term effects—including physical, mental, emotional, social, sexual
- the resources required to adjust to and cope with the disease
- appearance after surgery
- special clothing that may be required
- how to obtain special items, such as wigs and prostheses
- entitlements to benefits and services, such as subsidies for travel or prostheses

Not all this information need be provided at the first consultation, and considerable time may be spent in discussion with the surgeon and other members of the treatment team. Time is needed to reflect on opinions, to ask more questions and to consult with the family, friends and advisers.¹¹⁰ Some of the information can be provided in written form—the consumer version of these guidelines should be provided to women diagnosed with early breast cancer. State and territory cancer organisations are also good sources of such information and material.

* (For further information about costs, please refer to JRG Butler & A Howarth. *Out-of-pocket expenses incurred by women for diagnosis and treatment of breast cancer in Australia*. NHMRC National Breast Cancer Centre, 1999).

At diagnosis

Studies have shown that only a little of the initial consultation is remembered. In one study, women remembered only 25 per cent of the important facts given to them by their clinician with free recall, and only 33 per cent when prompted.¹¹³

It is not necessary to make treatment decisions at the initial consultation. This gives the woman time to accumulate and digest information which aids in understanding the disease and treatment options, and to receive support from family and friends. Waiting a week or two, to seek other opinions, will not have an adverse effect on outcome.

During the course of treatment

The need for information does not diminish after the initial consultation or after treatment decisions have been made, but increases during and following treatment.⁷ Women with breast cancer and their families will need further information as they assimilate that given initially. Treatment aims should be discussed each time the clinical situation changes.

Doctors and other health professionals should be aware of these changing needs, and give women and their families repeated opportunities to ask questions so that they don't feel they are being rushed into a decision regarding treatment. Doctors frequently underestimate the amount of information their patients want, and overestimate the amount of time they spend giving information.¹¹⁴ A question prompt sheet may help¹¹⁵—see Appendix E.

Withholding information

Information should be withheld in limited circumstances only. These are:

- if the doctor judges on reasonable grounds that the woman's physical or mental health might be harmed seriously by the information
- if the woman expressly directs the doctor to make the decisions and does not want the information offered—but even in this case, the doctor should give the woman basic information about her illness and the proposed intervention

It is inappropriate for a doctor to withhold relevant information because of a fear that the woman will be upset by it¹¹⁰ or because the woman's family requests it.

Assisting women to recall information

When confronted with a diagnosis of cancer couched in technical jargon, many people do not remember all that was discussed during a consultation. Research on how to best encourage recall has shown that recall of information increases when women are provided with: a breast care nurse or counsellor (**Level II**);¹¹⁶ patient-specific information, such as a tape recording of the consultation (**Level II**);¹¹⁷ a follow-up letter (**Level II**);¹¹⁸ and psychoeducational programs

(Level II).¹¹⁹ Both information recall and psychological wellbeing increases when the information is tailored to the woman's particular needs, as opposed to being given in a standard format **(Level I).**¹²⁰ Doctors should consider incorporating these findings into the consultation.

Women from non-English-speaking backgrounds

If the woman is not fluent in English, a qualified and appropriate interpreter should be used, rather than a family or staff member. Interpreters are available free of charge in both the public and private sectors, although they must be booked in advance of any consultation as their availability is frequently restricted. Only a qualified and appropriate interpreter can ensure that all the necessary information passes between doctor and patient. It is important to ensure that the interpreter is prepared to interpret conversation concerning the woman's prospects for survival, and is not restricted from doing so by cultural norms or constraints.

Written information for women from Greek-, Italian-, Arabic- and Chinese-speaking backgrounds is available from the iSource National Breast Cancer Centre.

(Other recommendations about assisting women from non-English-speaking backgrounds may be found in *NHMRC iSource National Breast Cancer Centre Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer*).⁹⁴

2.2.3 Preparing women for specific management, including surgery

In addition to adjusting to the diagnosis of breast cancer, women will undergo a number of invasive treatments for the disease.

Providing women with emotional support and information about the procedure that they are about to undergo and what they might expect to feel or experience reduces their emotional distress and improves their psychological and physical recovery **(Level I).**^{121,122} (The consumer version of these guidelines may assist in this process.)

Guidelines	Level of evidence	Reference
Providing women with support and detailed information about their diagnosis and treatment increases their emotional wellbeing and assists their physical and emotional recovery.	I	120–122
Strategies to improve recall of information are recommended, including: <ul style="list-style-type: none"> • the provision of a breast care nurse or counsellor • tape recording of the consultation • follow-up letter • psycho-educational programs 	II	116–119

2.3 COUNSELLING AND SUPPORT

Most women adjust better to having breast cancer if they have good emotional support from family and friends.^{89,90}

Appropriate counselling for women with breast cancer has been found to improve emotional wellbeing and quality of life (**Level I**).¹²⁰ The term ‘counselling’ refers generically to a form of supportive care delivered by all health professionals. There are differing levels of sophistication depending on the training and experience of the practitioner involved. Techniques encompassed by the term ‘psychological therapies’ and ‘counselling’ are varied and may include supportive listening, the provision of practical information and education, instruction in relaxation therapies, assistance with communication and relationship problems, training in assertiveness and advice on problem-solving. The selection of a particular therapy depends on the particular needs of the woman and her social context and the training and experience of the therapist. Central components of all psychological therapies are an empathic manner, non-judgemental listening, acknowledgment of concerns, reassurance and emotional support (see NHMRC iSource National Breast Cancer Centre *Psychosocial clinical practice guidelines: providing information, support and counselling to women with breast cancer*).⁹⁴

All members of the treatment team play a role in providing support and opportunities for women to disclose their concerns, feelings and fears. Women particularly value support provided by the doctors involved in their immediate care.

A number of trials have assessed the contribution of a breast care nurse and have shown that such nurses enhance the early recognition of support needs, decrease psychological distress, and improve continuity of care and understanding of the disease and its treatment (**Level II**).^{79,116,123} Breast care nurses can provide emotional support, recognise unmet needs, provide information about the patient's physical state and treatment and offer practical advice on available resources.

Support from sources such as family, friends and women who have or have had breast cancer (including the Breast Cancer Support Service) can be helpful. Accepting support from family members can be difficult because of some women's needs to conceal their own anxiety in order to protect the emotional wellbeing of those close to them (**Level III**).¹⁰⁴ It is important for doctors not to presume the nature of the woman's relationships and to respect her choice of support person.

While most women will want to see the doctor alone or with a family member or friend, some women may wish to have the counsellor or breast care nurse present during the consultation when the diagnosis is given. This will:

- recognise the importance of counselling in patient management
- allow the support process to begin immediately and establish a caring environment for the woman
- help the counsellor understand what has been discussed
- reduce the possibility of confusion because of conflicting information
- allow the woman to recognise the support from the doctor and the counsellor together (through the team approach)

Support needs for women with breast cancer and their families may include:

- counselling
- access to a support group or the Breast Cancer Support Service
- assistance with the care of children, elderly parents or an elderly spouse or partner
- assistance with transport
- the fitting of a prosthesis
- help with accommodation near the treatment centre

Different forms of counselling and support may be needed, depending upon the specific concern. Women whose primary concerns are associated with self-esteem, anxiety, body image and sexuality could benefit by personal counselling and psychological or psychiatric assessment and care. Women whose concerns relate mainly to treatment and the changes in their lives could benefit from short-term crisis counselling, the provision of information, advocacy and practical support.⁷ A recent Australian study of women with early breast cancer found that at the time of evaluation 45 per cent of women had a psychiatric disorder, most commonly depression or anxiety or both. It is possible that this study reported

high figures because women who were more likely to be depressed agreed to enter the study and agreed to participate in a trial of group therapy. However, it should be considered whether traditionally used self-report measures are less sensitive than a structured interview in diagnosing depression in women with breast cancer, and this may also account for the high figure **(Level III)**.⁸¹

Each state and territory operates a Breast Cancer Support Service made up of well trained volunteers who provide support on a one-to-one basis and who have the advantage of talking from personal experience. Many women find support groups and talking to women who have or have had breast cancer useful sources of information and support.^{109,124-126} Contact can be made through the local state or territory cancer organisation.

Depression

For most women the diagnosis of breast cancer represents a major blow. Although the majority of women will adjust to the diagnosis and treatment, a significant proportion will develop a depressive illness which requires treatment. The diagnosis of a major depressive episode in a patient with cancer is best evaluated by the severity of depressed mood, loss of interest and pleasure, the degree of feelings of hopelessness, guilt and worthlessness and the presence of suicidal thoughts.

Estimates of the proportion of women with breast cancer suffering from depression vary. This may relate to the assessment methods used and the particular group of women studied, including the stage of their disease. At three months post diagnosis, it has been estimated that 10-17 per cent of women meet criteria for a diagnosis of major depression. Other studies at 12-24 months post diagnosis have estimated rates of depression between 5 per cent and 20 per cent.^{79,80,127}

The diagnosis of recurrent disease is considered by many cancer patients to be more distressing than the original diagnosis of cancer. Rates of depression of up to 42 per cent of patients have been reported among women who have been diagnosed as having a recurrence.^{128,129}

A retrospective study of 57 patients with breast cancer showed a concordance of psychiatric diagnosis between the oncologist and the psychiatrist in only 23 per cent, with the oncologist failing to diagnose a major depression in a significant number of women.¹³⁰ Psychiatric morbidity may not always be recognised, particularly within the stressful context of diagnosis. Clinicians should, therefore, be alert for signs of depression or emotional distress in women diagnosed with breast cancer. When appropriate, referral should be considered to a psychiatric liaison clinic, counsellor, clinical psychologist or to a psychiatrist for treatment, including medication. Women with suicidal thoughts require immediate referral to a psychiatrist.

Women should be assured that depression is common in women with breast cancer, that it is not a sign of personal weakness and that treatments are usually highly effective. A more detailed discussion of depression in women with breast cancer can be found in the NHMRC iSource National Breast Cancer Centre *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer*.⁹⁴

Guidelines	Level of evidence	Reference
Counselling is recommended for women with breast cancer, as it improves quality of life.	I	120
The involvement of a breast care nurse in the treatment team is recommended, as this reduces psychological morbidity.	II	79, 116, 123

2.4 CHOOSING A SPECIALIST

General practitioners (GPs) frequently play a key role in recommending the specialist surgeon or clinical team. Eighty per cent of patients with early breast cancer were referred to surgeons by a GP and 13 per cent by a screening clinic.¹³¹ When choosing a specialist, women and GPs should consider the following factors:

- the clinician's experience in dealing with breast cancer
- access to multidisciplinary care
- location (local versus regional centre, especially for rural patients)
- decision-making style (collaborative versus directive)
- possible commitment to clinical research
- variations in cost

There is still considerable variation in the way specialists within a field manage breast cancer.^{132,133} In general it is beneficial for a woman to see a specialist who works with a multidisciplinary team; the evidence shows that the survival of women with breast cancer is better if they are treated by a specialist who also treats a large number of similar patients and who has access to a full range of treatment options in a multidisciplinary setting (**Level III**).¹³⁴ An Australian study has also shown that a rural setting was no impediment to breast conservation or to a multidisciplinary approach.¹³⁵

To help GPs provide the most appropriate referrals for their patients, breast surgeons, medical oncologists and radiation oncologists should be willing to

provide GPs with current information about their practices. This information could include:

- current management protocols
- use of patient support services
- accreditation status
- approximate fees and charges
- waiting times
- participation in quality assurance programs, including clinical trials, attendance at conferences and clinicopathological meetings

The provision of such information—perhaps annually through a personal newsletter—could be an important means of professional education and make for better communications about referral. Some of this information will be provided through the continuing education and re-certification requirements of the professional colleges.

In addition, the GP can bring his or her experience to bear. Previous patients may have reported their satisfaction or otherwise with particular specialists as regards the level of communication, their degree of involvement in the decision-making process, the treatment, the willingness of the specialist to deal with problems, and the availability of help after hours and on weekends.

The responsibility of the GP in the ongoing care of the whole patient is helped by the receipt of timely and comprehensive letters from specialists with adequate information about the management plan, including copies of pathology reports and other relevant investigations.

The referral letter from the GP should contain all the necessary information to aid in prompt and appropriate management by the specialist. Test results, films and other relevant data from the medical record should be forwarded with the referral letter.

The referral should also help establish good ongoing communication between the GP and the specialist. GPs require prompt, clear information in writing about management decisions, follow-up plans and patient progress.

Key point

When organising referral for women with breast cancer, GPs should consider both the preferences of the patient and the fact that patient outcomes are better if treated by clinicians who are part of a multidisciplinary team.

2.5 SECOND OPINION

Women have the right to obtain a second opinion at any time. This can help clear up any questions in their mind and help them decide which doctor they would prefer to manage their condition and which course of treatment to follow. It can also reinforce the accuracy of the advice given by their first doctor of contact.

Should any woman wish to obtain a second opinion, doctors should cooperate fully in providing all necessary information to the other doctor. This will save time and the unnecessary repetition of investigations.

Ideally the referral letter should come from the woman's usual doctor.

2.6 DISCLOSURE OF RISK

Doctors have a responsibility to give information about the risks of any treatment, especially those that may influence the woman's decision. Known risks should be disclosed when an adverse outcome is common even though the detriment is slight, or when an adverse outcome is severe even though the occurrence is rare.

The Bolam principle—usually summarised as the idea that a doctor is not negligent if he or she acts in accordance with the behaviour of a reasonable body of his or her peers—has not been upheld by Australian judges in superior courts in recent decisions.

Key point

The level of information required to be disclosed changed with the High Court decision in *Rogers v Whitaker* (1992).⁹⁷ The High Court said:

The law should recognise that a doctor has a duty to warn a patient of a material risk inherent in the proposed treatment; a risk is material if, in the circumstances of the particular case, a reasonable person in the patient's position, if warned of the risk, would be likely to attach significance to it or if the medical practitioner is or should be reasonably aware that the particular patient, if warned of the risk, would be likely to attach significance to it.

The NHMRC advises all involved in health care to take note of the spirit of the law, as well as the letter of the law. Women should be provided with as much information as they desire, and in a form that is appropriate to their education and culture. Only then can they make an informed decision regarding treatment.

2.7 CLINICAL TRIALS

Clinical trials are an essential component of the process of finding better treatments for breast cancer. Each of the three major advances that have been made to improve the outcome for women with breast cancer has only been demonstrated to be of clear value because it was first tested in well-conducted clinical trials. These major advances are:

- the demonstration that the addition of chemotherapy and hormone therapy to surgery improves survival
- the demonstration that breast conservation is a safe alternative to mastectomy in terms of survival
- the demonstration that the early detection of breast cancer by mammographic screening can lead to an overall reduction in the morbidity and mortality from breast cancer

In Australia, clinical trials are conducted on a large scale through national and international collaboration (such as the Australian New Zealand Breast Cancer Trials Group—ANZBCTG). Those trials encompass prevention, DCIS and most types of early and advanced breast cancer. Other trials in various institutions address specific questions. (For more information on the different types of clinical trials and a contact number for the ANZBCTG, see Appendix G.)

The national trials are planned on the basis of available laboratory and clinical research and are designed to:

- define optimum treatment programs
- test modifications to these programs that might improve outcome

In Australia clinical trials must be approved by an Institutional Ethics Committee (which might be known as an Institutional Review Board or a Research and Ethics Committee). Women must be provided with relevant and complete information about the trial protocol and provide their written consent before they take part. Entry into a trial must be entirely voluntary, and neither a refusal to enter a trial nor a decision to withdraw later without giving a reason must affect the woman's relationship with her treating practitioner.

Doctors should encourage women with breast cancer to consider participating in appropriate clinical trials for which they are eligible, as there is indirect evidence that women who participate in clinical trials have better outcomes than similar women given similar treatment outside trials.¹³⁶⁻¹³⁸ A high participation rate will enable outstanding research questions to be answered more quickly.

Guideline	Level of evidence	Reference
There is indirect evidence that women who participate in clinical trials have better outcomes than similar women given similar treatment outside trials.	III	136–138

Women's concerns about participation in clinical trials include that:¹³⁹

- the process of seeking participation compromises the role of the doctor in providing support and information appropriate to the particular woman
- they are being asked to make difficult choices at a time when they are physically and emotionally vulnerable
- the invitation to participate may be offered in an environment in which their capacity to give informed consent is compromised
- they won't know to which group they have been randomised
- they won't understand the research terms

In discussions about clinical trials, doctors should:

- reassure women that specialists participating in clinical trials are in touch with the best and most up-to-date treatments available, and are seeking to improve them
- take time to provide as much information as the woman needs and desires in a manner in which she can understand so she can make an informed decision
- explain that the control group in a randomised clinical trial is not a 'no treatment' group and does receive the therapy which would be offered outside a clinical trial
- not ask the woman to take part while she is in a vulnerable position, such as undressed or lying down
- not coerce
- allow time for the woman to decide
- inform the woman that she can withdraw from the trial at any time without prejudice

Key point

All clinical trials must be approved in advance by the ethics committee of each institution involved. These ethics committees have been established under guidelines developed by the NHMRC. They must include men and women from different age groups, and must include at least one of each of the following:

- a laywoman not associated with the institution
 - a layman not associated with the institution
 - a minister of religion
 - a lawyer
 - a medical graduate with research experience
-

2.8 PREGNANCY

Pregnancy needs to be considered in several different contexts. There is the treatment of cancer in pre-menopausal women who have the potential to become pregnant; there is the treatment of women who are pregnant when diagnosed; and there is the desire by some women to become pregnant after treatment is completed.

Prior to the commencement of treatment, women who have not yet had children may wish to consult with an obstetrician to consider their future options for fertility. For the woman and her partner to make a realistic decision about pregnancies, it is important for them to be given information about the most likely disease course, and risk of recurrence.

Treatment of women who may become pregnant

Although surgery can proceed, even in pregnancy, pre-menopausal women should be advised to avoid becoming pregnant while being treated with radiotherapy and chemotherapy or tamoxifen, as the treatment may not be tolerated and may be damaging to the foetus.

The woman may develop amenorrhoea, which may be temporary in women under 40 years of age.

Women will vary in the importance they place on fertility and having further children. Although these are sensitive issues it is important for women to feel that they can discuss concerns with their clinician. The limited evidence that is available about pregnancy after breast cancer treatment is presented below.

Treatment of pregnant women

Some studies of women who were pregnant at the time of diagnosis have shown these women to have lower rates of survival,¹⁴⁰⁻¹⁴² while others have not.^{143,144} The reasons for this poorer survival, if it exists, are unknown, but it is thought that the hormonal and immunological changes associated with concurrent or recent pregnancy may have an impact.¹⁴⁵

Surgery can be performed with minimal risk to the baby. The best time to operate is during the second trimester, although the increased risk of miscarriage from anaesthetics in the first trimester is fairly small.

Chemotherapy during the first trimester probably increases the risk of congenital malformations, but during the second and third trimesters this risk is probably small.

Radiotherapy should be avoided in pregnancy because of the risks to the foetus, including malignancy in childhood.

Because of the potential difficulties, the treatment of pregnant women should involve a multidisciplinary team including a surgeon, a radiation oncologist, a medical oncologist, an obstetrician and a family GP.

Pregnancy after treatment

The potential loss of fertility may be a source of distress for women and their partners. The decision to have further children after treatment for breast cancer and the optimal timing of such pregnancies are personal choices. The evidence from recent studies fails to show that women who become pregnant after treatment for breast cancer affect their risk of recurrence.¹⁴⁶⁻¹⁵³

The long-term potential teratogenic effects of chemotherapy and radiotherapy are not known, but are thought to be minimal.

Women who have had breast irradiation will almost certainly not be able to breastfeed on the irradiated side.

One study shows that women who have children after treatment for breast cancer do not suffer increased parental stress, and that for many of these women having children enhances their quality of life.¹⁵⁴

2.9 COMPLEMENTARY AND ALTERNATIVE THERAPIES

Most alternative or complementary therapies have not been tested in randomised clinical trials and proven to be effective. These therapies may involve some interference with conventional therapies and may cause harm.

However, many people with cancer turn to complementary and alternative therapies. Nearly 22 per cent of people attending one of three NSW oncology clinics were using these therapies.¹⁵⁵ Other studies overseas and in Australia have found that 9–54 per cent of adults with cancer^{156–160} and 46 per cent of children with cancer¹⁶¹ use complementary therapies. Most who do so use them as an adjunct to scientific medicine, while some do so instead of using scientific medicine. Some people use complementary and alternative therapies to create a feeling of control over the treatment of their disease, and decisions to use such therapies might not be based on the same philosophical approach as that used by doctors.

The main reasons for using complementary and alternative therapies given in the Begbie *et al.* study¹⁵⁵ were:

- new source of hope (49% of users of alternative therapies)
- preference for natural therapy (40%)
- impression that it is a non-toxic therapy (37%)
- supportive alternative practitioner (29%)
- try something different (23%)
- greater personal involvement (14%)

The main therapies used were:

- relaxation/meditation (59% of users of alternative therapies)
- diet therapy (57%)
- megavitamins (43%)
- positive imagery (44%)
- faith/spiritual healing (30%)
- naturopathy (27%)
- immune therapy (17%)
- homoeopathy (16%)
- acupuncture (11%)

Some therapies such as meditation, relaxation and a healthy lifestyle can work alongside conventional therapies. Randomised controlled trials of relaxation and meditation have shown these therapies to be of benefit to patients.¹⁶² Relaxation therapy is commonly utilised by psychiatrists and psychologists and is sometimes used by GPs and palliative care teams.

Discussing complementary and alternative therapies

Doctors should be aware of any complementary or alternative therapies being used by their patients and encourage discussion of the use of these therapies in an open and accepting manner. Women should be advised where the therapy may be harmful, ineffective or expensive. For example, women should be informed of

the potential interaction between certain unproven therapies (such as high-dose vitamin C) and some chemotherapy agents.

Patients may, however, perceive that their doctors will be opposed to the use of alternative or complementary therapies. Forty per cent of women with cancer who were using such therapies did not tell their doctors.¹⁵⁵

Key points

Some complementary or alternative therapies are evidence-based. However, the majority are not and may interfere with conventional treatment. Healthy living—including a good diet, exercise within limits, enough sleep and relaxation, and effective management of stress—is important for everybody, including women with breast cancer.

Doctors should encourage discussion of the use of complementary and alternative therapies in an open manner.

Further information on complementary and alternative therapies and their effectiveness, safety and costs is available in the section on alternative therapies in the iSource National Breast Cancer Centre's *Clinical practice guidelines for the management of advanced breast cancer* (2001).¹⁶²

CHAPTER 3 BEFORE DEFINITIVE TREATMENT

Optimal therapy for breast cancer is a multidisciplinary activity requiring input from the woman and the surgeon, the radiation oncologist, the medical oncologist, the diagnostic radiologist, the pathologist, the general practitioner, nurses and other health professionals. This may be provided in an integrated treatment centre or be accomplished elsewhere by consultation between professionals.

There is reasonable evidence that the survival of patients with breast and other cancers is better if they are treated by a specialist who also treats a significant number of similar patients, and who has access to the full range of treatment options in a multidisciplinary setting (**Level III**).^{134,135}

The service model favoured by women is one which:

- provides continuity of care
- uses a team approach
- offers psychosocial support
- ensures women's access to relevant health professionals from one location
- emphasises liaison with community supports such as GPs and community nurses¹⁶³

Although surgeons are usually the specialist clinicians of first contact in the management of a woman with early breast cancer, surgery is only one treatment modality. Since adjuvant radiotherapy or systemic therapy is also used in many cases, other specialists should become involved in the planning of definitive treatment.

Pre-operative consultation with a radiation oncologist should be considered if radiotherapy is thought to be likely. Because the need for systemic therapy is usually determined by the histology of the tumour and regional lymph nodes, it is reasonable to involve a medical oncologist in treatment planning at a later stage. In certain cases, it is appropriate for the medical oncologist to be involved before treatment begins.

In all cases the woman will require a varying degree of support, ranging from practical advice about obtaining a breast prosthesis after mastectomy to professional counselling when emotional or psychological problems occur. Clinicians who treat women with breast cancer should inform them how to access appropriate support services.¹⁶⁴

The woman herself has an important role in the planning of treatment for breast cancer. She should be encouraged to participate in the selection of surgical and subsequent treatment^{111,112} and should be informed fully about the appropriate treatment options. This may involve considerable time in discussion with the

surgeon and other members of the multidisciplinary team, but it is an essential step in the preparation for definitive treatment.

Australian doctors have a duty of disclosure which involves informing the patient of any material risks associated with any procedure. A material risk is defined as any risk which a reasonable person in the patient's position would regard as significant and which by implication might influence a decision in the selection of treatment.⁹⁷

Guideline	Level of evidence	Reference
The outcome of patients with breast and other cancers is better if they are treated by a clinician who has access to the full range of treatment options in a multidisciplinary setting.	III	134

3.1 HISTORY

A full clinical history can be of great value in the management of women with breast cancer. Apart from establishing a professional association, the doctor is able to obtain information about other relevant medical conditions.

Matters such as symptomatology (including pain) and menstrual, obstetric, family and medication history can be of importance, and such a record gives valuable information about the woman's background. In addition, obtaining details of the woman's social situation may provide valuable information about her risk of suffering increased emotional distress, given the known psychosocial risk factors (refer to section 1.5).

3.2 CLINICAL EXAMINATION

A thorough physical examination follows the history, and should precede other investigations. It should involve examination of both breasts and axillae for signs of primary cancer and local spread, and a thorough examination of the rest of the body for signs of distant spread.

A knowledge of the physical findings can be of value in sequencing investigations and making plans for therapeutic approaches. That knowledge can also assist in raising awareness of potential difficulties that could be avoided by good planning.

Clinical examination of the breast and of the regional lymph nodes is important in the assessment of the patient, but clinical examination is not completely reliable and needs supplementation from other diagnostic modalities. For

example, one small study showed that clinical examination had a sensitivity of only 37 per cent in women under the age of 35 (**Level III**).¹⁶⁵

The error rate in clinical assessment of axillary lymph node metastases is between 30 per cent and 50 per cent (**Level III**).^{166,167}

One study reviewed eight series totalling 2109 women and found that the triple test of clinical examination, breast imaging and aspiration biopsy provided an accuracy of 99.1 per cent. Due to the difficulties experienced with mammography in the dense breasts of young women, they suggested that an increased use of open biopsy was reasonable in women under 35 years of age.¹⁶⁸

3.3 INVESTIGATIONS

The following diagnostic modalities are currently used in the preoperative assessment of primary breast cancer. Since all are known to have limitations, they are usually used in combination. Diagnosis is established by:

- history and clinical examination
- breast imaging: mammography with/without ultrasound
- fine needle aspiration biopsy or core biopsy

Clear, accurate clinical information in the referral will assist the radiologist in providing the most appropriate targeted imaging.

