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Current Issues Background Paper

Breast Cancer

by

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Foreword

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Contents

1 Introduction

The purpose of this paper is to provide an overview of the extensive information available concerning breast cancer. It provides in **Part 2** and **Part 3**, information concerning breast cancer and breast disease generally. **Part 4** describes the pathology of breast cancer and presents information concerning the different types of common breast cancers. In **Part 5** the paper looks at the current statistics on incidence, mortality and survival of breast cancer and breast cancer patients. (Figures for New South Wales, Australia and overseas are provided).

In **Part 6**, knowledge concerning the cause of breast cancer is examined and evidence concerning risk factors for developing breast cancer is provided. **Part 7** briefly examines breast cancer in men, and **Part 8** looks at the control and treatment of breast cancer. Strategies for both primary and secondary prevention are discussed as are the conventional treatments. **Part 9** provides a brief overview of the research and other funding for breast cancer in Australia and New South Wales, and is followed by a brief conclusion.

2 Background

Cancer is a major cause of morbidity and mortality in Australians. Data from the Australian Bureau of Statistics indicate that cancer was the leading cause of death amongst Australians of all ages in 1991[1] and that one in four Australians will develop cancer during their lifetime.

Approximately 80 per cent of cancers are due to environmental factors such as sunlight, smoking, alcohol consumption, nutrition, reproduction and sexual behaviour, pollution and occupation.[2] Many cancers resulting from such causes are preventable and as such, education and screening programs feature largely in programs aimed at cancer prevention.

Breast cancer is the second most common cancer amongst Australian women and the most common cause of death from cancer. Lifetime (0-74) risk of developing breast cancer is 1 in 16 and the likelihood of a woman dying from breast cancer before 75 is 1 in 44.[3] The latest information from the NSW Cancer Council Registry indicates that these figures are even more grim for NSW women; in 1991 the lifetime risk of developing breast cancer was 1 in 13 and the risk of dying from

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1 Australian Bureau of Statistics, *Causes of Death, Australia*, October 1992.

2 NSW Cancer Council, *Cancer in New South Wales Incidence and Mortality 1990*, NSW Central Cancer Registry, December 1992, p8.

3 Australian Cancer Society, *National Cancer Prevention Policy 1993*, Sydney, 1993.

breast cancer before age 75 was 1 in 43.[4]

Breast cancer is thus a significant women's health problem and one which will impact upon the lives of most Australians. Recognition of the growing breast cancer 'epidemic' has prompted State, Federal and International authorities into action designed to facilitate early detection of breast cancer and thus improve prognosis, and to improve the management of breast cancer patients. Nevertheless, further action is needed, particularly in the areas of research and community and clinical practitioner education.

[4] NSW Cancer Council, *Cancer in New South Wales Incidence and Mortality 1991*, Sydney, January 1994.

3 Breast Disease

Breast cancer is not the only common breast disease. In fact, many women who detect lumps in their breasts do not have breast cancer, but may suffer from a number of other curable diseases or have a noncancerous lump.

Benign breast disease[5]

Benign breast disease, also known as mammary dysplasia and fibrocystic disease, is very common and may affect up to 40 per cent of women. Benign breast disease manifests itself as painful and lumpy breasts. The condition is the result of inflammation of the glandular, ductal and fibrous tissues of the breast. Symptoms of benign breast disease include the presence of multiple, painful small lumps in both breasts, although one breast may be more affected, swelling in the breasts with or without cysts, pain in the armpits, symptom exaggeration premenstrually or in association with the ingestion of high dose oestrogen contraceptives and nipple discharge. The condition is most common in women between the ages of 30 to 50 and often improves after menopause. Women who suffer benign breast disease have a slightly elevated risk of suffering breast cancer.[6]

Noncancerous breast lumps

Only one in ten breast lumps are actually cancerous. The most common causes of noncancerous breast lumps are fibroadenomas, fat degeneration or breast abscesses.

Fibroadenomas are common in women under the age of 40 and are characterised by mobile, firm and round lumps that are not painful and which may be as large as two inches in size (five centimetres). Fibroadenomas can easily be removed with surgery.

Trauma to the breast tissue, such as from a heavy blow, may result in death of fatty tissue which may form a lump. Such 'lumps' are often removed to ensure that they are not cancerous.

Breast abscesses commonly occur as a result of bacterial infections during breast feeding. Treatment of the infection with antibiotics and milk expression often alleviates the infection. However, pus accumulation may result in an abscess forming which will require surgical incision and drainage.

[5] For a review of benign breast disease, see Humeniuk, V., 'Benign breast disease. A practical guide.' *Australian Family Physician*, 1993, 22, 22 - 25.

[6] Cabot, S., *Women's Health*, Sydney, Pan Australia, 1994, pp 199 - 201.

4 Breast Cancer

Breast cancer is not just one disease, presenting in one form. There are a range of diverse malignancies which manifest as breast cancer, the classification of which was recently revised. It should be emphasised, however, that common histological[7] classification of cancers across individuals does not necessarily correspond to similar behavioural patterns of tumours; tumours that are similar histologically may follow entirely different progression paths in different individuals.

There are two subtypes of breast cancer - in situ (localised) and invasive (spread out). There are two main types of in situ breast cancer, namely ductal and lobular, and six types of invasive breast cancer - ductal, lobular, medullary, tubular, mucinous colloid and paget's disease. A short description of the symptoms and pathology of each of these follows.

Ductal in situ breast cancer

In situ cancers are described as a proliferation of malignant appearing cells in/around a duct or lobule occurring without invasion of the surrounding tissue. Breast cancers classified as in situ ductal cancers represent a ragbag of conditions loosely divided into two groups - comedo (cf. blackheads or pimples) which are monomorphic, and non-comedo which are polymorphic. All these cancers are pathologically characterised by proliferation of cells in the duct without invasion to surrounding tissue. All types of in situ ductal breast cancers contain microcalcifications which enable them to be detected using mammography. Ninety-nine per cent of in situ ductal breast cancers are cured by mastectomy. However, a recurrence rate of around 40 per cent is observed if treatment is by local incision and radiotherapy.

In situ lobular breast cancer

In situ lobular breast cancers are characterised by a solid proliferation of small cells occurring in the breast lobules. Almost invariably, in situ lobular breast cancer is identified incidentally (ie these cancers are not identified as lumps detected by either physical breast examination or mammography). These cancers may be pre-malignant or may be a marker for increased risk for the development of other cancers. Treatment strategies include monitoring the cancer; 30 per cent of cancers so tracked become invasive; or bilateral mastectomy.

Invasive ductal breast cancer

Invasive ductal breast cancers account for around 75 to 80 per cent of invasive cancers. These cancers are characterized by no specific histology but are identified by palpitation as stony hard lumps of 2-5 cm. These cancers have an appearance resembling an unripe pear and are accompanied by microcalcifications which permit their detection using mammography. Unfortunately these cancers have a very poor long term prognosis as the secondaries metastasise to the axilla, bone, liver and brain. In addition, micrometastases commonly occur; removal of the primary cancer and radiotherapy are thus unlikely to prevent the appearance of secondary cancers years later.

Invasive lobular breast cancer

Around 10 per cent of invasive breast cancers are lobular. These cancers are not well demarcated and are characterised by ill-defined cell thickening. Histological examination of the cells reveals that the cells are small and uniform, arranged in indian file strands around ducts and lobules in a targetoid fashion. These cancers are multi-centric and are spread via the lymphatic system. Prognosis with these cancers is also poor as secondaries tend to occur in unexpected and 'weird' places including the meninges and serosal surfaces.

Other invasive breast cancers

The four other types of invasive breast cancers are all much less common than ductal and lobular invasive breast cancer. However, these cancers have a much better prognosis. Invasive medullary breast cancer accounts for approximately five per cent of invasive breast cancers and is characterized by well-defined lymphocyte proliferation. Tubular invasive breast cancer makes up around two per cent of invasive breast cancers and mucinous colloidal around three per cent. These latter cancers are characterised by a slow build up of colloid around a slow growing tumour. The final sort of invasive breast cancer is Paget's disease[8]. However, Paget's disease occurs 100 per cent with either invasive or in situ ductal breast cancer. Invasive Paget's breast cancer affects the nipple and areolar. This cancer is often mistaken as eczema as the symptoms include reddening and peeling of the skin on and around the nipple.

Overall, about 95 per cent of breast cancers are adenocarcinomas. Across all ethnic groups, the majority of these are infiltrating duct carcinomas. However, there are differences in the incidence of different types of cancer across ethnic groups. Infiltrating duct carcinomas occur proportionately more often in Chinese and Japanese women (and may partially explain the better five year survival rates in these groups), lobular carcinomas occur most often amongst white women and medullary cancers occur more amongst Hispanic, black and Chinese women.[9]

In approximately one per cent of breast cancer cases bilateral primary tumours are reported. However, routine biopsy of the 'unaffected' breast reveals a bilateral rate of around 12-15 per cent. Interestingly, most investigators have reported that

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[7] Histological classification of breast cancers is based upon examination of the cells of the tumour and surrounding tissue and is performed by histologists and pathologists.

[8] Paget's disease also affects bones and results in the enlargement of the skull.