While most of these tests will be performed so a diagnosis can be made, some may be used for further refinement between the time of diagnosis and the commencement of treatment.

Each of these investigations will provide different information, and none used alone is able to identify all cases of breast cancer.¹⁶⁹ It is therefore recommended that the triple test be used in investigating breast symptoms. This approach is outlined in *The investigation of a new breast symptom: a guide for general practitioners*.¹⁷⁰ (Also refer to *The pathology reporting of breast cancer. A guide for pathologists, surgeons and radiologists*. 1997, Australian Cancer Network.)

Mammography

In women with clinically detected breast cancer, mammography should be performed to detect cancer in the contralateral breast. In the affected breast, it measures the extent of the primary tumour and may demonstrate multifocal disease.

In women with DCIS or extensive intraductal carcinoma (EIC) associated with an invasive tumour, mammography may give a more reliable preoperative assessment of the extent of the disease than clinical examination (**Level III**).¹⁷¹ But even

mammography is likely to underestimate the extent of the disease process in women with DCIS (**Level III**).¹⁷²

In women with clinically palpable breast cancer, the combined use of clinical examination and mammography is likely to provide the best available assessment of the extent of disease in the breast. A good working relationship between the surgeon and the diagnostic radiologist can assist in decision-making.

Breast ultrasound

Breast ultrasound provides a reliable method for the assessment of tumour size in most cases of invasive breast cancer, particularly in dense breast parenchyma where mammography may fail to demonstrate clearly the margins of the tumour (**Level III**).¹⁷³

Ultrasound has also been shown to be useful in the detection of small breast cancers, particularly in younger women with dense breast tissue which is not suitable for mammography.¹⁷⁴

Some types of breast cancer such as invasive lobular carcinoma may not be detectable by either mammography or ultrasound examination.

Breast ultrasound is not routinely used for screening.

Key point

Not all cancers can be detected by mammography or ultrasound. Even if both tests are negative, a persistent lump should be investigated. Mammography and ultrasound should never be relied upon exclusively to diagnose any condition in the breast.

Fine-needle aspiration biopsy

Cytological examination of material obtained by fine needle aspiration has been used for many years to establish a preoperative diagnosis in cases of palpable breast cancer.¹⁷⁵ In the case of an impalpable lesion, a cytological sample can be gained by fine needle aspiration guided by either mammography or breast ultrasound (**Level III**).¹⁷⁶ It may require hook wire localisation and imaging.

The accuracy of breast cytology is very high when carefully performed and the cytologist is expert.¹⁷⁷ When a diagnostic sample of malignant cells is obtained, it may be possible to proceed directly to definitive surgery without a preliminary open biopsy.¹⁷⁸

Fine-needle aspiration biopsy (FNAB) provides a cytological rather than histological diagnosis. Before definitive surgery, it is necessary to have clinical and imaging support for the cytological diagnosis.

Hormone receptor status can be determined using cytological aspirates.

Core biopsy

Core biopsy uses a wide bore needle to obtain a tissue sample which may provide a definitive histological diagnosis. As for fine needle aspiration, core biopsy may be performed on palpable lesions or, with mammographic or ultrasound guidance, on impalpable tumours (**Level III**).¹⁷⁹ Where calcification is present, it should be submitted for a specimen X-ray to ensure correct sampling of the lesion.

Core biopsies need to be done by those familiar with the technique and its application in patient care. If the lesion is palpable, core tracks should be placed in such a way as to enable surgical excision of the track. This is also preferable for stereotactic core biopsies of impalpable lesions, but not always possible. In this situation, prior planning should be conducted in conjunction with the treating surgeon or multidisciplinary team.

Key point

The use of either fine needle aspiration or core biopsy to establish a preoperative diagnosis allows detailed discussion with the woman about surgical management and may permit a one-stage surgical procedure.

(See iSource National Breast Cancer Centre guidelines on *Breast fine needle aspiration and core biopsy*, in preparation.)

Open biopsy

When a cytological or histological diagnosis has not been obtained prior to surgery and there is still a strong clinical suspicion of malignancy, an open biopsy can be used to obtain a tissue diagnosis. It can be done either as an independent procedure or as part of a planned treatment procedure.

It is preferable to obtain an open biopsy as an independent procedure. This provides detailed information about the type and extent of the tumour, together with material for the assessment of hormone receptor proteins and other prognostic indices, before treatment is discussed. Information about the extent of disease, including vascular or lymphatic permeation and the presence of EIC, is of value in planning further surgical procedures.^{180,181}

Where possible, a small lesion should be excised completely, when open biopsy is performed.

Impalpable lesions may require needle localisation under mammographic or ultrasound control before open biopsy to assist surgical location. Excised specimens should be submitted for a specimen X-ray or ultrasound. They should be oriented by the surgeon and the tissue must not be incised.

Frozen section histology

Frozen section examinations of breast specimens have a limited role in the management of the patient with a palpable breast lesion. However, it may be necessary for confirming the diagnosis of the malignancy at the time of surgery and prior to definitive treatment, when that diagnosis is strongly suspected on clinical or radiological grounds but has not been made by preoperative fine needle or core biopsy. It is not often indicated in the management of women with clinically impalpable lesions.¹⁸²

- Frozen sections should not be performed in cases where the pathologist believes that subsequent examination is likely to be prejudiced.¹⁸²
- Fine needle or core needle biopsies are now widely available and have been shown in many studies to be as accurate as frozen sections. Frozen sections are not recommended for needle localised excision biopsies unless preoperative diagnosis has not been made and the lesion is easily palpable within the resected specimen.¹⁸²
- While cytological analysis of malignancy may typically be conducted before definitive surgery, frozen section may be used intraoperatively to confirm histologically a preoperative cytological diagnosis. It may be used to obtain an immediate diagnostic report when an open biopsy is performed as an independent procedure. It should not be done unless the surgeon can preserve the integrity of the specimen so as not to compromise tumour margins or subsequent histology.
- When a preoperative diagnosis has not been obtained, the use of frozen section histology to determine immediate definitive treatment, such as mastectomy, does not allow adequate discussion with the woman about her surgical management. Such a policy should be rarely used. An exception to this is when other investigations have strongly indicated the presence of cancer, and the woman has expressed a preference to undergo definitive treatment as a one-stage procedure. This may occur when the woman has expressed a preference to proceed directly to axillary dissection if a breast conservation procedure is indicated. It may also occur when mastectomy is the treatment of choice based on clinical and radiological findings, but only if the woman is prepared to proceed with this management without further discussion.

While some women are prepared to give consent for defined surgery to proceed depending on intraoperative findings such as frozen section, most women would feel uncomfortable about making the decision for a possible mastectomy in this way.

Other pre-operative investigations

Apart from mammography, the selection of other investigations should be determined by the doctors involved in the patient's care.

Full blood count and serum biochemistry may give useful information in selected cases, but imaging investigations—including chest X-ray, bone scan, liver ultrasound and chest computed tomography (CT)—have a low diagnostic yield.¹⁸³ They should be used only when clinically indicated. Such indications include:

- symptoms of lung disease
- a palpable liver
- abnormal liver function tests
- bone pain
- bony tenderness

Serological tests for cancer-specific antigens, such as CEA and CA 15.3, are non-specific and unreliable as indices of active disease.¹⁸³

Key point

All diagnostic modalities have an error rate and it is advisable to use more than one modality to obtain a preoperative diagnosis. The combination of clinical examination, mammography, ultrasound and fine needle aspiration cytology provides the highest diagnostic accuracy and the lowest risk of diagnostic error, particularly in women over 35 years. An increased use of open biopsy is reasonable for suspicious or indeterminate lesions where a definite benign needle biopsy has not been obtained in women less than 35 years of age.

3.4 PATHOLOGY

Pathological examination of the specimen is an essential part of the management of breast cancer. The examination and reporting of breast specimens should be undertaken in line with the Australian Cancer Network's guidelines for *The pathology reporting of breast cancer*.¹⁸² (This document is currently being updated.)

Pathological examination has three main aims:

- to provide a diagnosis
- to confirm the complete removal of the lesion
- to provide extra information useful for management, such as tumour markers and oestrogen receptors

Re-excision should be performed if pathological examination shows the margins were involved.

Pathological examination is easier if diathermy is not used on the specimen. The excised specimen should be oriented by the surgeon at the time of excision.

Synoptic pathology reports should contain, as a minimum, the following information:

- tumour size
- type
- histological grade
- tumour margins
- presence or absence of multifocality
- the presence or absence of DCIS, both within the tumour and around it
- the presence or absence of vessel space invasion in the main tumour
- number of axillary nodes identified and examined^{182,184}
- extracapsular spread
- oestrogen receptor status
- progesterone receptor status

It is recommended that receptor analysis be routinely requested and obtained. Present evidence indicates that hormone receptor status from immunohistochemistry testing is reliable and can be extended to cytological aspirates.

For further information on pathological testing and reporting, refer to *The pathology reporting of breast cancer*.¹⁸²

To assist the pathologist, surgeons should send all excised lymph nodes for examination. Clinicians should specifically request hormone receptor status on the pathology form. If it is not requested, the hormone status will not be readily available for decision-making, and the woman will not be reimbursed for the test if it is done.

Note that oestrogen receptor status can be determined on cytological aspirates, freshly excised specimens and paraffin block specimens.

Other information—such as degree of angiogenesis, proliferative rate, cathepsin D expression, epidermal growth factor receptor expressions, pS2 expression and the presence of heat shock/stress proteins—can be obtained by special staining, but much of the data are yet to be proved clinically useful.

Key point

It is recommended that receptor analysis be routinely requested and obtained.

CHAPTER 4 SURGERY FOR INVASIVE BREAST CANCER

The aim of surgery for primary breast cancer is to eradicate the primary tumour and any local extension in the hope of achieving total disease control.

Indirect evidence suggests that surgical intervention may extend survival from the time of clinical detection. In an historical comparison, women treated by radical mastectomy appeared to survive longer than women whose breast cancer was untreated,¹⁸⁵ and in the long-term follow-up of women treated by radical mastectomy, about 30 per cent of women were alive 30 years after surgical treatment (**Level III**).¹⁸⁶

There have been two randomised trials involving women over 70 not having surgery. In the first, women were randomised to either tamoxifen 40mg daily or tamoxifen plus optimal surgery.¹⁸⁷ At a median follow-up of 34 months, many women on tamoxifen alone had progressed to surgery, but there was no demonstrable difference in quality of life or survival rate. The trial is continuing. However, a number of women over the age of 70 years are of good performance status and good prognosis and should probably be treated along standard treatment lines, which in most circumstances would be wide local excision followed by post-operative radiotherapy. There is no evidence to suggest that these patients have any greater difficulty coping with such treatment.

In the second trial,¹⁸⁸ women were randomised to either wedge resection or tamoxifen 40mg daily. At a mean follow-up of 65 months, significantly more women in the tamoxifen group had progression of their cancer. There was no difference in overall survival, cause of death, the rate of metastases or the site of initial metastasis.

Further evidence supporting the value of surgical excision is provided by randomised controlled trials of screening mammography. Women offered mammographic screening and treatment of screen detected cancers have significantly lower mortality than women in unscreened control groups in population-based trials of mammographic screening (**Level I**).¹⁸⁹

The surgical treatment of primary breast cancer has devolved into two basic procedures:

- complete local excision (CLE) with axillary dissection
- total mastectomy with axillary dissection

4.1 BREAST CONSERVING SURGERY

Breast conserving surgery demands CLE, which by definition means clear histological margins with a rim of normal breast tissue around the periphery of the primary tumour on all sides. This procedure is suitable for tumours which are

unifocal and in which clear margins can be obtained, if necessary by including overlying skin. All the requirements of treatment must be taken into account when planning the incision.

There is no absolute limit to the size of a tumour which can be locally excised without incurring a high risk of recurrence; 3–4cm is often regarded as a practical limit.¹⁹⁰ The aim of treatment is to maximise control of the disease and decrease the impact of breast cancer on the woman's quality of life. However, the relativity of tumour size to breast size and the achievement of an acceptable cosmetic result are equally important considerations.

A breast conserving protocol comprises CLE in which clear margins are obtained by any surgical technique (including segmentectomy and quadrantectomy),¹⁸² combined with axillary dissection and followed by adjuvant radiation therapy to the breast (see below). Completeness of excision minimises the risk of local recurrence. There are no reliable data to show a definite width of margin that is necessary for complete excision, but re-excision should be considered where the tumour extends to and or involves the margin.

For specimens of impalpable lesions that are accompanied by a specimen radiograph, it is essential to correlate the radiological and histological appearances. Blocks should be selected from the area of the radiological abnormality which can be identified, by either slicing or repeating an X-ray of the slices or by using a localisation device in which a grid reference is used to locate the areas of interest. Either method is acceptable. Any lesion present within the specimen should be described and its maximum dimension recorded in millimetres. The relationship of the lesion to the excision margins should be recorded and the distance to the nearest margin or margins, measured.¹⁸²

Very small, well differentiated tumours are associated with decreased levels of axillary involvement, and in such cases after discussion, consideration may be given to omission of axillary dissection. It should be noted that even in T1b tumours (6–10mm), the probability of lymph node involvement approaches 20 per cent (**Level III**).¹⁹¹ Studies of sentinel node biopsy may help to resolve this issue (see also section 4.4, Management of the axilla). (see Appendix C for TNM clinical classification).

When the omission of axillary dissection from a breast preserving protocol is considered, the woman should be fully informed of the risk of axillary node metastases being undetected. Radiotherapy could be offered as an alternative.

4.2 TOTAL MASTECTOMY

In clinical trials conducted in the 1960s, total mastectomy combined with axillary dissection or radiation treatment to the axilla achieved survival rates similar to those achieved by the Halsted radical mastectomy.¹⁹² Later studies confirmed this (**Level II**)^{193,194} and there is now essentially no role for Halsted therapy in modern care of breast cancer.¹⁹⁵

The surgical protocol for a total mastectomy includes complete excision of the breast parenchyma with preservation of the underlying pectoral muscles.

Total mastectomy is an appropriate treatment for women whose tumours extend widely within the breast, have ill defined margins which defy CLE, directly involve the nipple or overlying skin, or who do not choose breast conservation. Nipple involvement does not always preclude breast conservation. In such cases, excision of the central breast tissue, including the nipple, is often feasible. It is reasonable to reconstruct the nipple as a secondary procedure.¹⁹⁶

Skin sparing and nipple preserving mastectomy with immediate reconstruction may have a place in the treatment of early breast cancer. Although no long-term results of this technique are yet available, early data suggest no increase in the risk of local recurrence when tumours of comparable size are treated by skin sparing mastectomy as opposed to total mastectomy (**Level III**).¹⁹⁷⁻¹⁹⁹

4.3 COMPARISON OF BREAST CONSERVING SURGERY WITH MASTECTOMY

Pre-operatively, about 70 per cent of mammographically detected cancers and 50 per cent of clinically detected cancers appear suitable for breast conservation,²⁰⁰ and this option should be discussed with the woman.

Numerous randomised, controlled clinical trials have demonstrated no difference in distant metastases or survival among women with operable breast cancer treated by mastectomy compared with those treated by breast conserving surgery (**Level I**),^{195,201-203} when both have included axillary dissection.

The incidence of local recurrence is 1–2 per cent per year in women who have breast conserving surgery followed by radiotherapy.²⁰⁴ In comparable tumours, the incidence of local recurrence following mastectomy is 3–5 per cent at 10 years, or less than 0.5 per cent per year.²⁰⁵

The choice of surgery is an individual one and each woman should be fully informed of her options, including the risks and benefits of each procedure. The woman should be informed that local recurrence can occur even in surgery properly performed and she should be made aware of the potential need for further surgery if the margins are positive.

The cosmetic result of breast conserving surgery has a high level of acceptance,²⁰⁶ gives an opportunity to preserve the breast shape, avoids the need for a prosthesis or reconstructive surgery, facilitates a better fit of clothing and in general is associated with less impact on body image and sexuality. These are factors which may influence a woman's decision in favour of breast conserving surgery. In discussion of choice between breast conserving surgery and mastectomy, women should be informed that body image is better preserved with conservation surgery (**Level I**).²⁰⁷

Guideline	Level of evidence	Reference
In discussion of the choice between breast conserving surgery and mastectomy, women should be informed that body image is better preserved with conservation surgery.	I	207

Specific situations in which mastectomy may be preferred to breast conserving surgery include:

- a tumour of such a size relative to the breast that a satisfactory cosmetic result may not be obtained
- multifocal disease
- co-existence of extensive intraductal carcinoma or DCIS which is of high grade and which cannot be excised with clear margins
- prior radiation therapy to the breast
- previous history of collagen disease, particularly scleroderma
- widespread indeterminate micro-calcification within the breast, which may make mammographic follow-up difficult
- when the woman chooses mastectomy in the knowledge that the two treatments are equally effective

Studies comparing breast conserving surgery and mastectomy have shown similar psychosocial morbidity for both procedures, even twelve months after surgery (**Level III**).⁸⁰ However, an influential factor during the first twelve months appears to be choice, with those offered a choice of surgery experiencing fewer psychological difficulties in the first 12 months than those who were not (**Level III**);⁸⁰ this was not evident three years after surgery.²⁰⁸

Regardless of surgery type, some women will suffer problems with sexuality,^{129,209} although there is some evidence that this effect is less marked in women having breast conserving therapy.¹²⁹ The most consistent finding is that body image is much better in women who have breast conserving surgery.^{73,129,207} Further research is needed to elucidate the impact of different forms of surgery on physical health, anxiety, depression and global quality of life.

Overall, there is no evidence for a substantial difference in post-operative psychological health between women who have had breast conservation and those who have had mastectomy,^{80,210-215} although the focus of anxiety may be different.

Many women who have mastectomy will be able to have breast reconstruction. In some cases, this can be planned before mastectomy and carried out at the same time. Women with cancers suitable for immediate reconstruction should be informed of this option before surgery.

Guideline	Level of evidence	Reference
Where appropriate, women should be offered a choice of either breast conserving surgery followed by radiotherapy or mastectomy, as there is no difference in the rate of survival or distant metastasis.	I	195

4.4 MANAGEMENT OF THE AXILLA

Management of the axilla has several aims:

- eradication of metastatic disease within the axillary nodes
- assessment of nodal status for evaluation of prognosis
- assessment of nodal status to determine adjuvant therapy

Both dissection and irradiation are used in managing the axilla. The best approach needs to be considered, as there are side effects from both axillary dissection and axillary irradiation—in particular, lymphoedema. Reported estimates of rates of lymphoedema following axillary surgery (sampling or dissection) and/or axillary irradiation vary widely, reflecting the methodological weaknesses of many of the studies that have investigated the prevalence of lymphoedema following treatment for breast cancer.²¹⁶ Rates of between 0 per cent and 58 per cent for axillary dissection alone (six studies); between 0 per cent and 11 per cent for axillary sampling (two studies) and 8 per cent for women who received axillary irradiation alone (one study) have been reported.²¹⁶ When both axillary surgery (dissection or sampling) and irradiation are given, reported rates of lymphoedema range between 6 per cent and 60 per cent (nine studies).²¹⁶ However, analysis of the significance of much of this research is complicated by the lack of comparability between studies and measurement methods, small sample sizes, poor differentiation of subgroups and methodological problems in individual studies.²¹⁶

Axillary dissection

The extent of axillary dissection can be defined with reference to the pectoralis minor muscle:

- level 1: lower axilla up to the lower border of pectoralis minor
- level 2: axillary contents up to the upper border of pectoralis minor
- level 3: axillary contents extending to the apex of the axilla

All nodes removed should be sent to the pathologist for examination.

Survival

The benefits of axillary dissection in prolonging survival are unclear; studies have reported different effects on survival and most have some methodological flaws. For example, the NSABP 04 trial²⁰⁵ found that there was no difference in survival between women who had simple mastectomy and those who had radical mastectomy (including axillary dissection). However, 33 per cent of women in the non-dissected group had undergone some form of limited axillary surgery and the power of the study may have been insufficient to demonstrate a clinically significant difference between the groups.

Other studies have found overall long-term benefits in survival when axillary dissection was carried out.^{192,217,218} For example, Cabanes' study of lumpectomy plus breast and axillary irradiation without axillary dissection, versus lumpectomy plus breast irradiation with axillary dissection, showed a small but significant improvement in survival in women who had axillary surgery (92.6% vs 96.6%, $p=0.014$).²¹⁷ However, interpretation of these results is difficult since a significant proportion of the axillary dissection group received adjuvant systemic therapy based on their nodal status.

Prognostic information

Axillary dissection also provides information about nodal status for both prognosis and the planning of adjuvant treatment.

Axillary lymph node status is the most powerful single variable in the estimation of prognosis for primary breast cancer. Prognosis is related to the *number* of axillary nodes which contain metastases—this relationship applies to both disease-free interval and to survival.²¹⁹

As a means of selecting women for adjuvant systemic therapy, the number of nodes involved is important since the benefits of therapy are expressed as a reduction in risk. The probability of lymph node involvement is related directly to the size of the primary tumours. Larger tumours are more likely to have metastasised to axillary lymph nodes than smaller ones. But even in small primary tumours (T1a), the risk of nodal metastases approaches 20 per cent.¹⁹¹ In the presence of nodal involvement adjuvant radiotherapy has been shown to have a significant influence on disease-free survival, to reduce locoregional recurrence and, in a few studies, to improve overall survival.^{220,221} (See section on Axillary Irradiation below.)

At this time, axillary dissection is the only reliable technique for determining lymph node status.

Axillary sampling is an ill-defined procedure and is not recommended as an alternative to axillary dissection. Axillary sampling may imply the removal of a single lymph node for histological examination, or a dissection of the axillary

contents extending to level 1. Although there is now some evidence from randomised controlled trials^{222,223} which shows that this technique produces qualitative information about whether an axilla is histologically involved under some circumstances, the accuracy of the procedure has not been validated by other centres. At this time axillary sampling is considered unreliable in assessing the presence of axillary lymph node metastases because of the high false negative rate.²²⁴

Sentinel node biopsy

Sentinel node biopsy is being studied,^{225,226} but is not currently considered an alternative to axillary node dissection and the procedure should only be performed as part of a controlled study or as a prelude to dissection. In the future, after appropriate controlled randomised trials have been completed, sentinel node biopsy technologies may modify the approach to the axilla.

Axillary irradiation

The selective use of radiotherapy in patients with increased risk of recurrence is beneficial (Level II).^{220,227} Two studies^{220,227} have shown a survival benefit for post mastectomy radiotherapy that included the axilla (and the internal mammary chain and supraclavicular fossa), and another trial has shown a trend towards improved survival.²²¹ However, a large overview failed to demonstrate a survival benefit for post-operative radiotherapy.^{195,228}

Axillary irradiation following dissection in women with *limited* nodal involvement

Relevant data are provided by extrapolation of results from several large randomised trials²⁰¹⁻²⁰³ which compared breast conserving therapy and mastectomy. They suggest that there may be little benefit from adding axillary irradiation among women who have had axillary dissection and who have only a small number of involved lymph nodes.

For example, the NSABP-B06 trial²⁰² reported that 90 per cent of patients had less than four lymph nodes positive in a dissected axilla. Local axillary relapse in this entire series is low, at around 1-3 per cent. It is unlikely that the addition of radiotherapy will confer much benefit where rates of relapse are already very low.

This conclusion is supported by a strong body of retrospective data.^{201,229} Data from the Mayo Clinic suggest isolated locoregional recurrences (that is, recurrences on the chest wall or lymphatic areas) of only around 8 per cent of women with less than four lymph nodes involved.²³⁰ Similarly, Fowble *et al.*²³¹ suggest isolated locoregional recurrences of 7 per cent in this group. Of the 634 patients analysed in this study, only 1.3 per cent recurred in the axilla alone and another 1.3 per cent in multiple sites that included the axilla—that is, the total axillary recurrence rate was only 2.6 per cent.²³¹

Fisher²³² analysed patterns of recurrence in 320 patients who had been treated for Stage II or III breast cancer with surgery and chemotherapy without locoregional radiation therapy. Twenty-one isolated axillary recurrences were found (6.6 per cent) at a median follow-up of 77 months. The number of axillary nodes involved was not predictive of recurrence.

Axillary irradiation following dissection in women with greater lymph node involvement or remaining disease in the axilla

While these data suggest that there is little to be gained by axillary irradiation in women with only a small number of involved lymph nodes, it seems that there may be benefit from the addition of radiotherapy when it is likely that there is remaining disease in the axilla—for example, when the surgeon believes that macroscopic disease was left behind or transected, or when the pathologist indicates positive margins.

The addition of axillary irradiation with greater nodal involvement is more controversial.²³²⁻²³⁵ When there is greater nodal involvement, local relapse rates will be increased for surgery alone. For example, data from the Mayo Clinic²⁰³ suggest isolated locoregional recurrences at three years of 14 per cent among women with 4-7 positive nodes and 22 per cent for women with eight or more positive nodes. Similar data have been reported by Fowble *et al.*²³¹ However, not all of these relapses are axillary. Most studies have shown at least 50 per cent to be on the chest wall. These studies are unrandomised.²³²⁻²³⁵

The three randomised trials^{220,221,227} noted above which showed an improvement in survival in high-risk disease for patients irradiated to the entire lymphatics and chest wall, showed a reduction in locoregional relapse from 32 per cent to 9 per cent at ten years. Again, the distribution of local relapses was not given, but more than half were on the chest wall. Axillary recurrences remain uncommon even in patients with heavy nodal involvement. Not all analyses have demonstrated increased axillary relapse rates with increasing numbers of involved nodes.²³²

It is important, however, to consider the role of axillary irradiation in patients at high risk of local recurrence. Not all axillary recurrences can be salvaged. It is particularly difficult to salvage axillary recurrence with radiotherapy where the axilla has been previously selectively excluded from the chest wall and supraclavicular fossa volume. The prevention of recurrence is therefore a preferable option, although it carries the cost of increased risks of lymphoedema.

Guideline	Level of evidence	Reference
For most women with early breast cancer, a level 1 or level 2 axillary node dissection should be standard.*	II	205, 217

* See Table I for recommendation summary.

Summary

Treatment of the axilla by either dissection or irradiation will reduce rates of axillary recurrence. In practice, most women will be offered axillary dissection as the first choice since this will also provide information to assist in staging and in contributing to decisions about systemic and locoregional adjuvant treatment.

While data are limited, general agreement was reached on certain recommendations for the management of the axilla at the Meeting on Axillary Dissection and Irradiation held at the Gold Coast, Australia in September 1998 (see Table 1 for a summary).

For some women, irradiation rather than dissection will be the preferred method of axillary control. This includes selected women in whom the result of axillary dissection would be unlikely to influence the decisions about systemic adjuvant therapy. Other women may not wish to have further surgery, and any decision should involve consultation with appropriate members of the multidisciplinary team.

Some women at high risk of axillary recurrence will require both axillary dissection and axillary irradiation. In particular, this will include those women who have remaining axillary disease following dissection.

Table 1: Recommendations for management of the axilla*

-
- For women with early breast cancer, a level 1 or level 2 axillary node dissection should be standard.
 - The omission of axillary dissection can be considered for some women, including: selected patients in whom the result of axillary dissection would be unlikely to influence the decisions about systemic and locoregional adjuvant therapy; and women with an isolated small low grade carcinoma.
 - Axillary irradiation will reduce axillary recurrence.
 - Where the risk of axillary recurrence is high, both axillary dissection and axillary irradiation should be considered. In particular, this will include those women who have remaining axillary disease following dissection.
 - Management of the axilla should be determined by a multidisciplinary team in discussion with the patient. Patients should be informed of the benefits and risks of axillary dissection and axillary irradiation.
-

*Source: Recommendations from the Meeting on Axillary Dissection and Irradiation held at the Gold Coast, Australia, September 1998.

4.5 BREAST RECONSTRUCTION

After treatment for breast cancer, women may have concerns about their appearance. For example, in a recent Australian study, 29 per cent of women reported feeling substantially less attractive and 13 per cent were unable to look at themselves naked after treatment for breast cancer and had low self-esteem following a mastectomy.¹²⁹ The study included women who had had either breast conserving surgery (54 per cent) or mastectomy (46 per cent), but the data were not analysed separately.

Breast reconstruction involves the use of a prosthesis or of tissue from other parts of the body to rebuild a breast removed by mastectomy. It does not interfere with the treatment of breast cancer.

The decision to choose breast reconstruction is a complex one and opinions vary as to whether it should be done at the time of treatment or later. Women should be given the opportunity to consider the procedure, so they can balance the advantages and disadvantages of reconstruction after mastectomy.²³⁶⁻²³⁹

Methods of reconstruction

The actual method of reconstruction will depend on the nature of the problem.²⁴⁰ There is no single method that is suitable for all women.²⁴⁰

In women with small breasts, a prosthesis may be a satisfactory method and may be used alone, or in association with a tissue expander. This latter device is used to achieve a gradual increase in the amount of available skin cover. A second procedure may be required to replace the expander with a definitive prosthesis. Complications occur in about 10 per cent of patients (**Level III**).²⁴¹

In some selected women with large and heavy breasts, a breast sharing reconstruction may be possible. With this technique, tissue from the other breast is taken for the reconstruction. Infection and loss of tissue occurs in about 5 per cent of cases (**Level III**).²⁴²

Skin and fat may also be transferred from the back, using the latissimus dorsi muscle as a flap. Donor site morbidity is minimal and complications of infection and tissue loss occur in fewer than 5 per cent of patients. A prosthesis may be necessary to augment the breast volume, and complications occur in fewer than 5 per cent of patients.²⁴³

In women with a suitable amount of loose skin and fat on the abdomen, a transfer of this tissue, either as a pedicled flap or as a free microvascular transfer, may be used. This is known as the TRAM (transverse rectus abdominis myocutaneous) flap method of breast reconstruction. The complications of infection and loss of tissue occur in about 5 per cent of patients. A further 10 per cent suffer some weakness and bulging of the abdominal wall.²⁴⁴ Because more muscle is used in

the pedicled technique, the risk of abdominal weakness is potentially greater than with the microsurgical approach. Other potential complications of either the microsurgical or pedicled methods of reconstruction include fat necrosis in the reconstructed breast and asymmetry with the other breast.

There is no evidence that breast reconstruction increases the risk of recurrence of the original tumour, or that there is any significant impairment of the ability to detect any recurrence.²⁴⁵ However, continuing follow-up (including mammography) is advised, as all women who have had a cancer of the breast have a small but definite increased risk of developing a new cancer in the residual breast tissue.

Although there is no evidence that the use of silicone prostheses poses any long-term risk to general health,²⁴⁶ significant numbers of women have local reactions to the prostheses, which may develop a tight capsule, become hard or be rejected.²⁴⁶ Because of the controversy surrounding silicone breast implants, these have been replaced largely by saline-filled implants. Soft tissue reconstruction is preferred by many women, particularly if there have been complications from the use of prostheses.

Psychological issues

There is no evidence that women who seek breast reconstruction are, as a group, psychologically vulnerable.²⁴⁷

No randomised trials of the impact of breast reconstruction on patient wellbeing have been located. However, it appears that reconstruction may help women worry less about their health, as the surgery helps repair the constant reminder of the life threatening nature of the disease.²⁴⁸ Psychological health may be improved in the short term and body image may be improved at three and twelve months.²⁴⁹

Women who have breast reconstruction are almost always happy with their decision. They report a number of benefits, including: a feeling of being whole again, better psychological and social adjustment to their cancer and mastectomy, more positive body image, better sexual adjustment, less depression and feeling more comfortable without a prosthesis.²³⁷

4.6 EXTERNAL BREAST PROSTHESES

Specialists performing mastectomy should ensure that the woman is aware of services available which can organise the fitting of a temporary or permanent prosthesis (while some patients are suitable for immediate reconstruction, others who have delayed reconstruction will need to use an external prosthesis in the interim). Follow-up should include assessment of post-mastectomy wound oedema, neuralgia, and radiation skin change or swelling that may impair the

correct fitting and use of an external prosthesis. Clinicians should also be aware of the consequences of a poor fitting, such as postural pain.

There is little literature concerning consumer access to and satisfaction with the current range of external breast prostheses.²⁵⁰

4.7 COMPLICATIONS OF SURGERY

Breast surgery requiring general anaesthesia has a low risk of complications. The main risks are:

- post-operative wound infection
- haematoma
- deep venous thrombosis

Women who have other unrelated diseases may have increased risk associated with anaesthesia. In appropriate cases, this increased risk should be discussed prior to surgery.

Following mastectomy and axillary dissection, a woman may experience:

- seroma of the axilla (following axillary dissection) or skin flap
- pain in the upper medial aspect of the arm and chest wall
- impact of loss of the breast on body image, appearance and self-esteem;
- lymphoedema of the arm (following axillary dissection)—which can occur at any stage, even years after treatment
- chest wall discomfort—which should settle within six months

Following breast conservation and subsequent breast irradiation, a woman may experience:

- seroma of the axilla (following axillary dissection)
- breast oedema
- breast pain and/or chest wall pain—which may last from three months to up to several years in some cases
- lymphoedema of the arm (following axillary dissection and/or irradiation)—which can occur at any stage, even years after treatment

Following breast reconstruction, a woman may experience:

- partial necrosis (death of tissue) of a soft tissue reconstruction
- infection and delayed healing
- infection and rejection of a prosthesis (in prosthetic breast reconstruction)
- a second primary tumour in retained breast tissue
- weakness of the abdominal wall (where tissue is in the rectus flap method of reconstruction)

Women should be clearly informed of these potential side effects when treatment options are being discussed, so they may make an informed decision.

After either total mastectomy with axillary dissection or breast conservation with axillary dissection, limitation of shoulder movement (particularly abduction and elevation) may occur, usually during the first few weeks. Appropriate exercises with or without physiotherapy will usually restore full function. Frozen shoulder is a rare complication of these operations. Arm exercises to restore function should be commenced on the first post-operative day.

When axillary dissection has been performed, it is usual to have some sensory loss in the chest wall below or posterior to the axilla and in some cases on the medial and posterior aspect of the upper arm. Preservation at the intercosto-brachial nerve reduces the extent of sensory loss.

As a generalisation, radical surgery combined with radical radiotherapy to the axilla results in a significantly increased risk of late complications such as lymphoedema. The risk of morbidity from combined treatment is relatively constant, while the benefits (a reduction in the risk of death and/or a locoregional recurrence) increase the higher the risk of recurrence or death. The matter becomes one of individual choice as it is obvious that not all women will see these costs and benefits in the same light.

The predisposing factors to the development of lymphoedema remain poorly understood. Analysis of research about the prevalence of lymphoedema is complicated by the lack of comparability between studies and by methodological problems in individual studies (see section 4.4).²¹⁶

Evidence supporting many forms of proposed treatments for lymphoedema, such as compression techniques, physical therapy, and surgical techniques, is less than optimal.^{216,251} Higher quality research is needed to examine the most efficacious treatments for this condition. (See NHMRC National Breast Cancer Centre *Lymphoedema: prevalence, risk factors and management: a review of research*, 1997.)

Patients with lymphoedema are at high risk of psychological distress.²⁵²⁻²⁵⁴ A special garment designed to compress the limb, and regular massage to the arm may be recommended to reduce the swelling of lymphoedema; there is some evidence of the effectiveness of these techniques (**Level III**).²¹⁶ The management of lymphoedema requires the input of both medical practitioners and physiotherapists, and occasionally of occupational therapists.

Key point

Women who have lymphoedema, or who have had both surgery and radiotherapy to the axilla resulting in a high risk of developing lymphoedema, need to look after their arm as the risk of infection is high. Women should be advised that the risk of problems associated with lymphoedema may be decreased by adhering to the following:

- if the arm on the same side as the surgery is cut or infected, or becomes hot, red, or swollen, immediate medical advice should be sought, the area cleaned and oral antibiotics commenced at the earliest sign of infection
- if possible, avoid in the affected arm: having blood taken, blood pressure checked, a drip inserted and an injection or vaccination
- avoid cuts, burns and insect bites
- avoid washing the dishes without gloves
- avoid letting the arm become sunburnt
- avoid gardening without gloves and long sleeves
- avoid carrying anything heavy with the affected arm
- wear loose clothing and loose jewellery
- use skin cream to keep the skin of the arm moist
- keep cool during hot weather
- eat a healthy diet to maintain body weight within reasonable limits
- undertake regular gentle exercise

Any intervention in the affected arm should be very carefully considered.

Studies of the psychosocial impact of lymphoedema have found that lymphoedema is associated with a diminished quality of life and that women with lymphoedema may experience not just functional impairment but also psychological morbidity.^{252,253,255} A recent review of the literature also reports that studies have shown that women who develop lymphoedema exhibit higher levels of psychological, social, sexual and functional morbidity than women with breast cancer who do not develop this complication.²⁵⁶ The review concludes that it is important that information about the condition and its consequences is given to women early in the treatment cycle.²⁵⁶

4.8 THE ECONOMICS OF LOCOREGIONAL THERAPY

Breast conserving treatment is more expensive than mastectomy—three times as expensive in one study²⁵⁷—because of the need for radiotherapy to prevent local recurrence.^{257,258} However, these studies do not include the cost of reconstruction after mastectomy, which may tend to equalise the cost.

While mastectomy may be the lower cost option in monetary terms, quality of life is an important factor in the cost/benefit equation. If a woman believes that her quality of life will be improved by choosing one treatment instead of another, that choice confers a benefit and should, where possible, be met.²⁵⁹

4.9 PRACTICE AUDIT

The audit of practice outcomes provides valuable information for the clinician and health service providers. Clinicians are encouraged to audit their practice. The Royal Australasian College of Surgeons has a breast audit instrument for breast surgeons (for further information see Appendix I). A national audit tool has been developed for radiotherapy, and one for medical oncology is in the process of development. (For the radiotherapy audit tool, please refer to *Radiotherapy and breast cancer*. Prepared by the Radiation Oncology Advisory Group; NHMRC NBCC and Royal Australian and New Zealand College of Radiologists, 1999).

CHAPTER 5 RADIOTHERAPY

Radiotherapy has been used in the treatment of breast cancer since the late 1890s. Today it is used commonly after breast conserving surgery and less commonly after mastectomy.

In 1995 the Early Breast Cancer Trialists' Collaborative Group published a meta-analysis of the results of randomised trials of radiotherapy and surgery.¹⁹⁵ They concluded that the addition of radiotherapy to surgery resulted in a rate of local recurrence that was three times lower than the rate with surgery alone (Level I).¹⁹⁵ This meta-analysis was updated in 2000.²²⁸

However, they found no significant difference in 10-year survival: among a total of 17,273 women enrolled in such trials, mortality was 40.3 per cent with radiotherapy and 41.4 per cent without radiotherapy. Radiotherapy was associated with a reduced risk of death due to breast cancer (odds ratio, 0.94; 95% confidence intervals, 0.88–1.00) which indicates that after 10 years, there would be about 0–5 fewer deaths due to breast cancer per 100 women. However, there was an increased risk of death from other causes (odds ratio 1.24; 95% confidence interval 1.09–1.42).

5.1 RADIOTHERAPY TO THE BREAST AFTER BREAST CONSERVING SURGERY

The routine use of radiotherapy following breast conservation has been examined. In the Uppsala-Obrebro trial,²⁶⁰ women were selected on the basis of mammographic findings, had tumours ≤ 2 cm, were node-negative and had pathologically confirmed free margins. There was a statistically significant difference in favour of giving radiotherapy to reduce the risk of local recurrence and consequent mastectomy. The five-year actuarial recurrence rate was almost 20 per cent in women receiving no radiotherapy, compared with less than 3 per cent in women treated with radiotherapy. This local recurrence rate of almost 20 per cent has been shown to increase with time,²⁶¹ as has been the case in other randomised trials such as NSABP B06.²⁶²

In other studies involving women not so carefully selected, local recurrence reaches almost 10 per cent per year within the first two years²⁰⁴ and 40 per cent at eight years²⁶³ for breast conserving surgery without radiotherapy. The Uppsala-Obrebro trial mentioned above has demonstrated clearly that even when CLE is confirmed by meticulous histological examination in T1 tumours, the risk of local recurrence is substantially increased if adjuvant radiotherapy is omitted.²⁶⁰

The success of an approach which conserves the breast depends on pathological confirmation that the margins of the resected breast tissue are not involved by the tumour. It is not necessary for the pathologist to verify that the margin is of a

specific dimension, for example, 10mm. Re-operation to obtain this degree of clearance is not necessary but adds to cosmetic deformity.^{43,264}

While it is not uncommon clinical practice to omit radiotherapy in highly selected early cases, it has to be emphasised that the decision requires the woman to weigh the benefits of avoiding the side effects and inconvenience of radiotherapy against the risks of local recurrence and the possible need for later mastectomy. A group of women at sufficiently low risk of local recurrence to allow breast conservation without radiotherapy has not been defined. Sometimes it may be appropriate to omit radiotherapy. Full discussion with the individual patient is essential, including provision of information about the benefits and potential risks of this course of action.

Although adjuvant radiotherapy is frequently omitted in the elderly woman, there is no objective evidence to show that this does not incur an increased risk of local recurrence.²⁶⁵

(Please refer to Chapter 4 for further information about the role of radiotherapy in the management of the axilla).

Guideline	Level of evidence	Reference
Radiotherapy after complete local excision (CLE) is recommended as it significantly reduces the risk of local recurrence in the breast and the need for further surgery. It should not be omitted, even in selected patients.	I	195, 260, 266

5.2 RADIOTHERAPY AFTER MASTECTOMY

Radiotherapy to the chest wall and/or regional nodes is probably the most controversial area covered in these guidelines. It has been traditionally given with the dual aims of reducing local and regional recurrence and of improving survival.

The vast majority of clinical trials which have addressed the role of postmastectomy radiotherapy have done so when the radiotherapy has routinely, rather than selectively, followed surgery.

Studies such as the King's Cambridge trial^{229,267} and the Edinburgh trial²⁶⁸ have shown the importance of treating the axilla. Both studies revealed a significant increase in uncontrolled local recurrence when simple mastectomy and observation were compared with simple mastectomy and radiotherapy (**Level I**).²⁶⁹

Impact of postmastectomy radiotherapy on survival

Several meta-analyses have examined trials of postmastectomy radiotherapy. Interpretation of the results of these meta-analyses is difficult because of changes over time in radiotherapy techniques.

The National Breast Cancer Centre's Radiation Oncology Advisory Group (a joint group with the Royal Australian and New Zealand College of Radiologists) commissioned a further meta-analysis of trial data that would include the most recent information from those Danish and Canadian pre-menopausal patient trials.²⁶⁹

Based on meta-analyses²⁷⁰⁻²⁷² and a recently commissioned meta-analysis of trial data²⁶⁹ which includes the most recent randomised controlled trials,^{220,221,227} several conclusions can be drawn:

- There is clear evidence of a significant reduction in the risk of local recurrence following postmastectomy radiotherapy with the prevention of approximately two-thirds of recurrences (**Level I**).²⁶⁹ There is no evidence that the relative reduction in the risk of local recurrence varies according to various risk factors including age, nodal status, receptor status, tumour grade or tumour size.
- There is clear evidence of a reduction in the risk of breast cancer mortality after postmastectomy radiotherapy (**Level I**).^{228,269}
- The reduction in breast cancer mortality is offset to some extent by an increase in the relative risk of death from causes other than breast cancer. On balance, the evidence does not indicate a reduction in total mortality following radiotherapy. There is also no evidence that the effect of radiotherapy on mortality varies significantly according to the extent of the surgery, type of radiotherapy, the year trials commenced or completed recruitment, or whether or not systemic therapy was administered.²²⁸
- It is difficult to reconcile these findings; in particular, recent updates of two of the trials show a statistically significant increase in survival in those women receiving postmastectomy radiotherapy.^{220,221}

The overview considered non-selective use of radiotherapy either as a definitive treatment of the axilla or routinely as an adjuvant to definitive surgery. Logically, even the latter trials should have been combined with the Danish and Canadian studies. Furthermore, many of the older trials used obsolete techniques with little regard to dose and fractionation. It is thus not surprising that when combined in this way with all other trials, the important data provided by the updates of the two trials fail to confirm a statistically significant reduction in mortality overall.

Summary of the evidence

Postmastectomy radiotherapy reduces the risk of locoregional recurrence (**Level I**) and of cause-specific mortality (**Level I**).^{228,269} The impact of postmastectomy radiotherapy on all cause mortality remains unclear. A review of the most recent published data²⁷³ has shown a reduction in all cause mortality, but this is not supported by the results of the meta-analysis of all randomised controlled trials.²²⁸ It is therefore logical to recommend postmastectomy radiotherapy for those at high risk of local or regional relapse. The risk threshold at which radiotherapy should be considered will depend on the likely benefit and on any possible adverse effects of that radiotherapy (the latter may depend on age).²²⁸

Risk of locoregional relapse

Data that indicate the levels of risk of locoregional failure are difficult to obtain from the 32 trials included in the third meta-analysis.²⁶⁹ However, evidence from large, retrospective, well analysed series (Rutqvist personal communication, 1997) and a recent analysis²⁶⁹ would suggest that the following are important indicators of increased risk of locoregional recurrence:

- increasing number of positive nodes
- increasing tumour size
- involvement of margins
- high histological grade of tumour
- lymphovascular invasion

While the existence of extracapsular spread is an indicator of poor survival,²⁷⁴ it does not increase the risk of axillary recurrence.^{275,276} Another recent study has questioned the value of extra nodal spread as an indication for radiotherapy to the axilla (**Level III**).²⁷⁷

Summary

Postmastectomy radiotherapy may therefore be considered in the following circumstances:

- tumours greater than 5 cm
- axillary involvement of more than three nodes
- the presence of positive tumour margins

In addition, when smaller tumours are found or fewer nodes are involved but one or both of the following are present, postmastectomy radiotherapy may be considered:

- lymphovascular invasion
 - high grade — grade 3
-

More trials are required to establish the effect on overall survival of modern radiotherapy after mastectomy. Until such data exist, prevention of local recurrence remains an important goal of postmastectomy radiotherapy.

These issues are considered in detail in the publication *Radiotherapy and breast cancer*²⁷⁸ developed by the Radiation Oncology Advisory Group of the iSource National Breast Cancer Centre and the Royal Australian and New Zealand College of Radiologists.

Guideline	Level of evidence	Reference
Postmastectomy radiotherapy is recommended for women at high risk of local or regional relapse	I	269, 228

5.3 COMPLICATIONS OF RADIOTHERAPY

Radiotherapy has a number of early local and general side effects, as well as late morbidity. The extent and severity of complications from radiotherapy will depend mainly on:

- the anatomical extent of the radiation fields
- the field arrangement
- the fraction size
- the total dose

Side effects increase significantly where the fraction size is greater than 2Gy per day, where the dose is greater than 60Gy and where other than megavoltage therapy has been employed.

Radiation does not cause alopecia, unless directed at the head.

The studies examining adverse effects and quality of life are generally of poor quality.²⁷⁹ However, to enable patients to plan their lives, they should be alerted before treatment commences that tiredness, lassitude or fatigue during or following treatment may be experienced.

Local effects that occur during treatment include redness and soreness of the skin. These will extend over the area of treatment and may cause concern to women. They usually resolve within a week or two of completion of treatment.

Later effects may occur in the months or years after radiotherapy, including tight skin and lymphoedema (if the axilla is irradiated). Lymphoedema usually occurs between six months and several years after treatment.

Side effects

- **Lymphoedema**

Lymphoedema can occur in any woman who has had either radiotherapy to the axilla or lymph node dissection. It is far more common in women who have had both (see section 4.4, Management of the axilla).

- **Local side effects in the conserved breast**

Women who have radiotherapy to the conserved breast may experience abnormal sensation varying between discomfort and significant pain, particularly in the first two years. The end cosmetic result is affected by many factors. The most important determinant of cosmetic result is the extent of surgery, followed to a lesser extent by the following factors:^{280,281}

- the surgical technique and the positioning of the scars
- the dose of radiation
- the boost technique (boost to large areas runs the risk of producing fibrosis and distortion)
- the extent of axillary dissection (level 1, 2 and 3 dissection may increase oedema in the breast)
- size of the breast—the larger the breast, the more likely it is to show a post-radiation shrinkage
- other factors such as weight gain, which may result in a disproportionately small increase in the fat in the treated breast

There is conflicting evidence over whether chemotherapy given at the same time as radiotherapy affects the cosmetic result.

Breast-feeding is generally not possible from the irradiated breast, but cases where it has been possible have been reported.²⁸²

- **Cardiac/vascular damage**

A meta-analysis of trials of adjuvant postmastectomy radiotherapy showed that in the 15+ year survivors, there was a non-significant increase in cardiac deaths.²⁷² This segregated according to the side of the tumour and was related to inclusion of the heart in the high-dose volume.

Modern planning techniques, designed to irradiate only the chest wall ± the residual breast deliberately exclude the heart from dose volumes >10 per cent, appear to decrease the risk of cardiac damage.²⁸³ A cohort study of women treated with breast conserving surgery and post-operative radiation therapy found no indication of an increased risk of acute myocardial infarction associated with the radiation therapy.²⁸⁴ However, the study suggested that cardiac damage is related to the volume of heart irradiated.²⁸⁵

This is supported by the analysis of morbidity and mortality data from two Danish randomised controlled trials^{220,227} of post-mastectomy radiotherapy in high risk breast cancer patients. When radiotherapy is delivered to the chest wall, axilla, internal mammary chain and supraclavicular fossa and when due attention is paid to minimising cardiac dose, ischaemic heart disease morbidity and mortality are not increased at 12 years.²⁸⁶

In a more recent overview²²⁸ on the favourable and unfavourable effects of radiotherapy on the long-term survival of breast cancer patients, once again both breast cancer mortality and local recurrence were reduced. However other, particularly vascular, mortality was increased. This hazard of increased morbidity is most marked in women with a low risk of locoregional recurrence (and hence unlikely to experience a major benefit from adjuvant radiotherapy) and in older women.

- **Osteitis of the ribs**

This is a brittleness of the ribs which occurs in up to 2 per cent of cases²⁸⁷ and can lead to spontaneous fracture. However, this usually requires no treatment. The risk of stiffness of the shoulder can be reduced by appropriate shielding.

- **Acute radiation pneumonitis**

The risk of acute radiation pneumonitis is reported to range from 0.7-7 per cent.²⁸⁷ When the breast and axilla are irradiated, the risk will be at the upper end of the range because the risk increases with the amount of lung in the radiation field. It is, therefore, a rare complication. Small asymptomatic radiological changes,

often referred to as fibrosis, may be noted on the chest X-rays. They may cause confusion and may be mistaken for metastases.

- **Brachial plexopathy**

This is a very rare complication and will only occur when the axilla and supra-clavicular fossa are irradiated. The incidence is 0.3 per cent at five years with current doses and fractionation,²⁸⁸ but has exceeded 5 per cent when hypofractionated regimens have been used.²⁸⁹

- **Second malignancy**

Six studies involving about 150,000 women treated with radiotherapy have reported on the development of a second malignancy.²⁹⁰ These studies have shown a relative risk of 1.17 which was not statistically significant.

About half the series quote an increased incidence of colon, uterine and ovarian cancer in patients irradiated for breast cancer. These cancers are unlikely to have been caused by radiotherapy, as the host organ does not lie within the field irradiated. When site-specific associations such as colon, uterus and ovary are excluded, the risk of second malignancy becomes negligible in the clinical context (**Level III**).²⁹⁰

In terms of post-radiation sarcoma, only 24 cases have been reported in seven series involving nearly 34,000 patients with follow-up of 5–18 years. The best estimate of risk is of two cases of post-radiation sarcoma per 10,000 women years of follow-up. In the case of breast conservation, perhaps half of these cases will be an angiosarcoma of the breast.²⁹¹

Key points

The prescription of radiation and the techniques used to deliver it can be extremely complex.

The radiotherapeutic management of breast cancer following breast conservation is governed by two fundamental radiobiological principles. These are that:

- The tolerance of normal tissue is a function of the total dose of radiation received as well as of the dose received per fraction per day and the volume of tissue irradiated.
- The probability of eradicating disease is a function of the dose delivered and the magnitude of the disease burden — in other words, a larger dose is required to eradicate a larger tumour given equal radiosensitivity.

Radiotherapy after breast conservation involves irradiation of the whole breast with a moderate dose, often followed by a higher dose, or boost, to the site of excision of the primary lesion. The boost allows the delivery of a higher dose to a small volume within which the risk of residual tumour is greatest.

The side effects of radiotherapy are a function of the total dose, the number of fractions in which it is delivered (that is, dose per fraction) and the time over which it is delivered. It is possible to give radiotherapy more quickly than the usual five to six week schedules, but this would require a reduction in the total dose given, which may reduce its efficacy. It would also require giving larger doses each day, which could increase the risk of late tissue damage and poor cosmesis. Recent evidence suggests that shortened radiotherapy fractionation schedules can achieve high rates of local control with acceptable cosmesis.²⁹² Long-term results and additional results are awaited.

Chemotherapy given in conjunction with breast radiotherapy may increase morbidity (for example, anthracycline may increase risk of cardiac damage and concurrent chemotherapy may increase risk of acute skin toxicity). However, preliminary results indicate that radiotherapy can be given with cyclophosphamide, methotrexate and 5-fluorouracil (CMF) therapy.^{292,293}

These issues are considered in detail in the publication *Radiotherapy and breast cancer*²⁷⁸ developed by the Radiation Oncology Advisory Group of the iSource National Breast Cancer Centre and the Royal Australian and New Zealand College of Radiologists.

CHAPTER 6 SYSTEMIC ADJUVANT THERAPY

Systemic adjuvant therapy includes all forms of hormonal manipulation and/or cytotoxic chemotherapy administered in conjunction with local therapy for early breast cancer. The aim of such therapy is to treat undetectable remaining cancer, which will reduce the risk of clinically evident metastatic disease and local recurrence. Ultimately, this should improve survival. This is a rapidly evolving area of knowledge, and many new agents are currently in trial. As new data emerge this section will be updated. Decisions regarding adjuvant systemic therapy are most appropriately made in a multidisciplinary setting.

Key to evaluating the potential impact of adjuvant therapies is an assessment of the absolute risk of recurrence for individual women. Several prognostic formulations have been developed⁶⁴ based primarily on tumour size, grade and extent of nodal involvement. Data are also available from control groups in randomised trials of adjuvant therapy, published in overviews.²⁹⁷⁻²⁹⁸ These groups however may not represent the general population at risk, as they have been selected by trial entry criteria. Patients with small (<2cm), screen detected, node negative tumours are under-represented in these trials and will be expected to have a better outcome.

Overall survival at 10 years

	Age <50	Age 50–69
Node negative	71.9%	64.8%
Node positive	41.4%	46.3%

Data from Early Breast Cancer Trialists' Collaborative Group, 1998.²⁹⁸

There is strong evidence based on meta-analysis of all available randomised clinical trials²⁹⁴⁻²⁹⁸ to show that adjuvant systemic therapy with the anti-oestrogen tamoxifen reduces risk of recurrence and death after treatment for stage I and II breast cancer in women with oestrogen receptor positive tumours up to the age of 70 (**Level I**).²⁹⁷ In women aged under 50, ovarian ablation can offer similar benefits (**Level I**).²⁹⁹ There is now good evidence that the benefits of tamoxifen are limited to those patients whose tumours contain hormone receptors (either oestrogen or progesterone receptors),²⁹⁷ and some evidence that the benefits of ovarian ablation are similarly restricted.^{299,300} Many clinical trials use age, usually a cut-off of 50 years, as a surrogate for menopausal status. Given that the median age of menopause in Australia is about 52 years, this is not accurate. Those recommendations that are based on age should be viewed with caution if they exclude an assessment of the woman's menopausal status. For example, oophorectomy may be useful for pre-menopausal women independent of age. Tamoxifen can be recommended for suitable women regardless of age.

There is also evidence from meta-analyses²⁹⁴⁻²⁹⁸ that multi-agent chemotherapy also reduces the annual risk of recurrence and death in women with both node positive and node negative disease up to the age of 70 years. The average magnitude of these protective effects was approximately 25-30 per cent reduction in risk of recurrence, and approximately 15-20 per cent reduction in risk of death. It is important to look at these figures in terms of absolute reduction in risk.

For a given proportional benefit in death (or recurrence) rate, the absolute improvement in 10-year survival (or disease-free survival) will generally be greater for women at higher risk. In the trials included in the overview, the absolute difference in 10-year survival was about two-fifths of the proportional reduction for women with node positive disease, and one-fifth for those with node negative disease. Thus a 25 per cent reduction in death rate with treatment might correspond to a 10 per cent absolute difference for women with node positive disease, and 5 per cent for those with node negative disease.²⁹⁷ A smaller absolute reduction (approx 2 per cent) would be expected in the hypothetical good prognosis subset of node negative disease.

Guidelines	Level of evidence	Reference
Under the age of 50 years (pre-menopausal women), ovarian ablation reduces the risk of recurrence and death for women with breast cancer.*	I	299
Up to the age of 70 years, multi-agent chemotherapy reduces the risk of recurrence and death for women with breast cancer.*	I	298

* See Table 5 for information regarding nodal status.

Factors which may affect the magnitude of benefit from each form of systemic adjuvant therapy are considered below.

Before treatment begins, women who have not yet had children may wish to consult with an obstetrician to consider their future options for fertility.

6.1 PRE-OPERATIVE CHEMOTHERAPY

There have been a number of studies^{301,302} of chemotherapy given prior to definitive local treatment. In general, there is no additional benefit over the use of chemotherapy after surgery in terms of disease-free or overall survival.

There is Level II evidence³⁰¹ that this procedure can increase the overall breast conservation rate from 60 to 67 per cent. The greatest increase was noted in women with tumours greater than 5 cm in size. However, the rate of negative nodes is increased and therefore some prognostic information is not available.

This approach is not recommended except in restricted circumstances, particularly when breast conservation is sought in the presence of a large tumour.

6.2 POST-OPERATIVE ADJUVANT CHEMOTHERAPY

Evidence has shown that moderately prolonged (several months) combination chemotherapy is more effective than single agent therapy and treatment lasting less than one month (**Level I**).²⁹⁵ Accordingly, analyses in the Oxford overviews have concentrated on trials of moderately prolonged combination chemotherapy in which treatment lasted at least several months (mostly 6–12 months). Within this range, duration of therapy had no apparent impact on outcome.²⁹⁸

The most recent Oxford overview confirmed a highly significant improvement in recurrence-free survival, with absolute differences in 10-year recurrence-free survival ranging from 5.4%–15.4% in the various groups (see Table 2). The main divergence was observed during the first 5 years, with the curves remaining roughly parallel thereafter. Absolute improvements in overall survival ranged from 2.3–12.4% (see Table 2). The beneficial effect of chemotherapy on overall survival continued to increase between 5 and 10 years, especially in women aged under 50.

Table 2: Chemotherapy: effect on outcome

	Age	Relative risk reduction	Nodal status	Absolute difference at 10 years
Recurrence-free survival	All	24%		
	<50	35%	Node negative	10.4%
			Node positive	15.4%
	50–69	20%	Node negative	5.7%
Node positive			5.4%	
Overall survival	All	15%		
	<50	27%	Node negative	5.7%
			Node positive	12.4%
	50–69	11%	Node negative	6.4%
Node positive			2.3%	

Data from Early Breast Cancer Trialists' Collaborative Group, 1998.²⁹⁸

The data above were averaged over all chemotherapy combinations, with some proving more effective than others. In the most recent analysis, the combination of cyclophosphamide, methotrexate and 5-fluorouracil (CMF) was not significantly different from all other regimens combined. However, variations exist between CMF regimens, with some given entirely intravenously,³⁰³ though the classical CMF regimen uses cyclophosphamide by mouth.

There is no direct randomised comparison between CMF using oral or intravenous cyclophosphamide in the adjuvant setting. One European Organisation for Research and Treatment of Cancer (EORTC) randomised clinical trial of women with metastatic breast cancer³⁰⁴ reported superiority for the combination using oral cyclophosphamide, and a similar trend was reported in comparisons of adjuvant studies.^{305,306} In the absence of definitive data, the classical combination with oral cyclophosphamide is preferred where practical.

In the updated Oxford overview,²⁹⁸ the quantitative benefit of adjuvant cytotoxic therapy in women aged 50–69, although still highly significant, was about half the magnitude seen in younger women.

Anthracyclines were more frequently used in the newer trials included in the recent overview. This allowed the analysis of anthracycline-containing regimens against CMF. Anthracycline-containing regimens gave slightly superior results when compared to CMF, both for recurrence-free survival (risk reduction 12% SD=4; absolute difference at 5 years 3.2%; 2p=0.006) and overall survival (risk reduction 11% SD=5; absolute difference at 5 years 2.7%; 2p=0.02) (**Level I**). However, anthracycline-containing regimens are associated with increasing toxicity, including complete alopecia and increased risk of cardiac toxicity, particularly for patients receiving left-sided chest irradiation.²⁹⁸ This is also supported by recent individual trials in pre-menopausal node-positive women³⁰⁷ and in high-risk node-negative women:³⁰⁸ both trials confirmed greater toxicity, particularly febrile neutropenia. However, the overview noted that results from all trials exploring this issue were not yet available.

All the trials in the most recent Oxford overview commenced before 1990. They do not allow assessment of the value of increased dose intensity.

Once perioperative and preoperative regimens were excluded, the Oxford overview data found no evidence of a difference between cytotoxic regimens lasting a few months and longer treatments.²⁹⁸ Choice of standard adjuvant cytotoxic therapy outside of trials is now less clear than before the most recent overview. It could reasonably consist of either 6 cycles of CMF (using oral cyclophosphamide) or 4 cycles of adriamycin and cyclophosphamide (AC). However, one recent study with short-term follow-up has shown improved recurrence-free and overall survival in node-positive patients by the addition of paclitaxel following four cycles of AC.³⁰⁹

Guidelines	Level of evidence	Reference
Moderately prolonged (several months) combination chemotherapy is recommended as it is more effective than single agent therapy and than treatment lasting less than one month.	I	295
Anthracycline-containing regimes are superior to cyclophosphamide, methotrexate and 5-fluorouracil (CMF) for both recurrence-free survival and overall survival at the increased risk of alopecia, cardiac toxicity and febrile neutropenia.	I	298

Dose reduction

Because of the side effects of cytotoxic chemotherapy, there is a temptation to use lower doses. Retrospective analyses had suggested that lower doses were less effective (**Level III**),³¹⁰ but the potential for bias made interpretation difficult.

However, a large prospective randomised trial³¹¹ found that patients randomly assigned to higher doses of 5-fluorouracil, doxorubicin and cyclophosphamide (FAC) did better than those assigned to half the dose (**Level II**). No colony stimulating factor (CSF) support was required in the higher dose arm of this trial.

There is thus evidence (**Level II**)³¹¹ that dose intensity is important to outcome in adjuvant cytotoxic therapy, at least in the range of doses achievable without CSF support.

An alternative interpretation is that lower doses are ineffective.

Guideline	Level of evidence	Reference
Dose intensity is important to outcome in adjuvant cytotoxic therapy, at least in dose ranges achievable without colony stimulating factor (CSF) support.	II	311

High-dose chemotherapy requiring stem cell support

Although trials are in progress to compare high-dose and conventional chemotherapy,³¹² few have yet reported results. Weak evidence based on a historically controlled series (**Level III**)³¹³ suggests the use of high-dose therapy requiring autologous bone marrow or peripheral blood stem cell support in women at high risk of recurrence, such as those with 10 or more involved lymph nodes. However, two small randomised trials have not shown benefit for high-dose therapy (**Level II**).^{314,315}

Such therapy is expensive and potentially hazardous, although the initially high rates of toxic death have fallen with increasing experience of the technique. However, the use of high-dose chemotherapy remains controversial. A recent review of research into this area concluded that firm evidence is needed of the benefit of this treatment compared with conventional therapy.³¹⁶ Currently there is insufficient evidence to justify the delivery of high-dose chemotherapy to women with breast cancer outside of clinical trials.³¹⁶

Guideline	Level of evidence	Reference
Treatment with high-dose chemotherapy outside of clinical trials is not recommended.	II	314, 315

Granulocyte-colony stimulating factors

The evidence regarding the correct use of granulocyte-colony stimulating factors (G-CSFs) is still accumulating. Guidelines recently prepared by the American Society of Clinical Oncology for the use of G-CSF support³¹⁷ concluded that primary use of G-CSFs should be restricted to cytotoxic regimens expected to produce febrile neutropenia in at least 40 per cent of the patients treated. Since these levels are unlikely with conventional adjuvant cytotoxic therapy doses, routine G-CSF support is not recommended.

Secondary use of G-CSFs in patients who have experienced febrile neutropenia or whose therapy might otherwise be delayed or given in lower dosage because of neutropenia has been suggested, but remains of unproven value.

G-CSF support may be considered as an alternative to dose reduction in patients with a history of febrile neutropenia.

Side effects of cytotoxic chemotherapy

Nausea, vomiting, tiredness and alopecia are the side effects most frequently associated with cytotoxic therapy.³¹⁸ Newer anti-emetics have reduced the severity of nausea and vomiting.^{319,320}

Temporary alopecia sufficient to require a wig is common following anthracyclines,³²¹ although less common in women having CMF.³²² Alopecia may be very distressing for the woman and her family, as it is a highly visible reminder of the cancer for which she is being treated. Although hair usually grows back within three months of completing treatment, it may have a different texture and be curlier than before.

Chemotherapy has been associated with long-term impairment in sexual function and infertility associated with premature menopause^{323,324} (**Level III**), with studies reporting between 50–60 per cent of women treated for early breast cancer having sexual dysfunction beyond 12 months post-treatment.^{325,326} The causes of this may be direct, through gonadal and hormonal effects, and indirect, through fatigue, apathy, nausea, vomiting and sleep or appetite disturbances that interfere with libido.³²⁷ Change in sexual function is more evident in those women who become menopausal following chemotherapy,³²³ and this is a concern raised by women.³²⁸

Tiredness is another side-effect that may undermine the woman's ability to cope with family and other responsibilities, particularly if it persists after completion of chemotherapy. Another source of concern for women is the subjective sense of impaired thinking and poor concentration following chemotherapy. There is limited research in this area, but one study reported cognitive impairment in 75 per cent of women who had completed 3–18 months treatment with CMF, CAF or tamoxifen.³²⁹ High-dose chemotherapy appears to impair cognitive functioning more than standard-dose chemotherapy.³³⁰ Another study found that patients with breast cancer treated with adjuvant CMF have a significantly higher risk of late cognitive impairment than breast cancer patients not treated with chemotherapy.³³¹ These effects included problems with concentration and with memory.

Less common short-term side effects include mucositis, diarrhoea, conjunctivitis, chemical cystitis and anxiety about attending for treatment. Rarer side effects include febrile neutropenia, infection, venous thromboembolism and haemorrhage.³¹⁸

In the longer term, therapy-induced leukaemia is rare.³³²

The risk of death from adjuvant chemotherapy is very low.

Congestive cardiac failure is associated with higher cumulative doses of anthracyclines such as those of >500mg/m² of doxorubicin or >900mg/m² of epirubicin. It may be exacerbated by radiation therapy which includes the heart.

It is important that women should be fully informed of the short- and long-term effects of cytotoxic chemotherapy and of these potential side effects, including impact on body image and sexuality (**Level III**),³³³ as well as of the potential benefits of treatment. The provision of information on treatment and treatment side effects improves emotional wellbeing (**Level I**).¹²⁰

For information on menopausal symptoms see *Menopause and hormone replacement therapy: a booklet for women*, 1996 NHMRC and *Hormone replacement therapy for peri- and post-menopausal women: booklet for health professionals* 1996, NHMRC.

Guideline	Level of evidence	Reference
Women should be fully informed of the short- and long-term effects of cytotoxic chemotherapy on general functioning and on body image, sexuality and fertility.	III	333

6.3 TAMOXIFEN

In the most recent Oxford overview,²⁹⁷ tamoxifen was associated with a highly significant improvement in recurrence-free survival in women with ER-positive tumours. It was recognised that tamoxifen had little benefit in patients with ER-negative tumours. Analysis was therefore confined to those women whose tumours were ER-positive or unknown.

The magnitude of the benefit of tamoxifen was clearly dependent on the duration of adjuvant tamoxifen therapy, as shown in Table 3.

As with cytotoxic therapy, the main divergence in recurrence-free survival was in the first five years, while overall survival advantages continued to accrue during the second five years.

Table 3: Tamoxifen duration: effect on outcome

Tamoxifen duration	Recurrence-free survival		Overall survival	
	Risk reduction %	Absolute % difference at 10 yrs	Risk reduction %	Absolute difference at 10 yrs
Node negative				
~ 1 year	17 ± 8	4.7	13 ± 8	3.4
~ 2 years	28 ± 5	5.6	11 ± 6	2.2
~ 5 years	49 ± 4	14.9	25 ± 5	5.5
Node positive				
~ 1 year	21 ± 3	7.5	12 ± 4	4.5
~ 2 years	30 ± 3	10.0	19 ± 3	7.2
~ 5 years	43 ± 5	15.2	28 ± 6	10.9

Data from Early Breast Cancer Trialists' Collaborative Group, 1998.²⁹⁷

Most trials used a tamoxifen dose of 20mg/day. There is no evidence that higher doses offer better outcomes.²⁹⁴

In trials of one or two years duration of tamoxifen, there is a trend towards greater improvement in recurrence-free survival among older women, but this trend is weaker in the more recent trials involving about 5 years of adjuvant tamoxifen, where the analyses are limited to patients with positive or unknown ER.²⁹⁷

There is strong evidence that adjuvant tamoxifen therapy reduces the incidence of contralateral breast cancer (**Level I**).^{45,297} The protective effect is more marked with longer periods of adjuvant therapy, and 5 years of tamoxifen approximately halves this risk. This protective effect on contralateral breast cancer is similar in women whose first breast cancer was ER-positive or ER-negative.²⁹⁷

Tamoxifen's weak oestrogenic action also induces an increase in bone mineral density and altered blood lipid patterns. While these changes might lead to a reduction in cardiovascular events and deaths, no such reduction could be demonstrated (or refuted) in the most recent overview data.²⁹⁷

The Oxford overview concluded that currently available trial results still leave substantial uncertainty as to whether tamoxifen should continue to be routinely taken beyond 5 years.²⁹⁷

Side effects of tamoxifen

The best evidence about the side effects of tamoxifen comes from placebo-controlled trials, such as the B14 trial conducted by the NSABP.⁴⁵ While tamoxifen was associated with increased risk of hot flushes and vaginal symptoms (dryness and discharge), contrary to the impression from uncontrolled data it was not associated with excess weight gain (**Level II**).^{46,47} Ocular toxicity has also been reported³³⁴ as have ocular changes, but the latter are typically asymptomatic. The NSABP Breast Cancer Prevention Trial has reported that rates of stroke, pulmonary embolism and deep-vein thrombosis were elevated in women aged 50 years and over following treatment with tamoxifen (**Level II**).⁴⁸

A more significant problem is the increased incidence of endometrial cancer in post-menopausal women, about 1/1000/year.^{45,335-337} This effect was particularly marked in the NSABP trial,⁴⁵ which had an unexpectedly low incidence of endometrial cancer in the placebo group, and in a Swedish trial involving a higher tamoxifen dosage of 40mg/day.³³⁸ Among women receiving tamoxifen for prevention of breast cancer, the incidence of endometrial cancer was increased about 2.5-fold (**Level II**).³³⁹

Women on tamoxifen and their doctors should be aware of the risk of endometrial cancer. Abnormal bleeding should be investigated promptly, and although no good scientific basis for screening for endometrial cancer has been established, women on tamoxifen therapy should be considered for annual gynaecological review. Guidelines for the gynaecological surveillance of women on tamoxifen have been produced by the Royal Australasian College of Obstetricians and Gynaecologists. For more information on these guidelines refer to Appendix D.

Given that a similar increase in endometrial cancer has been noted with the use of unopposed oestrogen replacement therapy for menopausal symptoms,^{340,341} the effect of tamoxifen may reflect its weak oestrogen agonist properties.

Although the incidence of endometrial cancer is increased by tamoxifen therapy, and the increase may be greater with more prolonged therapy and tamoxifen doses above 20mg/day, the overall risk based on Australian incidence figures remains approximately 1 in 1000 women per year. Hysterectomy rates in the population will affect this risk, and additional data will be emerging from ongoing trials. This increased risk from endometrial cancer is vastly outweighed by the protective effect of tamoxifen against recurrence of breast cancer.

Data from the overview²⁹⁷ and from the breast cancer prevention trial³³⁹ indicate no increased risk of any other cancer among women taking tamoxifen.

Care should be exercised when tamoxifen is prescribed for patients taking warfarin as the metabolism of warfarin³⁴² is decreased, potentially leading to haemorrhagic complications.

Other anti-oestrogens

A number of other selective oestrogen-receptor modulators (SERMS) are under investigation. There are three studies in progress comparing toremifene with tamoxifen in the adjuvant setting.³⁴³ There are no data comparing its efficacy and toxicity to those of tamoxifen in this setting. Raloxifene is under investigation as a chemopreventive agent. There are no adjuvant studies under way at present.

Guidelines	Level of evidence	Reference
Tamoxifen is recommended for most women with oestrogen receptor positive tumours, as it significantly improves recurrence-free and overall survival in women of all age groups.	I	297
Tamoxifen reduces the incidence of contralateral breast cancer.	I	297
Women should be informed of the potential side effects of tamoxifen, including endometrial cancer, stroke, pulmonary embolism, deep vein thrombosis, hot flushes and vaginal dryness and discharge, but not excess weight gain. For most women, the protective effect of tamoxifen against the recurrence of breast cancer will vastly outweigh the increased risk of side effects.	II	45–48

6.4 OVARIAN ABLATION

Ovarian ablation involves destroying the function of the ovaries. This can be done by removing them surgically, by irradiating them or by suppressing their function using luteinizing hormone releasing hormone (LHRH) analogues such as goserelin.

Oophorectomy was the first effective systemic therapy for breast cancer.³⁴⁴ A number of relatively small trials in the 1950s, 1960s and 1970s failed to show an overall survival difference, so the method fell into disfavour.

The most recent Oxford overview included data from 12 of the 13 trials comparing surgical or radiotherapeutic ovarian ablation to no treatment, or to identical treatment without ablation. All these trials commenced before 1980. Trials of chemical ovarian suppression, all of which commenced after 1985, were not included. The trials involved 2102 women aged under 50 at randomisation,

among whom there were 1130 deaths and an additional 130 recurrences. At 15 years, recurrence-free survival was significantly improved in the group receiving ablation (45% vs 39%; $p=0.0007$), as was overall survival (52.4% vs 46.1%; $p=0.001$) (**Level I**).^{298,299} This effect was seen in both node negative and node positive women; oestrogen receptor status was not measured in all trials.

Not all patients underwent axillary dissection. The benefit of ovarian ablation was separately significant in patients assessed as being with or without axillary involvement at diagnosis.

Trials in which ovarian ablation was compared to no treatment showed a larger benefit than those in which chemotherapy was administered to both groups. In these latter trials, the additional benefit of ablation was not separately statistically significant (see Table 4), but the number of events was small, and there was no statistically significant interaction between the efficacy of ablation with or without chemotherapy. In this situation, the overall effect is more reliable than the subset analysis.^{298,299}

Table 4: Efficacy of adjuvant ovarian ablation in women under 50 years

Group	Recurrence-free survival		Overall survival	
	Risk reduction %	Absolute % difference at 10 yrs	Risk reduction %	Absolute difference at 10 yrs
All women < 50	18.5 ± 5.5	6.0 ± 2.3	18.4 ± 5.7	6.3 ± 2.3
Node negative		8.9 ± 4.2		5.6 ± 4.0
Node positive		13.4 ± 3.8		12.5 ± 3.9
No chemotherapy	25 ± 7		24 ± 7	
Both chemotherapy	10 ± 9		8 ± 10	

Data from Early Breast Cancer Trialists' Collaborative Group, 1996.^{298,299}

No significant benefit was seen among women aged 50 or over at randomisation.^{298,299} Ovarian ablation is not indicated after the menopause.

ER status was available for most of the trials with chemotherapy (which were in general more recent than those comparing ablation to no treatment). Among the 194 patients with ER negative tumours there was no evidence of benefit of ablation on recurrence-free survival or overall survival, while among the 550 women with ER positive tumours, there was a trend for ablation plus chemotherapy to be more effective than chemotherapy alone in both recurrence-free survival (odds reduction 13 ± 11%) and overall survival (17 ± 13%), though these differences were not statistically significant.

Evidence from one randomised trial indicated that ovarian ablation alone was superior to cytotoxic chemotherapy in pre-menopausal women with positive oestrogen receptors, while cytotoxic therapy was superior if the receptors were negative (**Level II**).³⁰⁰ This finding underlines the importance of obtaining receptor results in all cases. If it is accepted that ovarian ablation is more effective in women with receptor-positive tumours, the average results from the overview may underestimate the magnitude of benefit for such women.

The trials reviewed used surgical oophorectomy or ovarian irradiation to achieve ablation. Laparoscopic oophorectomy has made the operation more acceptable to some women.

LHRH agonists such as goserelin produce an endocrine status equivalent to that of oophorectomy, but are reversible on cessation of therapy. Their use and efficacy in the management of breast cancer is suggested by preliminary results of recent clinical trials.³⁴⁵⁻³⁴⁹ The optimum duration of treatment by goserelin is not known.

Guideline	Level of evidence	Reference
Ovarian ablation is more effective in women with oestrogen receptor positive tumours.	II	300

Adverse effects of ovarian ablation

Premature menopause is associated with significant vasomotor, sexual and other problems associated with oestrogen depletion, including increased risks of osteoporosis and cardiovascular disease. The overall survival benefit in ovarian ablation trials indicates that, at least within the first 15 years, the benefits of therapy outweigh any such adverse effects.

The safety of oestrogen replacement therapy in women with breast cancer has not been established. This is the subject of ongoing trials.

6.5 COMBINED MODALITIES

Much of the evidence for the value of using more than one adjuvant modality is indirect. Current clinical trials are addressing many questions about the combination of cytotoxic and endocrine treatments in various sub-groups of patients.

Does chemotherapy add to ovarian ablation?

Few trials have yet examined the need for cytotoxic adjuvant therapy in women receiving ovarian ablation.

Does ovarian ablation add to chemotherapy?

As noted above, there is insufficient evidence in the most recent Oxford overview to be certain. Although the impact of ovarian ablation appeared to be smaller in the presence of cytotoxic therapy, the interaction was not significant.

The most influential single trial was the Ludwig Breast Cancer Study,³⁵⁰ which supports the concept that the additional effect of ablation in the presence of chemotherapy may be greater in women with ER positive tumours.

Does chemotherapy add to tamoxifen?

Both in patients aged <50 and in those aged 50–69, the overview data²⁹⁸ suggest that the effects of tamoxifen and cytotoxic therapy are independent, so that the proportional benefits of chemotherapy on recurrence-free and overall survival are similar in the presence or absence of tamoxifen. A systematic review showed that trials comparing anthracycline-containing chemotherapies or ‘classical’ CMF³⁵¹ in combination with tamoxifen yielded better outcomes than tamoxifen alone (Level I),³⁵² while trials using modified ‘CMF’ regimens showed no benefit.^{305,352}

Guideline	Level of evidence	Reference
Chemotherapy in combination with tamoxifen yields an increase in disease-free survival compared with tamoxifen alone.	I	352

Does tamoxifen add to chemotherapy?

The beneficial effect of 5 years of adjuvant tamoxifen was similar in trials of tamoxifen versus nil, and in trials of tamoxifen plus chemotherapy versus chemotherapy alone.²⁹⁷

Guideline	Level of evidence	Reference
Tamoxifen in combination with chemotherapy yields an increase in disease-free survival compared with chemotherapy alone.	I	297

6.6 WHICH WOMEN SHOULD BE OFFERED SYSTEMIC ADJUVANT THERAPY?

Because systemic adjuvant therapies have been proven effective, they should be considered in the management of all women with high or moderate risk of recurrence after local therapy for early breast cancer.

In deciding whether or not to recommend such therapy to a woman, the potential benefit of systemic adjuvant therapy should be considered together with her age, general health and preferences. In determining the value of systemic adjuvant therapy, clinicians must initially determine prognosis without systemic adjuvant therapy.⁶⁴

Tables 2, 3 and 4 summarise the estimated benefits of systematic adjuvant therapy. Table 5 categorises the risk of recurrence associated with various prognostic factors. Table 6 matches these risk categories with recommended systemic adjuvant therapy. Systemic adjuvant therapy should be recommended to most women with involved axillary nodes, because this is an indicator of a high risk of recurrence after treatment for early breast cancer.

Women with node-negative breast cancer include a spectrum from those with large, high grade, receptor-negative tumours whose prognosis is similar to patients with involved nodes, to those with tiny, screen-detected tubular cancers with a very low risk of recurrence. At the 1998 St Gallen meeting, a classification of node-negative patients into low-, intermediate- and high-risk groups was adopted (see Table 5).³⁵³

Tamoxifen and ovarian ablation are not in general recommended for women with ER and progesterone receptor (PgR) negative tumours. Tamoxifen may be considered in women whose tumours, although classified as receptor-negative, contain some evidence of ER or PgR.³⁵³

Prognostic indicators

The size of the primary tumour affects the prognosis among node-negative women (**Level III**).⁶⁶ Women with ER-negative tumours have a poorer prognosis (**Level II**).^{354,355}

6.7 RECOMMENDATIONS

Clinical trials

Further delineation of optimum treatments for different subgroups requires that as many women as possible be entered into appropriately designed and approved clinical trials. These trials should seek to refine the indications for particular therapies or combinations of modalities in the various subgroups defined by patient and disease characteristics.

Treatment outside clinical trials

The willingness of patients to undergo adjuvant cytotoxic therapy is influenced by their family and social status and by the details of the treatment, but not (at least within a group who had all received treatment) by their age, educational level, employment status or the use of concurrent adjuvant endocrine therapy. In a study, women who had undergone adjuvant cytotoxic therapy regarded it as worthwhile for relatively small absolute improvements in survival.³⁵⁶

Selection of higher-risk node-negative women for adjuvant systemic therapy involves balancing the expected gains against the adverse effects. Detailed suggestions are tabulated below.

The following suggestions for adjuvant systemic therapies outside clinical trials are adapted from those defined at the 1998 St Gallen Adjuvant Breast Cancer Conference. Note that menopausal status per se is no longer a major deciding factor in the selection of adjuvant therapy, although the toxicity of therapy must be balanced against its efficacy, especially in older patients. The evidence supports the following general guidelines for women up to the age of 69. Borderline situations require a careful discussion of risks and benefits between the patient and the responsible clinician. The role of newer therapies, such as taxanes and aromatase inhibitors, and prognostic markers, such as Her2 status, have yet to be fully evaluated,³⁸⁶ and this section will be updated as results come to hand.

Table 6 has been arrived at on a consensus basis but some clinical experts believe this could lead to over treatment of some women. For example, a woman with a grade 1, node-negative 2cm carcinoma would be classified as being at intermediate risk according to the St Gallen recommendations and ovarian ablation with or without chemotherapy would be advised if the woman was

oestrogen receptor or progesterone receptor positive. Using the Nottingham group recommendations the same woman would have an index of 2.4, which approximates that of women in the general population, and adjuvant treatment would not be advised. Before embarking on either course, the benefits of both approaches should be discussed with the woman and the possibilities carefully explained.

Table 5: Definition of risk categories for patients with node-negative breast cancer

Factors	Minimal/low risk (all of the listed factors)	Intermediate risk	High risk (at least one of the listed factors)
Tumour size*	≤1 cm	1.1–2 cm	>2 cm
Oestrogen receptor (ER) and/or progesterone receptor (PgR) status**	Positive	Positive	Both negative
Grade	Grade I (uncertain relevance for tumours ≤1 cm)	Grade I–2	Grade 2–3
Age***	≥35 years		< 35 years

* It was generally agreed that pathological tumour size (of the invasive component) was the most important prognostic factor for defining additional risk of recurrence.

** Oestrogen receptor (ER) and progesterone receptor (PgR) status are important biological characteristics that identify responsiveness to endocrine therapies.

*** Patients who develop breast cancer at a young age are considered to be at high risk of recurrence, although an exact age threshold for this increased risk has not been defined. Younger women tend to have tumours of a higher grade and to have more positive nodes.

Table 6: Systemic adjuvant therapy recommendations outside clinical trials³⁵³

Node negative			
Patient group	Minimal/low risk	Intermediate risk	High risk
Pre-menopausal ER or PgR Positive	Nil or Tamoxifen	Tamoxifen ± Chemotherapy ¹ Ovarian ablation* LHRH analogue*	Chemotherapy [†] + Tamoxifen Ovarian ablation* LHRH analogue*
Pre-menopausal ER and PgR Negative	Not applicable	Not applicable	Chemotherapy
Post-menopausal ER or PgR Positive	Nil or Tamoxifen	Tamoxifen ± Chemotherapy ¹	Tamoxifen ± Chemotherapy ¹
Post-menopausal ER and PgR Negative	Not applicable	Not applicable	Chemotherapy ²
Elderly	Nil or Tamoxifen	Tamoxifen ± Chemotherapy	Tamoxifen ± Chemotherapy ³
Node positive			
Patient group			
Pre-menopausal ER or PgR Positive	Chemotherapy [†] + Tamoxifen Ovarian ablation or LHRH analogue ± Tamoxifen*		
Pre-menopausal ER and PgR Negative	Chemotherapy ^{†2}		
Post-menopausal ER or PgR Positive	Tamoxifen ± Chemotherapy ¹		
Post-menopausal ER and PgR Negative	Chemotherapy ²		
Elderly	Chemotherapy ± Tamoxifen ²		

* The St Gallen panel regarded these therapies as still being tested in clinical trials.

† Anthracycline based therapies were superior to CMF in the overview ²⁹⁸

¹ The addition of chemotherapy is effective,²⁹⁸ but consideration may be given to tamoxifen alone in patients with relatively lower risk of recurrence.

² The addition of tamoxifen may be considered in patients whose tumours show any evidence of ER or PgR.

³ Add chemotherapy if no expression of ER or PgR in tumour.

6.8 THE ECONOMICS OF SYSTEMIC ADJUVANT THERAPY

The treatment of women with node-positive, pre-menopausal breast cancer with systemic adjuvant chemotherapy is considered to be one of the most cost-effective interventions in contemporary medical practice.^{357,358} It has been estimated to cost US\$1000 per QALY (quality adjusted life year).³⁵⁷

However the use of chemotherapy for node-negative women, who generally have a lower risk of dying from breast cancer, is more controversial.^{257,357,359,360} While treatment of these women is also beneficial, it is relatively expensive per life prolonged or saved. It has been estimated to cost about US\$50,000 per QALY.³⁵⁷

As well, data to determine which node-negative women will benefit from chemotherapy are not available. With increasing use of screening mammography, the proportion of women with uninvolved axillary nodes is likely to rise.³⁶⁰

Financial considerations become more important when considering the use of tamoxifen. Using data from the Oxford overview, it has been suggested that tamoxifen provides reasonable value for money in the treatment of women with early breast cancer.³⁶¹ Considering tamoxifen's minimal toxicity, one of the main disadvantages in treating women whom it will not benefit is monetary.

Overall, data concerning toxicities and impairment of quality of life during systemic adjuvant therapy are insufficient to allow a true estimate of the cost of toxicity from chemotherapy and time lost from work or other important parts of life.²⁵⁷

The out-of-pocket expenses associated with adjuvant chemotherapy incurred by women with or without private health insurance are discussed in the Centre's publication *Out-of-pocket expenses incurred by women for diagnosis and treatment of breast cancer in Australia* (1999).²⁵⁹

CHAPTER 7 FOLLOW-UP

The follow-up procedures for women treated for breast cancer have evolved over time³⁶² with little data³⁶³ to validate the procedures employed. Surveys indicate that the majority of recurrences are detected in the context of signs or symptoms, and that a small percentage are detected in the asymptomatic phase.

It is desirable that follow-up procedures are defined to achieve specified outcomes in a cost-effective manner. Women need to be informed of the goals of follow-up. It should be reinforced that there is no evidence that intensive follow-up improves survival. It is important that women understand the risks of recurrence of disease, and that new symptoms should be assessed in the light of this.

The notional goals of follow-up include:

- the early detection of local recurrence
- screening for a new primary breast cancer
- detection of treatment-related toxicities
- provision of psychosocial support
- identification of family history

The following discussion examines each of these goals, their utility to the patient and the data supporting them.

EARLY DETECTION OF LOCAL RECURRENCE

With current treatment protocols,³⁶⁴ the in-breast recurrence rate is 1–2 per cent per annum and 1 per cent after mastectomy. For women who have had mastectomy, the majority of recurrences will be detected by clinical examination alone. For women who have had breast conserving surgery, a significant proportion will be detected by regular mammography.

The usual treatments for local recurrence—surgery and radiotherapy—are more effective if used in the earliest phases. Treatment is aimed at maximising the chance of long-term local control, as the effect of uncontrolled local recurrence on the woman's quality of life can be substantial.

Key point

Although there is a perception that early detection of distant recurrence is desirable in order to commence treatment early, this is based on the false notion that the goal of such therapy is cure. Unfortunately, this is almost never the case.

There have now been two clinical trials^{365,366} involving more than 2000 women with no survival benefit for women followed intensively compared to those with a minimal follow-up schedule. One of these studies showed no increase in quality of life from an intensive follow-up schedule (**Level II**).³⁶⁶

Guideline	Level of evidence	Reference
A minimal follow-up schedule is recommended, as there is no evidence that frequent intensive follow-up confers any survival benefit or increase in quality of life.	II	365,366

SCREENING FOR A NEW PRIMARY BREAST CANCER

A history of breast cancer increases the risk of a second primary breast cancer two- to five-fold.³⁶⁷ Approximately 5–10 per cent of US women with a first breast cancer have been estimated to develop a second primary breast cancer during their lifetime; half of these cancers will occur in the contralateral breast.³⁶⁷ This is much higher than the incidence in the general population for whom regular screening mammography is recommended. Accordingly, regular (at least annual) mammography is strongly recommended.³⁶⁸

DETECTION OF TREATMENT-RELATED TOXICITIES

Follow-up of patients affords opportunities for clinicians to review and reflect on their practice and to assist with maintaining high quality clinical care. Audit of patient outcomes can provide valuable data on the occurrence of treatment-related toxicities and also contribute to an understanding of treated breast cancer disease.

Lymphoedema

Lymphoedema of the arm occurs after either surgical axillary dissection or radiation or both (see Chapter 4, Section 4.4). Regular follow-up is unlikely to detect this before being noted by the woman. However, the opportunity can be taken at follow-up visits to remind women of the need to avoid injury to the upper limb or to assess any change and refer for treatment and management.

Systemic adjuvant therapy

Early complications of adjuvant chemotherapy include premature ovarian failure causing menopausal symptoms, which may be distressing. Premature onset of menopause as a result of such treatment may significantly influence sexual functioning, body image and self-esteem in women.³²⁸

Subsequently, the issue that arises for women is that of HRT. However, the use of HRT in women who have been treated with breast cancer is controversial, and it is currently not known whether oestrogen replacement therapy can be safely given to these women.

Decisions about management of menopausal symptoms should take into account both tumour-related factors and the woman's wishes.

It is possible that the wider use of anthracycline-containing regimens may be associated with delayed cardiac toxicity.

Long-term observation for such complications should take place in an organised manner, preferably as part of a clinical trial so that valid conclusions can be reached.

Tamoxifen

As previously described (see Chapter 6), there are now data to indicate that tamoxifen therapy is associated with an increased risk of cancer of the endometrium. The exact risk in the Australian context is uncertain, but overseas reports show the incidence of endometrial cancer was increased about 2.5-fold.³³⁹ No screening procedures are routinely recommended at present, but enquiry should be made about symptoms at each visit.

Psychological morbidity

Depression and anxiety are common following diagnosis and treatment of breast cancer, and may require specific pharmacological and/or psychological interventions. Doctors should enquire about the woman's mood and how she is coping, as it is rare for women to seek psychological assistance themselves.^{369,370}

PROVISION OF PSYCHOSOCIAL SUPPORT

There are data demonstrating a variety of long-term psychological sequelae to treatment for breast cancer. These include episodes of depression and anxiety, especially when the time comes to cease adjuvant systemic therapy.³⁷¹ Difficulties of body image and adjustment may be common. Anxiety does not necessarily abate with longer survival.^{73,372,373} However, there are insufficient longitudinal data to describe the long-term course of significant adjustment problems in women with breast cancer.

Some women find regular check-ups psychologically reassuring;³⁷⁴ others associate them with a reminder of their diagnosis, leading to increased anxiety (**Level III**).³⁷⁵ Check-ups provide opportunities for routine assessment of the emotional adjustment of both the woman and her partner, and to provide support and offer referral or counselling should the need arise.

Further information is contained in the NHMRC iSource National Breast Cancer Centre *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer*.⁹⁴

IDENTIFICATION OF FAMILY HISTORY

Follow-up provides an opportunity to assess the risk of breast cancer in a woman's family. Some women identified as high-risk for breast cancer may wish to clarify the genetic risk of family members and be referred to familial cancer clinics (see Chapter 1).

ECONOMICS OF FOLLOW-UP

Given the large numbers of women with diagnosed and potentially curable cancers, the care of these women has a large impact on the health care dollar.

As noted above, intensive follow-up affords no survival benefit over a minimal schedule.^{365,366} Intensive follow-up also consumes extra resources because of dubious results of tests performed by protocol.³⁴ However, it does have the potential to improve the knowledge and care of women. Women in clinical trials need to be followed up closely, and the cost of follow-up should be built into the cost of the trial.

One study³⁷⁶ suggests that if American doctors had adopted a minimal surveillance strategy, they would have saved the US health care system (which covers about 250 million people compared to Australia's 19 million) \$US636m in 1990. By 2000 this annual figure was expected to rise to more than \$US1 billion (in 1990 US dollars).

WHO SHOULD PERFORM THIS FOLLOW-UP?

With the involvement of various specialists as well as the GP in the treatment of an individual woman, it is important that follow-up be coordinated to ensure patients are not subjected to an excessive number of visits.

Each treating team should develop a protocol which will result in rational follow-up procedures and provide information regarding the outcomes of particular treatment programs. For example, this may include alternating visits every six

months between treating doctors in the first two years so that women see one or other specialist each three months.

In some parts of Australia, follow-up of people with cancer is the responsibility of the GP. Under such circumstances, it is essential that the medical practitioner is aware of an appropriate schedule of follow-up, such as that described in these guidelines. The minimal requirement for regular follow-up of a primary breast cancer is a clinical review every three months for the first year, then six monthly to five years, then an annual review thereafter (see Table 7). A UK randomised controlled trial with an 18 month follow-up, in which women received routine follow-up either in hospital or in general practice, found that general practice follow-up of women with breast cancer in remission is not associated with increase in time to diagnosis, increase in anxiety or deterioration in health-related quality of life.³⁷⁷

It is essential that the woman's current GP is kept informed of the outcome of visits and of any investigations undertaken. To ensure adequate audit, it is recommended that all involved clinicians be informed of each others' activities.

Some women will change doctors over the many years of follow-up. It is essential that sufficient details of her medical history are available to ensure continuity of care.

Women should be aware that they will have mammography as part of their follow-up and that they do not need to respond to invitations from BreastScreen Australia.

Table 7: Recommended follow-up schedule^{183,365,366}

	1–2 years	3–5 years	After 5 years
History and examination	every three months	every six months	every year
Mammography (and ultrasound if indicated)	at 6–12 months after radiotherapy for conserved breast	every year	every year
Chest X-ray	only if clinically indicated		
Bone scan blood count and biochemistry			

Not every clinician involved in the care of a woman will be closely involved in her follow-up.

Symptoms should be assessed as they arise.

Women with early breast cancer should also be advised not to neglect other aspects of their health care.

Note that this follow-up schedule may change, due for example to the detection of recurrence or the development of other illnesses. The schedule needs to be tailored to individual situations.

Although women taking part in a clinical trial may be subjected to variations in these recommendations, many trial protocols currently prescribe a similar schedule.

Information on the follow-up of women with advanced breast cancer is provided in the NHMRC iSource National Breast Cancer Centre *Clinical practice guidelines for the management of advanced breast cancer, 2001*.

CHAPTER 8 REQUIREMENTS FOR SPECIAL GROUPS

8.1 WOMEN FROM RURAL AND REMOTE AREAS

About 30 per cent of Australian women who develop breast cancer live in regional, rural or remote areas. Women living in regional towns generally have good access to a range of services. However, women living far from urban centres sometimes have difficult choices. They must undertake treatment locally or travel far from family and friends. In a recent study, rural women with breast cancer in Australia reported spending an average of six weeks away from home.³⁷⁸ Many of these women would prefer to be treated in their local or regional area, rather than having to travel to a metropolitan centre. The cost of opting for local treatment is that choices may be limited. Most women, apart from those in remote areas, will have reasonable access to a surgeon who can operate on the primary cancer, remove it and stage the disease.

Increasingly, some general surgeons in rural areas have undertaken the considerable effort required to develop a special interest in breast cancer surgery. All surgeons who elect to manage women with breast cancer should keep themselves and their colleagues up to date with the current knowledge and treatment of all aspects of the disease, including current clinical trials. An audit of patient treatments and outcomes should also be maintained.

Particularly in rural and remote areas, GPs play a key role in the initial diagnosis of women with breast cancer. They also have an ongoing and important role in the women's post-operative management, including clinical follow-up, and in palliative care where that proves necessary.

With the exception of a few major towns, radiotherapy is not available outside capital cities, and resident medical oncologists are usually not available. Given that radiotherapy usually requires six weeks away from home, this influences some women to opt for mastectomy instead of breast conservation plus radiotherapy. This decision is often made for pragmatic, financial, work, family and social reasons.

Rural/regional surgeons managing breast cancer need a close liaison or networking with appropriate medical oncologists, radiation oncologists and a 'breast surgeon' in a metropolitan breast unit. Preferably, these should be doctors who either visit their region or have a specific interest or expertise in breast cancer management for rural women. For most rural women this should facilitate effective and efficient multidisciplinary assessment and management. The oncologist's recommended systemic adjuvant therapy can usually be administered locally and should not require travel.

Women travelling for treatment benefit from being accompanied by a carer who can provide support during their time away. The costs of travel to a regional or urban centre are financial hardship, social dislocation and emotional strain. Women who have treatment away from home may also find that communication between their local doctors and the treating specialists is not adequate.

Out-of-pocket expenses for women in rural and remote areas

A recent report examined out-of-pocket expenses incurred by women for diagnosis and treatment of breast cancer in Australia.²⁵⁹ It found that compared with their urban counterparts, women residing in non-urban, rural and remote areas do not appear to incur substantially greater out-of-pocket expenses for medical services involved in screening, diagnosing and treating breast cancer in their region. However, the evidence does suggest that many such women travel to urban or metropolitan areas in order to receive these services and therefore incur additional travel and accommodation costs.²⁵⁹

A shortage of plastic and reconstructive surgical services in regional and rural Australia may create a barrier for having reconstructive surgery. Again, the woman may have to consider travelling for treatment if immediate reconstruction is desired. (Appendix H lists breast cancer support services throughout Australia.)

Although most states have a travel and accommodation scheme, in current practice many women do not receive the financial assistance to which they are entitled.³⁷⁸ The treatment team should assist women to access adequate financial support. It should be noted that there appear to be substantial differences in the patient travel and accommodation assistance schemes run by state and territory governments.²⁵⁹

8.2 CULTURAL ISSUES

Qualitative research exploring the views of women from non-English-speaking and indigenous backgrounds has highlighted a range of issues.^{378,379}

These include:

- **Cultural issues:** Immigrant women and those from some cultural backgrounds may have specific beliefs that affect their attitudes to treatment. For example, in some communities, breast cancer is viewed as fatal and/or shameful. The role of the woman's religious beliefs and those of her family should be explored.^{379,380}
- **Female providers:** In some communities, women may have a strong preference for care from a female provider. This is the case in some indigenous communities where breast cancer is perceived as 'women's business'. Special care should be taken with these women to discuss treatment options and to provide female doctors where possible. The use of

Aboriginal Health Workers may also be of value in assisting indigenous women during treatment.

- **Use of interpreters:** If the woman is not fluent in English, it is important to use a qualified and appropriate interpreter, rather than a family or staff member. Interpreters are available free of charge in both the public and private sectors, although they must be booked in advance of any consultation. A telephone interpreter through the Translating and Interpreter Service (TIS) can usually be provided within a few minutes, although it is preferable to give some notice (phone: 13 14 50).
- **Provision of information:** Women from non-English-speaking and indigenous backgrounds need access to information about breast cancer. Some states have a telephone information service for women who are not proficient in English; state and territory cancer organisations can provide contact details (phone: 13 11 20 for local information from state cancer councils).

Although the **Multicultural Breast Cancer Information Service** (MBCIS) is located at the NSW Cancer Council, women who live in other states/territories are welcome to contact this service (1300 300 935).

Lesbian women and their partners may have special needs and problems. These are addressed in more detail in the iSource National Breast Cancer Centre consumer guide for women with early breast cancer (in preparation).

(Refer to NHMRC iSource National Breast Cancer Centre *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer*, 2000.)⁹⁴

CHAPTER 9 AREAS WHERE RESEARCH IS NEEDED

Since the House of Representatives Report on the Management and Treatment of Breast Cancer in Australia,³⁸¹ many of its recommendations related to research, policy and the organisation of breast cancer care have been addressed. The iSource National Breast Cancer Centre has been involved in many of these activities, which include:

- developing clinical practice guidelines
- developing resources for undergraduate medical training, GPs and consumers
- surveys of surgeons and consumers
- review of radiotherapy after mastectomy
- commissioning research and reviews on a wide range of topics (see Appendix F), including the psychosocial needs of women with breast cancer
- organising a rural surgeons program
- guideline implementation and dissemination
- convening a lymphoedema summit to ascertain research priorities into this area
- providing communication skills training for health professionals

However, much more research is needed into breast cancer. Topics which have been identified include:

- **The disease:**
 - the pathogenesis of the disease
 - women with metastatic disease
 - risk factors and profile
 - genetics of breast cancer
 - sentinel node biopsy
- **The impact of the disease and treatment:**
 - the impact of breast cancer treatment on quality of life
 - the identification and development of interventions to assist women in coping with body image changes
 - whether or not participation in a support group improves survival
 - the identification of women at high risk of a poor recovery

The Australian New Zealand Breast Cancer Trials Group (ANZBCTG) and the International Breast Cancer Group (IBCG) are conducting a number of trials investigating breast cancer treatment.

Below are listed completed or ongoing projects conducted by the iSource National Breast Cancer Centre and relating to the impact of the disease:

- the psychosocial impact of breast cancer as it is measured by health professionals: A literature review on the detection of psychological problems is currently under way.
- the impact of breast cancer treatment on body image and sexuality: The results of focus groups and interviews is currently in draft form.
- the psychosocial impact of breast cancer on families, including the development and evaluation of resources for children and partners of women with breast cancer: There is an ongoing series of projects from 1998, with reviews and interview-based projects examining the needs of children and issues encountered by women in talking to/supporting their families. A partners' support resource has been developed, and current work is focusing on the development and evaluation of informational resources for adolescent children of women with breast cancer.
- lymphoedema prevention and treatment. A lymphoedema summit was held in February 2000 to consider national research priorities on issues related to lymphoedema.

(Further information is contained in the NHMRC iSource National Breast Cancer Centre's *Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer*.)⁹⁴

- **Deciding on treatment:**
 - systematic literature reviews on the validity, reliability and utility of clinical examination and mammography, breast ultrasound, fine needle aspiration biopsy, core biopsy, open biopsy and frozen section histology
 - better markers of responsiveness to therapy, disease progression and patient survival
 - the optimal method of combining chemotherapy, hormonal and locoregional therapy
 - factors influencing participation in clinical trials
- **Treatment:**
 - systematic literature review on CLE with axillary dissection
 - HRT in women with breast cancer
 - the cost-effectiveness of interventions in breast cancer

- the role of radiotherapy in women with small, well differentiated tumours
- factors that mediate outcome
- **The consumer view:**
 - the consumer perspective in the Australian literature
 - consumer initiated research
 - the experience of specific groups, such as women of non-English-speaking backgrounds, Aboriginal and Torres Strait Islander women and women of low socio-economic status
 - the decision-making process and how it is affected by stress
 - levels of support best able to assist adjustment
- **Prevention:**
 - prevention trials, such as that involving tamoxifen
 - screening in women aged 40–49
 - what will help women at high risk
- **Cost-effectiveness:**
 - the collection of Australian cost data to allow analysis of the costs of treatment options
 - appraisal of the impact of treatment options on quality of life
- **Outcomes:**
 - collection of Australian outcome data relating to breast cancer treatment

The iSource National Breast Cancer Centre is currently engaged in:

- targeted strategies to implement early breast cancer guidelines (for example, randomised controlled trial of a quality improvement kit for hospitals)
- a national demonstration project on multidisciplinary care in breast cancer
- developing and disseminating guidelines on advanced breast cancer; DCIS, LCIS and AH; fine needle and core biopsy; and diagnostic imaging of the breast.

APPENDIX A: DEVELOPMENT OF THE FIRST EDITION (1995)

The need for procedures to ensure effective clinical practice and focus the health system more directly on health outcomes was identified by both the National Health Strategy and the Australian Health Ministers' Advisory Council.

The National Health and Medical Research Council (NHMRC) subsequently established a Standing Committee of the National Health Advisory Committee (formerly the Health Care Committee) to undertake the task. Initially named the Quality of Health Care Committee, the Standing Committee was later re-named the Quality of Care and Health Outcomes Committee (QCHOC) to reflect its emphasis on outcomes of care. QCHOC was given the task of:

- establishing a recommended national approach to the development of clinical practice guidelines which are focused on improving patient health outcomes
- working with the clinical colleges and other expert groups to encourage and facilitate the development of such guidelines and outcome measures by these groups

Having drafted guideline for clinical guidelines development,³⁸² the Standing Committee then set up a number of pilot working parties with the dual role of developing clinical practice guidelines in selected areas and trialing the proposed methodology for developing guidelines. The Standing Committee agreed on the following criteria for selecting pilot projects:

- high health burden imposed by the disease
- high cost of treatment interventions
- the existence of significant variation in current practice for similar conditions
- a reasonable expectation that guidelines would lead to an improvement in the quality of care and health outcomes
- the existence of a receptive group interested in taking on the development of guidelines for a particular issue of concern
- pilot projects should represent the four focus areas under the Commonwealth Department of Human Services and Health's National Health Goals and Targets (currently cardiovascular health; cancer control; injury prevention and control; and mental health)
- guidelines should be achievable: in some areas, guidelines cannot be developed while in others, guidelines are not required
- given the rising costs of health care, the area chosen for guideline development should offer some degree of potential for achieving cost-effectiveness in treatment

The treatment of diagnosed breast cancer was selected for guideline development because it met the above criteria, and because there were concerns that knowledge of the treatment options was not well disseminated among health professionals. It was also felt that not all women with breast cancer were being presented with the range of appropriate treatment options, and that guidelines would help women make informed choices.

TERMS OF REFERENCE FOR THE WORKING PARTY

A Working Party was established to draft the guidelines with the following terms of reference:

- Undertake the development and implementation of clinical practice guidelines for the treatment of breast cancer, following the procedures recommended by the QCHOC's draft first edition of *Guidelines for the development and implementation of clinical practice guidelines*.²
- Provide advice on this process to the QCHOC.

MEMBERSHIP OF THE WORKING PARTY (FIRST EDITION, 1995)

Membership of the Working Party reflected the multidisciplinary nature of breast cancer treatment. It comprised representatives from all aspects of clinical practice as well as consumer and breast cancer support groups; nurses; counsellors; and other related experts such as epidemiologists, health economists and medical educators.

The Working Party had the following members:

Emeritus Professor Tom Reeve (Chair)	Surgeon; Member, Quality of Care and Health Outcomes Committee
Dr Roger Allison	Radiation oncologist
Associate Professor Raja Bandaranayake	Medical educator
Professor Bruce Barraclough	Surgeon
Dr Michael Bilous	Pathologist
Professor Alan Coates	Medical oncologist
Ms Mary Draper	Policy activist
Professor John Forbes	Surgeon
Mr Colin Furnival	Surgeon
Dr Michael Green	Medical oncologist

Mr Tony Green	Surgeon; expert on remote/rural access issues
Dr Jane Hall	Health economist
Associate Professor Les Irwig	Epidemiologist
Dr Michael Jones	Radiologist
Professor Allan Langlands	Radiation oncologist
Associate Professor Donald Marshall	Surgeon (reconstructive surgery)
Ms Marcia O'Keefe	Engineer; breast cancer consumer advocate (Deceased October 1997)
Ms Beverley Rees	Nurse; counselling and support
Mr Ian Russell	Surgeon
Dr Angela Rutherford	General practitioner
Dr Raymond Snyder	Medical oncologist
Professor Robert Sutherland	Biologist
Dr Jane Turner	Psychiatrist
Mr Michael Wertheimer	Surgeon
Ms Marion Powall (observer)	Health Advancement Division Commonwealth Department of Human Services and Health
Ms Jayne Ross	Secretary, Quality of Care and Health Outcomes Committee
Ms Jane-Ann Jones	Executive Secretary, Working Party on the Treatment of Diagnosed Breast Cancer
Dr Mark Ragg	Consultant writer and editor

The Working Party also maintained close links with other groups currently working in this area, such as the Australian Cancer Network and the Clinical Oncologist Society of Australia.

PURPOSE AND SCOPE OF THE GUIDELINES

In order to maintain achievable terms of reference, the Working Party confined its scope to the management of early breast cancer, both in situ and invasive cancer. However, some introductory information was also included.

The objective of the guidelines is to assist clinician and patient decisions by providing a framework within which to apply clinical judgement and to consider

the needs of each individual woman. The guidelines are not rigid procedural paths; rather, their objective is to ensure that clinicians and women are well informed about the risks and benefits of the recommended interventions.

The full guidelines document covers best practice for the management of breast cancer from the point of initial diagnosis. While it aims to be a document useful for both health professionals and consumers, a separate book, derived largely from the main document, has been produced specifically in order to provide information for women who have breast cancer and their relatives.

The guidelines are based on the following key principles which form the basis of QCHOC's approach to guideline development and implementation:

- a proper evaluation of the latest scientific evidence
- a focus on the improvement of patient outcomes
- the adoption of a multidisciplinary approach which involves all stakeholders, including consumers

Target audience

These guidelines were developed to equip the treatment team with evidence-based recommendations for optimal management of early breast cancer care, according to the needs of the individual.

Scope of the guidelines

Topics covered include general principles of care, preoperative examinations, surgical management, the use of radiotherapy and systematic adjuvant therapy and follow-up requirements in relation to early breast cancer.

Outcomes

The guidelines are aimed at improving health and quality of life outcomes for women diagnosed with early breast cancer. Key outcomes may include the following:

- reduction in recurrence rates
- decreases in morbidity and mortality
- improved quality of life and psychological wellbeing
- improved communication between patients and clinicians
- improved knowledge and access to information for patients

PROCESSES EMPLOYED

The Working Party approached the development of the guidelines by setting itself four key tasks:

- Task 1: Identification of the known clinical problems and areas of uncertainty in each of the disciplines involved in breast cancer treatment.
- Task 2: Collection and review of the scientific evidence, including meta-analyses, to identify best and most appropriate practice for the various interventions in breast cancer treatment.
- Task 3: Establishment of a sub-group to review the literature and gather information on best practice from the woman's perspective.
- Task 4: Development of a glossary of technical terms in the breast cancer area, for incorporation in both documents.

Most of the work of the Working Party was conducted out of session, with meetings used primarily to identify the direction to follow and to review out-of-session activity. A technical writer was then contracted to prepare the document and draw all the information together in consultation with the Working Party.

Task 1

At initial Working Party meetings, various individuals and groups identified known clinical problems or issues in their respective fields. A specialists' sub-group was then formed to advance the clinical group's input to the guidelines in the surgical, medical oncological and radiotherapy areas.

Task 2

A member of the Working Party, Associate Professor Les Irwig, conducted systematic reviews of randomised controlled trials in the following areas:

- the treatment for early breast cancer: its effects on mortality and recurrence, its impact on quality of life and the effects of intensive monitoring of patients after initial treatment
- the impact of counselling and other psychological interventions on quality of life
- the impact of radiotherapy on quality of life

The findings from these reviews were incorporated into the guidelines.

The Working Party decided that it was important to give a clear indication in the guidelines as to the strength of the evidence for recommendations, and to provide references where appropriate. The rating system is discussed in detail under 'Levels of evidence' in the introduction to these guidelines, and evidence

which has been rated as either Level I or II is presented in tabular form throughout the text.

Task 3

At the request of the Working Party chairman, a Women's Perspective sub-group of the Working Party was convened in order to identify key issues in breast cancer treatment from the woman's perspective. From their knowledge of the literature and their experiences as users and providers of breast cancer services, the sub-group identified a number of issues it believed to be relevant to the process of guideline development. These included:

- information needs
- choice and control
- counselling and support
- communication between women and health care providers
- the treatment process
- treatment outcomes
- access issues
- recurrent metastatic disease

The sub-group then commissioned a search of the professional and consumer literature which addressed these aspects. Treatment outcomes and quality of life issues were excluded from the literature review because this aspect was included in the overall meta-analysis of treatment undertaken for the Working Party, discussed above.

Analysis of the literature elicited a number of principles which were incorporated in the guidelines, thereby ensuring that the guidelines reflect the preferences of women.

Task 4

All members of the Working Party contributed to the compilation of a glossary of breast cancer terms, which forms an Appendix to both documents.

COSTING ISSUES

A preliminary review was undertaken of the existing literature on the economic evaluation of breast cancer treatment. The review was not exhaustive, and focused only on those articles which considered options for treatment discussed in the guidelines. Cost-effectiveness information is included for locoregional therapy, adjuvant therapy and follow-up care. However, only one of the studies examined was Australian in origin, and population characteristics and costs (in

particular) are therefore likely to differ. Nevertheless, while the results cannot be generalised to the local setting, there is some commonality in existing treatment patterns. The information is therefore included as some indication as to where further research in the Australian setting may be worthwhile.

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APPENDIX B: REVISION OF THE FIRST EDITION (1995) AND PRODUCTION OF THE SECOND EDITION (2001)

In keeping with NHMRC recommendations, the guidelines have been reviewed and updated to provide a new edition for 2001 onwards.

The steps taken in reviewing the guidelines are described below.

THE REVISION TEAM

A multidisciplinary sub-group of the first edition Working Party was established to undertake a detailed review of the guidelines. The sub-group was chaired by Emeritus Professor Tom Reeve, and included Associate Professor Alan Coates, Mr Colin Furnival, Professor Allan Langlands (member until April 2000) and Ms Jayne Ross. This group met on a number of occasions to develop directions, consider specific issues and rewrite sections as required.

The Revision Team sought comment and collected reviews of the evidence as detailed below. These were then reviewed and incorporated into the revised guidelines.

Update of the evidence: overview

A review of the scientific findings on which the original guidelines were based was completed by the Cochrane Review Group in Breast Cancer. The update was conducted in December 1996 and repeated in December 1997. The accuracy of the statements in the guidelines, the supporting references and the levels of evidence were reviewed. This review included consideration of the new overviews published by the Early Breast Cancer Trialists Collaborative Group since the release of the first edition, addressing ovarian ablation, tamoxifen and poly-chemotherapy.²⁹⁷⁻²⁹⁹

Specific areas

The Revision Group identified a number of areas where a special review was required and requested individuals to provide these reviews as shown:

- Incidence and survival figures (Dr Anne Krickler)
- Genetics (Associate Professor John Hopper)
- Alternative and complementary therapies (amended with chapter from draft the iSource National Breast Cancer Centre's *Clinical practice guidelines on the management of advanced breast cancer*, 2001)

- Pathology (Dr Michael Bilous)
- DCIS and LCIS (Dr Michael Bilous, Dr Geoff Delaney, Associate Professor John Boyages, Dr Stephen Cahill)
- Breast conserving surgery with mastectomy (Mr Colin Furnival, Mr Donald Marshall)
- Axillary dissection and lymphoedema (Professor Alan Rodger, Mr Colin Furnival, Dr Sue Pendlebury, Mr Owen Ung)
- Postmastectomy radiotherapy (Professor Alan Rodger)
- Adjuvant therapy (Dr Ray Snyder, Professor Michael Green, Professor Alan Coates)

Individuals were required to provide critical appraisal of key papers that had been published since the first edition of the guidelines. These findings were incorporated into the guidelines. Draft reviews were then sent to the working party for consideration and final interpretation of evidence, and formulation of recommendations was reached through discussion. In addition, the NHRMC public consultation process provided a means of external review of the updated chapters.

Levels of evidence

The Working Group decided that it was important to give a clear indication in the guidelines as to the strength of the evidence for guidelines and key statements, and to provide references where appropriate.

The levels of evidence and associated guidelines are presented in tabular form throughout the text. The evidence cited in the guidelines has been classified as accurately as possible into four levels, as follows:

- Level I** Evidence is obtained from a systematic review of all relevant randomised controlled trials.
- Level II** Evidence is obtained from at least one properly designed randomised controlled trial.
- Level III** Evidence is obtained from well-designed controlled trials without randomisation; OR from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group; OR from multiple time series with or without the intervention.
- Level IV** This represents the opinions of respected authorities based on clinical experience, descriptive studies or reports of expert committees.

This rating system is recommended by the Quality of Care and Health Outcomes Committee (QCHOC) and has been adapted from the system developed by the US Preventive Services Task Force.²

The amount and strength of supporting evidence available for particular topics varies, partly reflecting the fact that research has tended to focus on some issues more than others. Since clinical decisions must often be made in the absence of published evidence, a number of recommendations are based on Level III and IV evidence. All recommendations were informed by the considered opinion of clinical experts and were considered to be best practice. The processes used in developing these guidelines were designed to ensure that, as well as being based on the best available evidence, the recommendations reflect a consensus view of early breast cancer treatment in Australia.

REVIEWS OF EVIDENCE AND RECOMMENDATIONS DEVELOPED BY THE ISOURCE NATIONAL BREAST CANCER CENTRE AND OTHER GROUPS

Since the publication of the first edition, the iSource National Breast Cancer Centre (the Centre) and others have produced a number of reviews of specific issues. While many of these issues were addressed in the first edition, there have been additional evidence reviews and reports on areas concerning the management of women with early breast cancer. Many of these were accessed for the revision of these guidelines and are shown in the reference section of this document. These include:

- The prognosis and management of women with ductal carcinoma in situ of the breast. A review by Ghersi D and Simes J, NHMRC National Breast Cancer Centre 1998
- Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer, NHMRC National Breast Cancer Centre 2000
- Report of the effectiveness of post-mastectomy radiotherapy and risk factors for local recurrence in early breast cancer, Radiation Oncology Advisory Group of the National Breast Cancer Centre and the Faculty of Radiation Oncology of the Royal Australian and New Zealand College of Radiologists in association with Ghersi D and Simes J (NHMRC Clinical Trials Centre), in Radiotherapy and Breast Cancer, NHMRC National Breast Cancer Centre 1999
- *Lymphoedema: prevalence, risk factors and management: a review of research*, by Collete Browning and Associates, NHMRC National Breast Cancer Centre 1997
- *Review of high-dose chemotherapy as a treatment strategy for breast cancer*, Talbot S, Basser R, Boyle F, Gallelari M, Rolfe F, iSource National Breast Cancer Centre, (in preparation)

CONSULTATION AND FEEDBACK

Issues raised by major stakeholders were taken into account as described. First, the guidelines were submitted to the NHMRC who oversaw the first and second public consultation processes. A number of submissions were received from experts, representatives of professional colleges and consumer representatives. These were reviewed and considered by a sub-group of the Working Party (including frontline clinicians, experts and consumers who have considered the clinical relevance and validity of the evidence and decided on its implications for practice) and modifications or inclusions were made if deemed to reflect best practice and the available evidence. After revision, the final drafts were approved by the sub-group. A consensus-building process was used to achieve agreement on the resulting recommendations.

Early breast cancer guidelines sub-group

This multidisciplinary group reviewed drafts of the guidelines and was comprised of:

Emeritus Professor Tom Reeve (Australian Cancer Network), Chair

Dr Roger Allison (Radiation oncologist)

Professor Bruce Barraclough (Surgeon)

Professor Alan Coates (The Cancer Council, Australia)

Ms Mary Draper (Department of Health, Victoria)

Mr Colin Furnival (Surgeon)

Mr Anthony Green (Surgeon)

Associate Professor Michael Green (Medical oncologist)

Ms Vanessa Lambert (Consumer representative)

Professor Allan Langlands (Radiation oncologist—member until April 2000)

Ms Jayne Ross (NSW cervical screening program)

Dr Raymond Snyder (Medical oncologist)

Dr Jane Turner (Psychiatrist)

Consumers have been involved in all stages of guideline development. Consumers are permanent members of the Early Breast Cancer Working Group, which has overseen the development of the guidelines. Consumers unconnected to the iSource National Breast Cancer Centre were also able to respond to the NHMRC call for submissions on the guideline.

Feedback on the first edition of the guidelines was sought at the end of 1997 and the beginning of 1998 from a broad range of agencies involved in breast cancer control. The organisations consulted included:

Original Working Party (see Appendix A)

Cancer organisations

ACT Cancer Society

Anti-Cancer Council of Victoria

Australian Cancer Network

Breast Cancer Action Group of Victoria

Cancer Council of NT

Cancer Foundation of WA

Counselling and support services from each state and territory cancer organisation (Breast Cancer Support Service and Cancer Information Service)

Medical Oncology Group

NSW Breast Cancer Institute

NSW Cancer Council

Queensland Cancer Fund

iSource National Breast Cancer Centre representatives from the professional colleges

Royal Australian College of General Practitioners

Royal College of Pathologists of Australasia

Royal Australasian College of Radiologists

Royal Australasian College of Surgeons

Royal College of Nursing, Australia

iSource National Breast Cancer Centre's Consumer Advisory Group

Other selected individuals from the following disciplines

Reconstructive surgery

Medical oncology

Consumers

Radiation oncology

Surgery

Psychiatry

General practice

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Comments and contributions were also received from the following individuals and groups:

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Dr Michael Bilous	Pathologist
Ms Carol Bishop	Coordinator, Breast Cancer Support Service
Associate Professor John Boyages	Radiation oncologist
Dr Fran Boyle	Medical Oncologist
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Ms Julie Burdis	Consumer representative
Ms Louise Burton	Manager Supportive Care, NSW Cancer Council
Dr Stephen Cahill	Radiologist
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IMPLEMENTATION AND DISSEMINATION OF THE GUIDELINES

The Centre will be responsible for disseminating, implementing, evaluating and updating the revised guidelines. The implementation plan has been developed on the basis of experience obtained through the implementation of the first edition of the guidelines.

An initial print run of the guidelines will be disseminated to relevant professional groups free of charge. Copies will also be made available to allied health organisations, state and territory health authorities, breast cancer treatment centres, consumer and patient groups, professional colleges and associations, public policy makers, health economists and professional journals.

To assist electronic dissemination, the Centre will include these guidelines on the its web page, enabling Internet access. The availability of the guidelines will be advertised through the Centre's newsletters, published frequently throughout the year. The guidelines will also be distributed to professional colleges across Australia.

Lastly, the guidelines will be promoted through national seminar series, presentations at relevant professional meetings and conferences and submissions to professional journals.

CONSIDERATION OF LOCAL CONDITIONAL AND RESOURCE CONSTRAINTS

Implementation of the guidelines will, in some cases, depend on the availability of expertise and resources. Unfortunately, little specific evidence is available concerning the range of local treatment options available for remote or rural women with early breast cancer, although these services are known to be often limited.

To assist with such issues, the Centre has been involved in the preparation of guideline implementation kits to help address issues of local variability, and in establishing pilot projects for electronically linking remotely located clinicians into a network of expertise. Ideally, such a network is multidisciplinary in nature, offering a range of expertise and assistance as well as continuity of care for management of the disease. Clinicians and other carers from non-urban areas are also encouraged to interact with multidisciplinary teams in the larger cities. Other projects aimed at alleviating rural and remote isolation have included the establishment of a Rural Surgeons Fellowship Scheme.

The guidelines have been framed in a manner that is flexible and mindful of variations in local conditions and resource considerations. Some of the recommendations may be difficult to implement, particularly the psychosocial recommendations—for instance, the provision of interventions which require a psychiatrist or clinical psychologist. However, many of these recommendations do not require additional infrastructure, and rather call for changes in style and approaches to the provision of information. The Centre is currently promoting evidence-based communication skills training at a national level, and has initiated a number of projects to explore what is required by specific treatment centres to meet needs and develop resources (such as specialist breast nurses) in diverse settings.

Throughout the text, reference is made to economic and cost/benefit issues. However, there is a lack of primary research on these areas. The resources required for additional studies to identify and test a range of economic evaluations (cost-effectiveness and cost-utility analyses) and cost comparisons of interventions in all possible service settings is quite significant and would constitute a major research undertaking of several years duration. This is beyond the scope of Centre's resources. In Chapter 9, it is recommended that Australian cost data are collected to allow for comprehensive analysis of the costs of treatment options, and also that research is conducted appraising the impact of treatment options on quality of life.

However, the Centre has commissioned two reports which have examined costs in relation to breast cancer management. The first²⁵⁹ provides estimates of the out-of-pocket expenses incurred by women in Australia in obtaining breast cancer screening, diagnosis and treatment services outside the BreastScreen Australia Program, based on data pertaining to the period 1995–1997. In- and out-of-hospital medical service costs were estimated, and costs of adjuvant radiotherapy and chemotherapy under different scenarios are presented.²⁵⁹ This report emphasises that, in the Australian health care system, a woman can gain virtually complete financial protection against the cost of medical, hospital and support services by opting to be treated as a public outpatient or a public inpatient in a public hospital. Further details of cost breakdowns can be found in the report.²⁵⁹

A second study described the average costs of diagnostic management at a Sydney-based breast clinic in the context of clinical practice guidelines for the diagnosis of women presenting with symptoms which may be caused by breast cancer.³⁸³ For this clinic the average costs of diagnostic management and the average cost of diagnostic procedures are detailed in the report of the study.³⁸³ It was concluded that the cost of diagnosis for women with breast problems cannot be compartmentalised into a set of procedural based events, and that overall clinical management plays an important role in the process of diagnosis. Although this study achieved a first step in estimating the marginal cost-effectiveness of implementing evidence-based guidelines for the management of women presenting with breast symptoms, it is not generalisable to the rest of the state or the country.³⁸³

For discussion of the economics and costs and benefits of different treatments, readers are referred to the chapters on surgery, radiotherapy, systemic adjuvant therapy and follow-up.

EVALUATION AND UPDATING

An essential part of the guideline development and implementation process is an evaluation of their effectiveness. An evaluation strategy will be drafted at the implementation stage and will include the collection of data to determine the impact of the guidelines on clinician behaviour and patient health outcomes.

The Centre has already undertaken key steps to facilitate this process. Baseline data have already been collected on women's perceptions of care through the Centre's National Consumer Survey (NCS). The NCS was based on a representative national sample of women treated for breast cancer in the preceding 12 months. This information will assist the development of an implementation strategy.

The guidelines reflect the best available knowledge at the time of their publication. However, they will require regular revision in order to maintain validity as new evidence emerges from systematic reviews. The Centre proposes to investigate the most cost-effective way of achieving this. Collaboration between the Centre's Treatment team and the Early Breast Cancer Working Group (which meets quarterly) provides an established mechanism to review advances in the field and implications for revising the guidelines.

In addition, the Centre's experience with the evaluation and revision of the early breast cancer guidelines and with the Cochrane Review Group in Breast Cancer will assist with the guideline review process. The Centre will continue to foster close links with the Australasian Cochrane Centre and relevant international guideline bodies in order to facilitate the updating of the guidelines.

APPENDIX C: TNM CLINICAL CLASSIFICATION

The most widely used classification for breast carcinomas is the TNM classification.¹ T, N and M categories (tumour, nodes and metastases respectively) are assessed by the combination of physical examination and imaging such as mammography.

T—Primary tumour categories

- TX Primary tumour cannot be assessed
- T0 No evidence of primary tumour
- Tis Carcinoma in situ: intraductal carcinoma, or lobular carcinoma in situ, or Paget disease of the nipple with no tumour
- Note: Paget disease associated with a tumour is classified according to the size of the tumour.
- T1 Tumour 2 cm or less in greatest dimension
- T1mic — Microinvasion 0.1 cm or less in greatest dimension.
- T1a — More than 0.1 cm but not more than 0.5 cm in greatest dimension
- T1b — More than 0.5 cm but not more than 1 cm in greatest dimension
- T1c — More than 1 cm but not more than 2 cm in greatest dimension
- T2 Tumour more than 2 cm but not more than 5 cm in greatest dimension
- T3 Tumour more than 5 cm in greatest dimension
- T4 Tumour of any size with direct extension to chest wall or skin
- Note: Chest wall includes ribs, intercostal muscles and serratus anterior muscle but not pectoral muscle.
- T4a — Extension to chest wall
- T4b — Oedema (including peau d'orange), or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast
- T4c — Both 4a and 4b above
- T4d — Inflammatory carcinoma

N—Node categories

- NX Regional lymph nodes cannot be assessed (eg because previously removed)
- N0 No regional lymph nodes metastasis
- N1 Metastasis to movable ipsilateral axillary lymph node/s

N2 Metastasis to ipsilateral axillary lymph node/s fixed to one another or to other structures

N3 Metastasis to ipsilateral internal mammary lymph node/s

M—Metastases categories

MX Distant metastasis cannot be assessed

M0 No distant metastasis

M1 Distant metastases (includes metastasis to supraclavicular lymph nodes)

Stage grouping

Stage	T classⁿ	N classⁿ	M classⁿ
Stage 0	Tis	N0	M0
Stage I	T1 ¹	N0	M0
Stage IIA	T0	N1	M0
	T1 ¹	N1 ²	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1 ¹	N2	M0
	T2	N2	M0
	T3	N1, N2	M0
Stage IIIB	T4	Any N	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1

Note:

1. T1 includes T1mic

2. The prognosis of patients with pN1a is similar to that of patients with pN0.

Note that these are clinical categories. It is also possible to use the pTNM system of classification based on pathological examination of the tumour and axillary lymph nodes.

APPENDIX D: RACOG BULLETIN VOL 10, NO 1, MAY 1996

FROM THE WORKING PARTY ON TAMOXIFEN AND THE ENDOMETRIUM*

Tamoxifen is the endocrine treatment of choice for selected patients with breast cancer, and is presently being trialed in Australia and elsewhere for its prophylactic value in healthy women at increased risk of developing breast cancer. Although tamoxifen functions as an anti-estrogen, it also has weak and variable estrogenic effects.

Because of its weak estrogenic activity, tamoxifen produces a number of side effects on the female genital tract. These may include:

- Estrogen-like changes in the vaginal epithelium of some patients.
- Stimulation of endometriosis, with worsening of symptoms in some patients. There has been one case report of an endometroid carcinoma arising from an ovarian endometriotic focus.
- Stimulation of the growth of benign fibroids.
- An increased incidence of benign endometrial polyps.
- An increase of benign endometrial proliferation. In post-menopausal women, it would seem that the incidence of atrophic endometrium is about 36 per cent in women on tamoxifen, compared to 73 per cent in control patients, while the incidence of proliferate endometrium is about 20 per cent (10 per cent in controls), endometrial polyps 11 per cent (3 per cent in controls) and endometrial hyperplasia 6 per cent (0.6 per cent in controls).
- A two- to three-fold increase in incidence of endometrial carcinoma. There have been about 250 reported cases of endometrial carcinoma in tamoxifen-treated patients and only one case was in a pre-menopausal woman. About 80 per cent of these cancers were stage 1 and either Grade 1 or 2, which is comparable to the situation in non tamoxifen-treated women. The risk increases with increasing duration of use, being about 3 fold for patients on tamoxifen longer than 5 years.
- There have been isolated reports of uterine sarcomas in women on tamoxifen and a single case of fallopian tube cancer.

Opinions vary widely in the literature and amongst clinicians on the surveillance of patients on tamoxifen therapy who have an intact uterus. Trans-vaginal ultrasonography is relatively non-invasive and will detect a relatively high

* Reproduced with permission from the RACOG (Royal Australian College of Obstetricians and Gynaecologists) Gynaecological Oncology Subspecialty Committee.

proportion of abnormalities. Biopsy of these lesions has produced a wide range of mainly benign pathologies and demonstrated that many of the ultrasonic abnormalities in fact appear to be located in the myometrium. Outpatient hysteroscopy and/or endometrial biopsy are more invasive and less well tolerated in post-menopausal women. Withdrawal bleeding following administration of progestogens is another possible method of screening asymptomatic women for endometrial proliferation. The specificity, sensitivity and cost-effectiveness of these various methods of monitoring are presently unknown.

Because the incidence of endometrial carcinoma is very low (2-3/1000 women per year) during or after tamoxifen therapy, and because there is no convincing evidence that the stage or grade of these tumours differs from that seen in the general population, the working party felt there were no data to support active investigation of asymptomatic women at the present time.

The working party resolved that:

- All women taking tamoxifen should be informed of its potential side effects, including specifically two to three fold increased incidence of endometrial cancer. They should be warned of the possible symptoms of endometrial cancer, including inter-menstrual or post-menopausal bleeding, abnormal vaginal discharge or pelvic pain.
- All patients on tamoxifen should have a baseline pelvic examination. This should include a speculum examination to determine the presence or absence of a cervix and to take a pap smear (if appropriate), and a bimanual examination to evaluate the size of the uterus and the adnexae.
- Any woman complaining of symptoms should be actively investigated immediately.
- If an individual patient expresses particular concern about the possibility of developing endometrial cancer, or is felt to be at additional risk because of a family history of breast, ovarian, endometrial or bowel cancer, the patient should be referred to a gynaecologist and offered investigation at the discretion of the gynaecologist. A vaginal ultrasound performed by a skilled gynaecological ultrasonographer would seem to be the least invasive and most useful initial investigation. Ultrasonography may select out those women with atrophic or inactive endometrium from those with possible pathology, who may require further intervention.
- Because of the absence of data establishing the sensitivity, specificity, clinical value and cost effectiveness of active investigation of asymptomatic women, such research should be encouraged and supported.

These recommendations, which apply to both the therapeutic and prophylactic use of tamoxifen, will be reviewed regularly in the light of any new evidence which may emerge.

Members of the Working Party

Professor Neville Hacker	(Convenor)
Dr Margaret Davy	(In absentia)
Mr Arthur Day	
Dr John Eden	
Dr James Grimwade	
Dr Michael Quinn	
Mr Robert Rome	
Dr Mandy Samson	
Dr Peter Warren	(In absentia)
Dr Barry Wren	
Dr Tom Jobling	(In absentia)

In attendance (representing the Australia-New Zealand Breast Cancer Trials Group):

Professor Alan Coates
Professor John Forbes

APPENDIX E: QUESTIONS YOU MAY BE ASKED

For many women, being diagnosed with breast cancer is a great shock. Most women know little about breast cancer and its treatment. In many cases, they don't even know where to start asking questions.

Following is a list of questions which women may ask about their cancer, treatment and prognosis:

General questions

- Do you mind if I tape record this consultation?
- Do you mind if my friend/relative comes in with me?
- Why did I get breast cancer?
- What type of breast cancer have I got? Where exactly is it? Is it only in the breast or has it spread?
- Am I hormone receptor-positive or receptor-negative? What does this mean?
- Do I need more tests? What sort of tests? Why do I need them? What do you expect them to show?
- With each test, what happens? What are the risks? The benefits? Is the test conventional or experimental? Who will do it? What other options exist?
- When will the results be available?
- How certain are you that the results of these tests will be accurate?
- Are there any specialist centres for the treatment of breast cancer?
- How can I find a doctor/surgeon/oncologist/counsellor I feel comfortable with?
- In everything you tell me about tests and treatment, how much uncertainty is there?
- How will the cancer affect my personal and sexual relationships?
- What emotions might I experience?

Surgery

- Do I have a choice between breast conserving surgery and mastectomy?
- Exactly what is involved in each type of surgery? Exactly how much will you remove? Will you remove the lymph nodes under my arm? Will you remove either of my chest muscles? Where will the scar/s be and what will they look like? Can you show me pictures?
- How will I feel after surgery? How long will I take to recover?

- Where can I go for a prosthesis? Who can help fit it?
- Can I see photographs of women who have had mastectomies, lumpectomies, partial mastectomies and/or reconstructions?
- If I have a mastectomy, can I have breast reconstruction? Can this be done during the same operation?

Radiotherapy

- Why do you think I should (or should not) have radiotherapy?
- If I have radiotherapy, what type of radiotherapy will I have?
- Who will do it? When? Where?
- How long will it take?

Chemotherapy

- Why do you think I should (or should not) have chemotherapy?
- If I have chemotherapy, how will it be given? For how long?
- Will the drugs make me sick? Will it make my hair fall out?
- Will I still be able to work?

Hormone therapy

- Why do you think I should (or should not) have hormone therapy?
- If I have hormone therapy, what type of hormone therapy will it be?
- Can I have a form of hormone therapy that does not induce permanent menopause?

Deciding about treatment

- What treatment do you recommend? Why?
- What happens if I choose a different treatment? Or no treatment?
- For all these treatments, what benefits would you expect for the average woman?
Am I the average woman?
- For all these treatments, what are the risks?
- How successful are these treatments for my type of breast cancer? Will they cure me, or will they control the cancer? In what way will they control the cancer? Will they mean I live longer? Will they reduce any problems the cancer's giving me? What will my life be like during and after treatment?
- Will there be any permanent damage? Will I still be able to have children? Will I be able to breast feed? Will I get my menopause early? Will my sex life be affected?
- I would like at least a week to make a decision—are you comfortable with this?

Questions relating to treatment

- How much time will all this take? Will I have to stay in hospital?
- How long will I be away from work?
- How much will it all cost?
- Do I need to use contraception during my treatment? Will I have to wait for a while after my treatment before I can become pregnant?
- Is there anything I need to be particularly careful about during my treatment?
- Is there anything I can do to help during my treatment? Should I eat special foods? How can I reduce stress?
- If I need a wig or breast prosthesis, how will I get one? Will I need special clothing?
- Am I entitled to any benefits and services, such as subsidies for travel or prostheses?
- What side effects can I expect? What can I do about them?
- Are there any side effects or problems I should tell you about immediately? How do I get in touch with you to do this? What if the problem occurs out of hours?
- How will you know if the treatment's working? What sort of tests will you do? How often will you do them? How long will they take to do? When will you have the results?

Lymph nodes

- What are lymph nodes? Why are they important in breast cancer?
- Will the surgery involve removing the lymph nodes? If so, what are the risks, side effects and complications of the operation?
- Can I prevent these complications?
- If I get them, how do I treat them?

Reconstruction

- Is reconstruction possible? What are the advantages and disadvantages of having reconstruction?
- If I choose to have a breast reconstruction, what is the best time for it—straight away or later?
- How would it be done? Who would do it?
- Would you have to operate on my other breast? Can you construct a nipple? How would you do this?
- Can you show me photographs of breasts you have reconstructed?
- How long would I have to stay in hospital? How many operations would I need?

- How long would it take me to recover? What side effects can I expect? Are there likely to be any complications or problems?

After treatment

- What long-term effects—physical, mental, emotional, social, sexual or anything else—may occur?
- Is there anything I should be particularly careful about after my treatment ends? Will I need to come back for a check-up? When should I come back? How often should I have mammograms?
- Is the cancer likely to come back? Where would it come back, if it does come back? Will I get it in the other breast? What signs should I look out for? What can I ignore?

Support

- Do you know of any local support groups? Where can I find out what support services are available?
- Can I talk to a counsellor? Is there a counsellor available to talk to my family?
- Can I talk to someone who has been in my situation and who has had treatment similar to the treatment you are recommending for me?
- What should I tell my family? What should I tell my children?

Information

- Where can I get more information on breast cancer and its treatment?
- Who can I contact if I have more questions between now and my next consultation with you?
- Can you show me how to examine my own breasts?

APPENDIX F: NATIONAL BREAST CANCER CENTRE PUBLICATIONS LIST AND ORDER FORM

WEBSITE

Breast cancer information on the internet. The Centre's website is a 'one-stop shop' for information about breast health and breast cancer in Australia. Updated regularly, the website features information about the Centre's projects and resources, breast cancer news, personal stories and viewpoints and publications. Visit the Centre's website at www.nbcc.org.au

NEWSLETTERS

Clinical Update

For surgeons, medical oncologists and radiation oncologists. A quarterly newsletter which reviews recent research articles with immediate significance to clinical practice.

Breast News

Quarterly newsletter of the National Breast Cancer Centre, featuring information about the Centre's projects and resources, new policy and program developments, recent key research papers, and current issues and debates, as well as upcoming breast cancer meetings in Australia and overseas.

Breast Fax

Monthly newsletter of the National Breast Cancer Centre, with the latest in the Centre's activities and projects. This one-page update includes information about the Centre's launches and new projects. Sent as a fax or can be sent as an email and viewed with Acrobat Reader.

PUBLICATIONS ORDER FORM

How to order

 iSource National Breast Cancer Centre,
PO Box 572,
Kings Cross NSW 1340

 National publications line:
(voicemail) on 1800 624 973
OR (02) 9334 1882

 National Publications Line:
(facsimile) on (02) 9326 9329

 Online order form at:
www.nbcc.org.au/pages/info/resource/nbccpubs/nbccpubs.htm

NB: The Centre's written materials are available for preview or downloading from www.nbcc.org.au

Costs

Free of charge unless otherwise stated.

Order Limits

Limits are shown beside the title. To discuss orders which exceed the stated limits call (02) 9334 1805

Delivery

Orders will be processed within 2 weeks.

isOURCE National Breast Cancer Centre Publications Order Form

Patterns of breast cancer

Guidelines and recommendations

	ICP	Ascertainment and reporting of interval cancers within the BreastScreen Australia Program ❶
	RCS	Current recording and registration practices for carcinoma in situ of the breast in Australasian State and Territory cancer registries.
	NPR	National protocol for recording 1. size, nodal status and grade of invasive breast cancer, 2. carcinoma in situ

Reports, research and data reviews

	BC1	Breast cancer in Australian women, 1921-1994
	BC2	Breast cancer in Australian women, 1982-1996
	DCA	Ductal carcinoma in situ (DCIS): Cancer Monitoring No 1 ❶
	SAW	Breast cancer survival in Australian women 1982-1994
	NSW	Breast cancer survival in NSW in 1973 to 1995
	DCN	Ductal carcinoma in situ in NSW women in 1995 to 1997
	NTS	Surgical management of breast cancer in Australia in 1995 ❶
	WAS	Trends in the incidence, surgical management and survival of breast cancer patients over 13 years in WA 1982-1994 ❶
WEBSITE ONLY		Report on the 1996 breast health survey

Breast cancer: general

Reports, research and data reviews

	MAD	Australia's first national breast cancer conference for women – Making a difference: actions recommended by women with breast cancer for the benefit of the Australian community ❶
	RR	Breast cancer research in Australia: current research and future priorities
	CIA	Catalogue of resources on breast health and breast cancer Part 1: Australian resources (1998) ❶
	DAO	Don't ask for an opinion – ask for a scalpel: print media coverage of breast cancer in Australia in 1995
	ITP	Evaluation of a breast cancer information training package for the Cancer Information Service
WEBSITE ONLY		Review of public materials intended for general dissemination: executive summary

Information for consumers

	RAD	Women and breast cancer (set of 5 radio programs on cassette) \$22 each* (incl. GST)
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Risk factors

Guidelines and recommendations

	BOG	Advice about familial aspects of breast cancer and ovarian cancer: a guide for health professionals (card)
WEBSITE ONLY		Current best advice about familial aspects of breast cancer: a guide for general practitioners (card)

Reports, research and data reviews

	PSC	Psychosocial factors and the risk of developing breast cancer (review)
	SPU	Some public health issues in the current state of genetic testing for breast cancer in Australia
	SRF	Summary of risk factors for breast cancer ❶

Information for consumers

	BCF	Breast cancer and family history: what you need to know (booklet) ❺
	PMF	Information for women considering preventive mastectomy because of a strong family history of cancer. NB This booklet is intended for use primarily by breast surgeons, breast specialists, oncologists, family cancer clinics and genetic counselling services.
WEBSITE ONLY		Best advice on familial aspects of breast cancer: a guide for general practitioners. Phase 2: Evaluation
WEBSITE ONLY		Diet and breast cancer (review)
WEBSITE ONLY		Evaluation of best advice on familial aspects of breast cancer for general practitioners

Early detection and diagnosis

Guidelines and recommendations

	BSP	Breast-self examination: a position statement from the National Breast Cancer Centre.
	IBS	Investigation of a new breast symptom: a guide for general practitioners. (card) ❷
	PAT	Pathology reporting of breast cancer: a guide for pathologists, surgeons and radiologists. (ACN) ❷
	HP1	Screening women aged 40-49 years: a summary of the evidence for health professionals

Report, research and data reviews

	BSS	Breast self examination and the early detection of breast cancer: a summary of the evidence for health professionals
	BSE	Effectiveness of breast self-examination: a literature review. ❶
	SYM	Evidence relevant to guidelines for the investigation of breast symptoms ❶
	IBA	Investigation of a new breast symptom: an audit in general practice ❶
	NAP	National audit of pathology reporting of breast cancer: a summary ❶
	PSM	Perceptions of screening mammography amongst women aged 40-49 ❶
	AHL	Prevalence, screening and management of atypical hyperplasia and lobular carcinoma in situ ❶
	DCI	Prognosis and management of women with ductal carcinoma in situ of the breast: a review ❶

	MMG	Review of the evidence about the value of mammographic screening in 40-49 year old women ❶
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Information for consumers

	BCB	Breast changes: what you need to know (booklet)
	WEBSITE ONLY	New technologies in breast cancer diagnosis: information update

Corporate

	AR5	Annual report 1999-2000: Achieving sustainable change
	AR4	Annual report 1998-1999: Partnerships to improve breast cancer control
	SD	Strategic Directions June 1999 – June 2003
	WEBSITE ONLY	Annual report 1995-1996: Translating research into action
	WEBSITE ONLY	Annual report 1996-1997: Improving breast cancer control
	WEBSITE ONLY	Annual report 1997-1998. National directions in breast cancer control
	WEBSITE ONLY	Consultative report: summary and outcomes. Volume 1
	WEBSITE ONLY	Consultative report: reports from State/Territory workshops Volume 2

Professional

Guidelines and recommendations

	CAK	Cameo-B: A model curriculum for medical students: breast cancer modules \$54.95 each* (incl. GST)
	LIC	Legal implications of clinical practice guidelines (a recommendations paper) ❷
	MLG	Medicolegal implications of clinical practice guidelines in the diagnosis and treatment of breast cancer and legal implications of clinical practice guidelines (a recommendation paper) ❶
		Medicolegal implications of clinical practice guidelines in the diagnosis and treatment of breast cancer and legal implications of clinical practice guidelines: an executive summary ❶

Reports, research and data reviews

	DRV	Drivetime radio with Dr John D'Arcy. Medical edition #33. Side B: Living with breast cancer: key issues in familial aspects of breast cancer; determining risk factors and patient counselling; the management of early breast cancer
	DR2	Drivetime radio with Dr John D'Arcy. Medical edition #39. Side A: Breast cancer guidelines for the diagnosis of symptomatic women
		Medicine and the Law (MJA Article)

Treatment

Guidelines and recommendations

	CPG	Clinical practice guidelines for the management of early breast cancer (NB guideline is being revised) ❶
	ADV	Clinical practice guidelines for the management of advanced breast cancer ❶
	MBC	Management of early breast cancer for GPs: action based on evidence. (card) (NB guideline is being revised) ❶
	RUK	Systemic adjuvant therapy for women with early breast cancer: An educational kit for health care professionals practising in regional areas of Australia ❶ (NB due to limited numbers, the Kit is limited to one copy per organisation)
	RBC	Radiotherapy and breast cancer ❶

Reports, research and data reviews

	MAX	Management of the Axilla in women with breast cancer
	NRT	New radiotherapy techniques
	CYT	Management of advanced breast cancer: systematic reviews of randomised controlled trials regarding the use of cytotoxic chemotherapy and endocrine therapy ❶
	SWT	Should women take part in clinical trials in breast cancer? The issues and some solutions

Information for consumers

	MCG	A guide for women with metastatic breast cancer (booklet) ❺
	AAB	All about early breast cancer (booklet) (NB: booklet is being revised) ❺
	AAC	All about early breast cancer (cassette) ❺
	AAR	All about early breast cancer (CD ROM) ❺ \$16.50 (incl. GST)

Support

Guidelines and recommendations

	PCG	Psychosocial clinical practice guidelines: providing information, support and counselling for women with breast cancer ❶
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Reports, research and data reviews

	PRM	An examination of procedures reimbursed under Medicare for breast disease and breast cancer in Australia, 1985 to 1996 ❶
	DSW	Cost of diagnostic investigations for women presenting with breast symptoms, The ❶
	DCX	Experience of diagnosis; information and support needs of women diagnosed with ductal carcinoma in situ
	LRS	Encouraging research into lymphoedema: a report on the summit held on 25 and 26 February 2000 ❶
	LRR	Encouraging research into lymphoedema: a register of lymphoedema research ❶
	LYM	Lymphoedema: prevalence, risk factors and management: a review of research ❶
	LPD	Lymphoedema prevention, diagnosis and treatment. Literature search

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patients and an observed response rate of 33 per cent has a 95 per cent confidence interval of 16–55%. While tumour response rate is a reasonable endpoint for assessing the anticancer activity of a drug, it is not an adequate surrogate for patient benefit.

Phase II trials are suitable for guiding decisions about further research, but are not suitable for making or guiding decisions about patient management. The literature is often confusing on this point, because phase II trials are often reported and interpreted as if they do provide answers to questions about patient management.³⁸⁵

Phase III trials are pragmatic since they are designed to answer questions about the usefulness of treatments in patient management. Questions about patient management tend to be comparative since they involve choices between alternatives, that is, an experimental management versus the current standard. The current standard may include other anticancer treatments, or may be the best supportive care without specific anticancer therapy.

The aim of a phase III trial is to estimate the difference in outcomes associated with a difference in treatments, sometimes referred to as the treatment effect. Ideally, alternative treatments are compared by administering them to groups of patients which are equivalent in all other respects. Randomised controlled phase III trials are the best, and often only reliable, means of determining the usefulness of treatments in patient management.

Table 8: Classification of clinical trials

Characteristic	Explanatory	Pragmatic
Purpose	To guide research and provide information about mechanisms and specific effects of treatment	To guide patient management and provide information about net effects and patient benefit
Primary focus	The treatment	The patient
Conditions	Idealised	Real
Treatment	Chosen to accentuate the phenomenon under study	Chosen with tolerance of the target population in mind
Controls	Chosen to isolate the phenomenon of interest	Chosen according to standard practice
Assessment criteria	Direct measures of biological activity, such as tumour response and host toxicity	Direct measures of patient benefit such as survival, quality of life and functional capacity
Choice of patients	Those most likely to demonstrate an effect	Those most typical of the patients to whom the results will be applied

The contact numbers for the Australian New Zealand Breast Cancer Trials Group (ANZBCTG) are phone: 02 4921 1896; fax: 02 4967 2351.

APPENDIX H: BREAST CANCER SUPPORT SERVICES

To find out about breast cancer support groups and other local services, contact your state or territory cancer organisations and the Cancer Information Service. The Cancer Information Service can be contacted in any state/territory by telephone on: **13 11 20**.

- The Cancer Council ACT
159 Maribyrnong Avenue
KALEEN ACT 2617
Phone: 06 6262 2222
Fax: 06 6262 2223
Email: chl@actcancer.org
Website: www.actcancer.org.au
- Anti-Cancer Council of Victoria
Rathdowne Street
CARLTON SOUTH VIC 3053
Phone: 03 9635 5000
Fax: 03 9635 5270
Email: enquiries@accv.org.au
Website: www.accv.org.au
- Anti-Cancer Foundation of South Australia
202 Greenhill Road
EASTWOOD SA 5063
Phone: 08 8291 4111
Fax: 08 8291 4122
Email: acf@cancersa.org.au
Website: www.cancersa.org.au
- The Cancer Council Tasmania
140 Bathurst Street
HOBART TAS 7000
Phone: 03 6233 2030
Fax: 093 6233 2123
Email: Iride@courier.tas.gov.au
Website: www.cancer.org.au/tas

- Cancer Foundation of Western Australia Inc
 46 Ventnor Avenue
 WEST PERTH WA 6005
 Phone: 089212 4333
 Fax: 08 9212 4334
 Email: cancerwa@cancerwa.asn.au
 Website: www.cancerwa.asn.au
- The Cancer Council Northern Territory
 Unit 1-3
 23 Vanderlin Drive
 CASUARINA NT 0810
 Phone: 08 8927 4888
 Fax: 08 8972 4990
 Email: uvstop@cancernt.org.au
 Website: www.cancercouncilnt.citysearch.com.au
- The Cancer Council, New South Wales
 153 Dowling Street
 WOOLLOOMOOLOO NSW 2011
 Phone: 02 9334 1900
 Fax: 02 9357 2676
 Email: feedback@nswcc.org.au
 Website: www.nswcc.org.au
- Queensland Cancer Fund
 553 Gregory Terrace
 FORTITUDE VALLEY QLD 4006
 Phone: 07 3258 2200
 Fax: 07 3257 1306
 Email: qldcf@qldcancer.com.au
 Website: www.qldcancer.com.au

Other breast cancer services for women

- Breast Cancer Network of Australia (BCNA)
PO Box 4082
AUBURN SOUTH VIC 3122
Phone: (03) 9805 2500
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Lymphoedema Associations & Support Groups

These groups provide information on lymphoedema, local services and resources and support to women with lymphoedema.

- The Australian Lymphology Association
8 Kergo Place
WANTIRNA SOUTH VIC 3152
- ACT Lymphoedema Support Group
66 Bindaga Street
ARANDA ACT 2614
Phone: (02) 6251 1294
- Darwin Lymphoedema Support Group
PO Box 4127
CASUARINA NT 0811
Phone: (08) 8927 4888
Fax: (08) 8927 4990
- Lymphoedema Support Group of NSW
79 Beechworth Road
PYMBLE NSW 2073
Phone: 02 9402 5625
- Lymphoedema Support Group of SA
PO Box 1006
KENT TOWN SA 5071
Phone: (08) 8204 4711
- Tasmanian Lymphoedema Support Group
C/- 42 Stanley Street
BELLERIVE HOBART TAS 7018
Phone: (03) 62444634

- Lymphoedema Association of Victoria
PO Box 2412
NORTH RINGWOOD VIC 3134
Phone: 1300 852 850
- Lymphoedema Association of Western Australia
C/- Crawford House
15 Bedbrook Place
SHENTON PARK WA 6008
Phone: (08) 9381 2070

Useful web sites:

Breast Cancer Network of Australia
www.bcna.org

iSource National Breast Cancer Centre
www.nbcc.org.au

The Cancer Council Australia
www.cancer.org.au

APPENDIX I: ROYAL AUSTRALASIAN COLLEGE OF SURGEONS BREAST AUDIT

The Royal Australasian College of Surgeons, (RACS) Breast Audit, set up as a collaborative venture with the iSource National Breast Cancer Centre, is now the recommended audit instrument for breast surgeons who are members of the Section of Breast Surgery, RACS. Use of this audit is an obligatory component of membership of the Section.

Information can be obtained from:

Ms Sarah Tyson, Project Manager

PO Box 688

NORTH ADELAIDE SA 5006

Phone: (08) 8361 9077

Fax: (08) 8239 1244

Email: breast.audit@racs.edu.au

GLOSSARY

Adjuvant chemotherapy/hormone therapy

The use of either chemotherapy or hormone therapy after primary treatment either by surgery or radiotherapy, or a combination of these (usually within six weeks) to eradicate micrometastatic cancer. A way of having one treatment assist another.

Alopecia

Hair loss. In the context of breast cancer, usually caused by one of the chemotherapeutic drugs. It is usually partial and short-term, and full recovery usually occurs.

Anti-oncogene

See **tumour suppressor gene** or **anti-oncogene**.

ANZBCTG

Australian New Zealand Breast Cancer Trials Group. National clinical trials group which conducts research on new treatments.

Anxiety

A diffuse, highly unpleasant, often vague feeling of apprehension, accompanied by bodily sensations such as pounding heart and sweating. There is an associated anticipation of future misfortune or danger, external or internal.

Atypia

Histological or cytological abnormal changes in epithelial cells. See also **dysplasia**.

Atypical ductal hyperplasia

Increased numbers of ductal epithelial cells which show some but not all the features of in situ carcinoma: associated with a significant risk of developing subsequent carcinoma in either breast.

Axilla

Fossa axillaris; armpit.

Axillary dissection

Surgical excision of the axillary contents (fat and lymph nodes) en bloc with mastectomy or as an independent procedure. The extent of the axillary dissection is further defined in the following way:

Level 1—excision of the axillary contents up to the inferior border of the pectoralis minor muscle.

Level 2—excision of the axillary contents up to the superior border of the pectoralis minor muscle.

Level 3—excision of the axillary contents up to the apex of the axilla.

Axillary sampling

An ill-defined procedure which varies from the excision of a single, low axillary node to the excision of the lower axillary contents as in a Level 1 axillary dissection.

Biopsy

Removal of a sample of tissue or cells from the body by excision or aspiration for microscopic examination to assist in diagnosis of a disease.

Body image

The individual's conception of and feelings about their body — its overall integrity, its physical characteristics such as form, size and shape, and its conformity to societal values and norms. Self-esteem, psychosocial functioning and sexuality are intimately linked with body image.

Bone scan

An investigation carried out to assess the presence or absence of metastatic disease. The uptake of a radio-nuclide in bone is determined. Sites of increased activity frequently represent metastatic disease.

Boost

An additional dose of radiation given to a smaller volume, usually the local excision site, after the remainder of the breast has been irradiated.

Brachytherapy

The use of isotopes inserted into tissue to deliver radiation to a limited volume. See also **teletherapy**.

BRCA1

Breast cancer gene 1. It is identified as a gene on the long arm of chromosome 17 which is mutated or lost in 2–4 per cent of women with breast cancer. See also **familial breast cancer**.

BRCA2

Breast cancer gene 2 has been identified recently on chromosome 13. See also **familial breast cancer**.

Breast conserving surgery

Surgery where the breast cancer is excised together with a margin of normal breast tissue. The whole breast is not removed.

Breast reconstruction

The creation or insertion of a breast shape or mound using surgical techniques, after a total mastectomy.

Breast sharing

This is a method of reconstruction in which some of the opposite breast is used to reconstruct the missing breast.

Calcification

The deposition of calcium salts in body tissues. In the breast, calcification can be seen in normal and abnormal ducts and in association with some carcinomas, both invasive and in situ.

Carcinoma

A malignant tumour arising from epithelial cells, which are cells lining the external or internal surfaces of the body. Carcinomas spread by local infiltration and may also spread to distant sites such as lung, liver, lymph nodes and bone. See also **metastasis**.

Carcinoma in situ

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.

Carcinoma NOS

Invasive ductal carcinoma not otherwise specified. Comprises 70 per cent of all breast cancers.

Cathepsin D

A protein with proteolytic and mitogenic activity secreted by breast cancer cells and postulated to be a marker of poor prognosis.

Centigray

1 centigray = 1 rad. This is a system used in the United Kingdom which allows the actual numbers to remain unchanged with the move from RAD to GRAY. For example, 4500 rads is 45 Gray or 4500 centigray.

Chemotherapy

The use of medications (drugs) to kill cancer cells, or to prevent or slow their growth.

Chromosome

A body in the cell nucleus carrying genes. See **gene**.

CLE

See complete local excision.

Clinical trial

Research conducted with the patient's permission which usually involves a comparison of two or more treatments or diagnostic methods. The aim is to gain better understanding of the underlying disease process and/or methods to treat it. A clinical trial is conducted with rigorous scientific method for determining the effectiveness of a proposed treatment.

Combined modality treatment

The integration of two or more forms of treatment to combat the cancer. For example: radiation and surgery; radiation and chemotherapy; surgery, radiation and chemotherapy.

Comedo carcinoma in situ

A high grade type of in situ breast carcinoma with large poorly differentiated cells and central necrosis. Also known as large cell in situ carcinoma.

Complete local excision (CLE)

The complete excision of an entire tumour mass, surrounded on every aspect by a margin of normal breast tissue, confirmed by histological examination of the margins.

Coping strategies

Mental strategies or behaviours employed to maximise functioning and reduce or eliminate psychological distress in response to stressful situations. Coping strategies may be influenced by personality style and the specific situation, and may change over time.

Core biopsy

The sampling of breast tissue with a cutting needle, 18 gauge or larger, to give a tiny cylinder of tissue for histological examination. This technique may involve a mechanical device to drive the cutting needle.

Cosmesis

The appearance of the breast following conservative treatment. It is generally accepted that one goal of conservative treatment is to retain a breast with an appearance as close to normal as is compatible with effective treatment.

Counselling

Refers generically to a form of supportive care delivered by health professionals. There are differing levels of sophistication depending on the training and experiences of the practitioner involved.

Cribriiform

See Non-comedo carcinoma in situ.

Cycle

Chemotherapy is usually administered at regular intervals depending on the type of drugs. A cycle commences with the administration of the chemotherapy and ends when the nadir has passed and the white blood and platelet counts have returned to pretreatment values. Then the next dose of chemotherapy is given.

Cytology

Assessment of cellular detail and abnormalities in a preparation of cells obtained by fine needle aspiration (FNA), or by other methods such as imprint or duct discharge cytology.

DCIS

Ductal carcinoma in situ.

Denial

Failure to acknowledge some aspect of external reality that would be apparent to others. This is an involuntary reaction (as opposed to lying) which aims to avoid anxiety.

Depression

A pervasive and sustained lowering of mood, often associated with tearfulness, guilt or irritability. May also include loss of interest in activities, lowered energy levels, impaired concentration and disturbance of sleep and appetite.

Determination of disease extent

The use of clinical examination, imaging (X-rays, bone scans), biochemical and pathologic information to determine the extent of the underlying cancer.

Differentiation

The degree to which a tumour resembles normal tissue. In general, the closer the resemblance, the better the prognosis. Well differentiated tumours closely resemble normal tissue.

Disease-free survival

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

DNA ploidy

A measure of the DNA content of a cell. Tumour growth is commonly accompanied by accumulation of genetic abnormalities including changes in the total amount of DNA per cell. From this comes the terms diploid (normal complement of chromosomes), tetraploid, aneuploid or polyploid.

Dry desquamation

A healing erythematous reaction with the shedding of dry skin.

Dysplasia

An abnormal growth of cells which have some of the features of carcinoma cells but which have insufficient changes to warrant a diagnosis of carcinoma. See also **atypia**. Note that this is a pathological term and should be differentiated from the radiological term 'dysplasia', which refers to an abnormal radiological appearance usually due to fibrocystic disease.

ECOG

Eastern Cooperative Oncology Group. A United States group of university and community oncologists funded to conduct trials to combat cancer.

ECOG performance status

An arbitrary scale of symptoms and ambulation based on a five-point scale developed by the United States Eastern Cooperative Oncology Group:

- 0—No symptoms of cancer
- 1—Presence of cancer-related symptoms
- 2—Spends less than 50 per cent of daylight hours in bed
- 3—Spends more than 50 per cent, but less than 100 per cent of daylight hours in bed
- 4—Totally confined to bed

EGF-R

Epidermal growth factor receptor. A cell surface growth factor receptor which binds several peptide ligands, including EGF. A high expression of EGF-R is associated with a poor prognosis. See also *erbB-2*.

Electron

The smallest particle of negative electricity. Electrons have a useful property of finite penetration of tissue, as opposed to the exponential absorption which occurs with X-rays.

EORTC

European Organization for Research and Treatment of Cancer. An oncology cooperative which carries out multicentre clinical trials across Europe.

EORTC core quality of life questionnaire (QLQ)

Developed by the EORTC study group for quality of life, QLQ - C30 is a generic 'core questionnaire' relevant to any cancer to be used with modules specific to a particular cancer. It has undergone extensive translation and testing for interpretation and is available in most European languages. A breast cancer module was field tested in 1995 in Germany, Belgium, Denmark, Sweden, Spain, Portugal, France, Italy, Poland, Bulgaria, Greece, Holland, Turkey and in all English-speaking countries.

Epidermal growth factor receptor

See **EGF-R**.

ER

Oestrogen receptor. An intracellular receptor protein that binds oestrogens and antioestrogens and mediates their effects by subsequently binding to DNA and altering the expression of specific genes. It is an indicator of responsiveness to hormonal therapies. High ER expression is associated with a good prognosis and with a response to hormonal therapy.

erbB-2

Also known as *HER2/neu*. A cell surface receptor related to EGF-R. Activation of EGF-R and *erbB-2* signal transduction pathways results in a mitogenic response. High expression of *erbB-2* is associated with a poor prognosis.

Erythema

Redness of the skin which is the earliest sign of radiation reaction. It usually occurs after a conventionally fractionated dose of about 40 Gray has been delivered.

Extensive intraductal carcinoma (EIC)

EIC is generally said to exist when 25 per cent or more of the primary invasive tumour mass is comprised of ductal carcinoma in situ (DCIS), and when areas of DCIS co-exist in the adjacent breast tissue. EIC is a predictor for high relapse rates following wide local excision and radiotherapy.

Familial breast cancer

Breast cancer that generally occurs in the setting of a first degree relative who has had breast cancer, particularly in pre-menopausal disease, implying an inherited disposition. The two best described syndromes of familial breast cancer are due to mutations of the BRCA1 gene (where there may also be a predisposition to ovarian cancer) and mutations of the p53 gene (Li-Fraumeni syndrome). Familial breast cancers are thought to comprise less than 10 per cent of all breast cancers. Recently a second gene BRCA2, on chromosome 13, has also been identified.

Fear

Anxiety due to a consciously recognised *external* threat or danger.

Fine needle aspiration biopsy (FNA or FNAB)

See **fine needle biopsy**.

Fine needle biopsy (FNB)

The sampling of cells from breast tissue for cytological examination using a needle of size 23 gauge or smaller. When suction is applied during the sampling, this is referred to as fine needle aspiration biopsy (FNA or FNAB).

Fraction

The total dose of radiation to be given is usually delivered over several weeks. That dose which is delivered each day is known as a fraction.

Free flap reconstruction

Soft tissue reconstruction where the tissue (such as the latissimus dorsi or a TRAM flap) is separated from its donor site and a new blood supply established using microsurgical techniques.

Frozen section

A rapid method of obtaining a histological diagnosis of tissue during an operation. This is not routinely done for breast cancer.

G-CSF

Granulocyte cell stimulating factor. A natural substance which promotes the release of mature white cells following their suppression, usually by chemotherapy.

Genes

The functional units of heredity, each occupying a fixed location on a chromosome within the cell nucleus.

Gene amplification

A process of DNA duplication that results in a chromosome having more than one copy of a gene or genes and which can result in inappropriate gene activation. It is a common mechanism of activation of oncogenes such as *erbB-2* and *c-myc* in breast cancer.

Grade

A relationship has been demonstrated between prognosis and degree of differentiation of breast carcinoma. This degree of differentiation is called the grade. 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.

Gray

The modern unit of radiation dosage. Doses used in curative breast cancer management would usually vary between 45 and 65 Gray. See also **rad**.

Grief

The normal emotional response to loss, which may include a complex range of painful feelings such as sadness, anger, helplessness, guilt and despair.

Halsted mastectomy

See **radical mastectomy**.

HER2/*neu*

See ***erbB-2***.

Histology

Assessment of cellular features by light microscopy of sections from paraffin-embedded tissue.

Hormone receptors

Hormone receptors are proteins residing within the cell which specifically bind to the appropriate hormone. This hormone receptor complex subsequently stimulates the cell to undergo a physiological function such as cell division. In women with breast cancer, these receptors are present in approximately 50 per cent of all women and are powerful prognostic indicators of survival and response to hormone (or antihormonal) therapy.

Hormone replacement therapy (HRT)

The use of exogenous female hormones as a substitute for natural hormones in women.

Hormone therapy

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

Hyperplasia

Increased numbers of epithelial cells. If florid, there is a slightly increased risk of developing subsequent breast carcinoma.

Immediate reconstruction

The reconstruction of the breast at the time of mastectomy.

In situ carcinoma

See **carcinoma in situ**.

Increment

See **fraction**.

International Breast Cancer Study Group

An international cooperative group which includes many Australian clinical researchers. The group conducts multicentre trials, especially in the area of adjuvant therapy.

Iridium (wire)

A radioactive wire sometimes used to deliver the boost to the operative site in breast conserving techniques.

Karnofsky index

An index based on simple percentages ranging from 10-100, 100 being totally normal and capable of full activity, and 10 being totally confined to bed and close to death. See **ECOG**.

Ki67

Immunohistochemical marker of proliferative activity.

Labelling index

Also known as thymidine labelling index. A measure of proliferative activity. The proportion of cells which incorporates radioactively labelled thymidine over a given time. It is a method of estimating DNA synthesis.

Large cell in situ carcinoma

See **comedo carcinoma in situ**.

Latissimus dorsi flap

Method of soft tissue reconstruction employing the skin of the back carried on the latissimus dorsi muscle. A prosthesis may also be inserted to provide greater volume.

LCIS

Lobular carcinoma in situ. It is a misnomer which describes a benign proliferative process in the lobular units. It does not have specific mammographic features and is usually detected by chance in the course of a breast biopsy for another lesion.

Limited axillary dissection

Less than complete axillary clearance equivalent to low axillary dissection.

Linear accelerator

Modern radiation equipment capable of delivering X-rays at very high energies of up to 25 million electron volts (25MeV).

Loss of heterozygosity

The absence of one copy (allele) of a gene or of part of one copy of a chromosome. In some circumstances, this may imply the presence of a tumour suppressor gene in the lost genetic material.

Lumpectomy

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

Lymph nodes/lymph glands

Collections of lymphoid tissue at intervals throughout the body. A common site or the early spread of breast cancer is to the axillary lymph nodes.

Malignant

A tumour having the capacity to destroy locally, spread and cause death.

Mammogram

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

Mammography

That process whereby soft tissue X-rays of the breast are obtained.

Margins of resection

The surgical margins of the excised tumour. See **complete local excision**.

Mastectomy

Surgical removal of the breast. May be total (all of the breast) or partial. See also **radical (Halsted) mastectomy**.

Megavoltage

Megavoltage applies to machines delivering X-rays of high energy. This includes Cobalt 60 apparatus and modern linear accelerators.

Meta-analysis

A quantitative synthesis of the results of two or more primary studies which have addressed the same hypothesis in the same way.

Metastasis

The process by which carcinoma cells are disseminated from the tumour origin (primary tumour) to form a new tumour (secondary tumour) at a distant site. Transportation of the cells is generally via lymphatics or blood vessels.

Metastasise

See **metastasis**.

Metastatic cancer

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

Micrometastases

Metastatic cancer which cannot be detected by conventional imaging (X-ray, bone scans) or biochemical or haematological tests.

Micropapillary

See **non-comedo carcinoma**.

Mitosis

The process of cell division. The number of mitoses indicates the number of tumour cells in replicative mode.

Modified radical mastectomy

Total mastectomy in continuity with a Level 2 or 3 axillary dissection, without excision of the pectoralis major muscle and with or without excision of the pectoralis minor muscles. See also **Patey's operation**.

Moist desquamation

A response to radiation therapy characterised by denudation of the epithelium. It can be exacerbated by friction and sweat and should *never* be referred to as 'radiation burn'.

Nadir

The lowest measured value. Usually used in the context of evaluating the effect of chemotherapy or radiotherapy on the white blood cell and platelet count.

Necrosis

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

Neutropenia (febrile)

That condition which exists when the numbers of circulating neutrophil leucocytes are reduced. If the numbers fall to very low levels, there is the risk of supervening infection and the syndrome is then known as febrile neutropenia or neutropenic sepsis.

Nodal status

Indicates the histological presence or not of metastases in the axillary nodes. (Node +ve = one or more nodes involved. Node -ve = no nodes involved.)

Non-comedo carcinoma in situ

A low-grade type of in situ carcinoma comprising small cells. Includes cribriform, micropapillary or small cell carcinoma depending on pattern.

Occult metastases

Metastases not yet apparent.

Oestrogen receptor

See ER.

Oncogene

Literally, a cancer-causing gene. A gene, often with a normal function in controlling growth or differentiation, which when functioning abnormally (activated, for example, by amplification or mutation) confers on normal cells immortality or the ability to form tumours (transformation). Oncogenes that are commonly overexpressed or amplified in breast cancer include EGF-R, *erbB-2*, *c-myc*, *c-myb* and *int-2/cyclin D1*.

Open biopsy

A surgical procedure performed under local or general anaesthetic in which a sample of breast tissue for histological examination is obtained in a conventional surgical procedure, using an open incision.

Orthovoltage

X-rays delivered from generators operating at less than 500,000 volts and usually in the region of 250,000–300,000 volts.

Ovarian ablation

Treatment which destroys ovarian function.

Overall survival

The time from the primary treatment of the breast cancer to the death of the patient.

p53

A protein with complex functions that include mediating cell cycle arrest after DNA damage. Li-Fraumeni syndrome (which results in a marked increase in the risk of breast cancer) is associated with inherited mutations of the p53 gene. Most p53 mutations result in an abnormal protein which accumulates in cells and is thus easily identified immunohistochemically. Acquired (somatic) mutations are found in approximately 50 per cent of breast cancers.

Paget's Disease of the Nipple

This is an eczematoid change of the nipple associated with an underlying breast malignancy. About 1–2 per cent of patients with breast cancer have it (from JM Dixon. *ABC of breast disease* BMJ Publishing Group, 1995: p.35).

Palliation

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

Parallel pair

An arrangement of X-ray fields which allows radiation to be given in one direction and in the reverse direction, and thus balance absorption with depth.

Partial mastectomy

Excision of part of the breast. In practice synonymous with complete local excision. See also **mastectomy**.

Patey's operation

A modified radical operation for carcinoma of the breast in which the breast and axillary lymph nodes are removed in continuity, as in the Halsted operation, but without removal of the pectoralis major muscle. See also **modified radical mastectomy**.

PCNA

Proliferating cell nuclear antigen. Protein expressed during S-phase and therefore potentially a marker of proliferative fraction.

PR

Progesterone receptor. The intracellular receptor which binds progestins and antiprogestins. It is an oestrogen-induced protein, so it can be used as a marker of functional ER status. High expression of PR is associated with a good prognosis.

Predictive factor

Frequently confused as a prognostic factor. An example is the oestrogen receptor which is usually found in patients with good prognosis but which is a predictive factor for response to hormone therapy.

Primary breast tumour

Tumour arising in the breast.

Progesterone receptor

See **PR**.

Prognostic factors

Patient or tumour parameters that are associated with, but not necessarily causally related to, better or worse disease outcomes.

Progression

The continuing growth of the cancer. Often used when discussing treatment failure. Also known as disease progression.

Prosthetic breast reconstruction

Creation of a breast shape using an artificial prosthesis, usually consisting of a silicone envelope containing normal saline or silicone gel.

Protocol

A well defined program for treatment.

pS2

An oestrogen-induced protein and therefore used as a marker of functioning ER status. High expression of pS2 is associated with a good prognosis.

Quadrantectomy

Strictly, excision of an entire quadrant of the breast. The term is often incorrectly interchanged with segmentectomy or complete local excision.

Quality of life

An individual's overall appraisal of their situation and subjective sense of wellbeing. Quality of life encompasses symptoms of disease and side effects of treatment, functional capacity, social interactions and relationships, and occupational functioning. Key psychological aspects

include subjective distress, satisfaction with treatment, existential issues, and the impact of illness and treatment on sexuality and body image.

There are a number of standardised measures of quality of life, ranging in sophistication from the simple visual scale through to comprehensive self-administered questionnaires. Some questionnaires have been designed for specific diseases or conditions, including several directed specifically at cancer. These standardised measures have demonstrated validity and reliability.

QLQ

See **EORTC Core Quality of Life Questionnaire (QLQ)**.

Rad

An old unit of radiation dose, now superseded by the Gray. 1 Gray = 100 rads.

Radical (Halsted) mastectomy

Total mastectomy in continuity with a Level 3 axillary dissection and complete excision of the pectoralis major and minor muscles. This operation is now largely obsolete and rarely performed.

Radiotherapy

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

Rectus flap reconstruction

Soft tissue reconstruction using skin and fat from the abdomen carried on the rectus abdominis muscle. Also known as TRAM — transverse rectus abdominis myocutaneous flap.

Recurrence

Reappearance of the cancer after a period of remission.

Relapse

Reappearance of disease after observed response to treatment.

Response to therapy — complete response

The disappearance of all detectable cancer for a minimum of one month. Also known as remission.

Response to therapy — disease progression

Increase of at least 25 per cent in the sum of the products (of the largest diameter and its perpendicular) of all measurable disease for at least one month, and no appearance of new lesions.

Response to therapy — partial response (partial remission)

A 50 per cent or greater reduction of the sum of the products (of the largest diameter and its perpendicular) of all measurable disease for at least one month, and no appearance of new lesions.

Response to therapy — stable disease

Measurable cancers (as defined above) without either response to treatment or progression.

S-Phase fraction

A measure of proliferative activity. The proportion of cells synthesising DNA (ie in the S-phase of the cell cycle), as estimated by flow cytometry.

Scleroderma

A connective tissue disorder, primarily affecting the skin, oesophagus and heart.

Secondary reconstruction

Reconstruction of the breast carried out some time after the original mastectomy.

Secondary tumour

A deposit of breast cancer away from the breast (such as in the lung, bone or lymph node). See **metastasis**.

Segmentectomy

The excision of an entire (radial) segment of the breast.

Sentinel node biopsy

Sampling of the first set of lymph nodes that receives drainage from the tumour cells. A combination of radioactive tracer and colour dye is used to localise the nodes. The biopsy technique is less extensive and can reduce the need for axillary clearance in node negative patients. It is not, at present, a standard procedure.

Simulator

Apparatus resembling a linear accelerator which allows rehearsal of the treatment position and allows the calculation of the radiation treatment prior to its commencement on a linear accelerator.

Small cell carcinoma

See **non-comedo carcinoma in situ**.

Soft tissue reconstruction

Method of reconstruction using the patient's own tissue, transferred from another area of the body.

Specimen X-ray

X-ray of a surgically removed specimen to confirm that a mammographically detected lesion has been removed. Also used for selection of histological sampling in impalpable lesions and a guide to whether margins are adequate.

Staging

Conventionally refers to the allocation of categories (0, I, II, III, IV) to groupings of tumours defined by internationally agreed criteria. Frequently these are based on the tumour, the nodes and the metastases (TNM). Staging may be based on clinical or pathological features.

Stereotaxis

A radiological technique to accurately localise a lesion in the breast. Used to permit precise insertion of a needle in order to obtain material for cytology (fine needle) or histology (core biopsy), or as an aid to surgical excision of an impalpable lesion.

Subcutaneous mastectomy

Surgical excision of the entire breast parenchyma, including the axillary tail of the breast, with preservation of the entire breast skin, including the nipple and areola.

Support group

The existence or availability of people on whom an individual can rely for the provision of emotional caring and concern, and reinforcement of a sense of personal worth and value. Other components of support may include provision of practical or material aid, information, guidance, feedback and validation of the individual's stressful experiences and coping choices.

Systemic

Involving the whole body.

Tangents

Fields (radiotherapy target areas) which are planned in such a way that the irradiation of a sector of the chest wall following mastectomy or chest wall and breast following breast conserving surgery minimises irradiation of the underlying lung.

Telangiectasia

Small dilated vessels which appear in heavily irradiated mucosal or epithelial surfaces.

Teletherapy

Radiation therapy delivered from a distance by either Cobalt 60 apparatus or a linear accelerator.

Thymidine labelling index

See **labelling index**.

Tissue expansion

Creation of a breast shape using an inflatable silicone envelope placed beneath the skin and muscle, which is gradually expanded over several weeks by repeated injections of saline.

Total mastectomy

Surgical excision of the entire breast parenchyma including the axillary tail of the breast, together with an ellipse of overlying skin which encloses the nipple and areola.

Toxicity

Side effects which are due to the treatment administered. The side effects range from mild to severe and are usually controllable, and in some women are preventable.

Transverse rectus abdominis myocutaneous flap (TRAM)

See **rectus flap reconstruction**.

Treatment failure

The inability of the cancer therapy (whether surgery, radiation or chemotherapy) to halt the growth or spread of the cancer.

Tubular carcinoma

A very well differentiated carcinoma seen increasingly as a result of mammographic screening. The tumour needs to be 90 per cent tubular to merit the term.

Tumour

An abnormal growth of tissue. It may be localised (benign) or invade adjacent tissues (malignant) or distant tissues (metastatic).

Tumour suppressor gene

A gene which, when down-regulated, inactivated or lost (see **loss of heterozygosity**), contributes to cell proliferation or ceases its activity in blocking cell proliferation. Examples are p53 in breast cancer, RB protein in retinoblastoma and possibly BRCA1 in breast cancer. See **anti-oncogene**.

Tumour type

The overall histological pattern of the tumour.

Vascular infiltration

Invasion by carcinoma cells of peritumoral lymphatics or veins indicating a propensity for distant spread.

Wedge

A beam modifying device which is used to correct for varying thickness in a field of radiation. It is used in radiotherapy for breast cancer because the thickness of the breast will vary from its apex to its base.

X-rays

X-rays are electromagnetic radiations with wave lengths in the range of 0.1-100 angstroms. X-rays are absorbed exponentially by the irradiated tissue. See also **electron**.

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