[9] Kelsey, J. and Horn-Ross, P., 'Breast cancer: magnitude of the problem and descriptive epidemiology', *Epidemiologic Reviews*, 15, 7 - 16, 1993.

unilateral breast cancer occurs most often in the left breast (a left to right ratio of 1.05 to 1.2 has been reported) with the left excess reported in both whites and blacks. Speculation concerning reasons for this excess include the observation that the left breast is often larger than the right breast and thus a greater amount of tissue may potentially be able to be affected. Most types of breast cancer, except perhaps medullary cancer, occur more often in the left breast. The left excess also seems to be more apparent in perimenopausal and post-menopausal women than in pre-menopausal women.[10]

Definitive diagnosis of breast cancer is made by either fine needle biopsy[11] or entire lump excision. Fine needle biopsy has become more popular over recent years and involves insertion of a needle into the lump to extract some cells which are then examined for characteristic cancer-like changes. Whole lump excision may also occur under local anaesthetic, although this is less common, and involves the surgical removal of the entire lump which is then examined pathologically. Around 65 per cent of breast biopsies are found to be benign, that is noncancerous.[12]

[10] Kelsey and Horn-Ross, 1993 op cit, p7.

[11] Koss, L.G., 'The palpable breast nodule: a cost-effectiveness analysis of alternate diagnostic approaches', *Cancer*, 72, 1499 - 1502, 1993, presents an history of fine needle biopsy and also assessment of its utility and accuracy.

[12] Cabot, S., 1994 op cit, p208.

5 Incidence, Mortality and Survival

Incidence

Incidence of, and mortality from, breast cancer increase with age. Risk of developing cancer at age 30 is estimated to be 1 in 2000, at age 50, 1 in 55, at age 74, 1 in 14. Cases of breast cancer in women in their 20s and 30s are rare in comparison to cases in women in their 40s and 50s. The breast is the most common site for cancer in women aged 30 and over in the Western world. Women in the age range 45 - 65 seem to be most at risk of developing breast cancer.

World

Breast cancer incidence differs considerably across continents. In general, the incidence is lower in Asia and Third World countries than it is in North America and Europe. Japan consistently has the lowest rate of around 18.6 per 100 000 women and white residents of San Francisco Bay area in the USA the highest rate - 87.0 per 100 000 women. Switzerland has a rate of around 66.8 per 100 000 women, New Zealand a rate of 59.5 per 100 000 Maori women and 57.7 per 100 000 non-Maori women and Finland a rate of 44.7 per 100 000 women. There are also differences between ethnic groups within countries; black American women have a lower rate than the San Francisco Bay women but a higher rate than black African women and Japanese and Chinese immigrants to the USA. There is little change in the incidence of breast cancer in Japanese women who migrate to Hawaii and mainland USA in their lifetime. However, breast cancer incidence in the daughters and grand-daughters of these women gradually increases until it is on a par with white American women even if these women marry Japanese men.[13] There are also differences in the incidence patterns and survival rates between the East and West. The incidence of breast cancer in premenopausal women tends to be similar across the world. However, where there is a pronounced increase in breast cancer incidence in Western post-menopausal women, there is a decrease amongst Japanese post-menopausal women. Furthermore, the overall survival rate of Japanese women with breast cancer is better than that of British women, despite a lack of difference in survival time for pre-menopausal women.[14]

Worldwide, in both industrialised and developing countries, the incidence of breast cancer is rising.[15] For example, between 1973-77 and 1988-91 in NSW, the age-standardised rates of breast cancer increased 25 per cent with most of the

[13] Henderson, I.C., 'Risk factors for breast cancer development', *Cancer Supplement*, 71, 2127-2140, 1993.

[14] Henderson, I., 1993, op cit , 2135.

[15] The recorded incidence of breast cancer in America grew markedly in the mid-1970s after Betty Ford and Margaretta Rockefeller were diagnosed as having the disease. It seems that highly visible cases of the illness encouraged many women to be screened. This event does not, however, explain the surge in incidence in the 1980s.

increase occurring in the late 1980's.[16] In 1972, on average, 1424 new cases of breast cancer were identified in females. By 1991 this figure had risen to 2807. Similar, although earlier and sometimes larger, increases were observed throughout the Western world. Age-adjusted breast cancer incidence rates in the USA increased from 82.4 cases per 100 000 women in 1973 to 112.4/100 000 women in 1987, an increase of 36 per cent.[17] On the basis of current incident rates, the American Cancer Society estimates that 1 in every 9 women in the USA will develop breast cancer during her life; 180 000 new cases of breast cancer were diagnosed in women in the USA in 1992 (1000 new cases in men were also diagnosed).[18]

The cause of this rise in breast cancer incidence is not clear as only around 25 per cent of the increase can be attributed to better record keeping.[19] In addition, there are indications that at least part of the rise may be due to the increased use of mammographic screening and the earlier diagnosis of tumours. Several pieces of evidence support this hypothesis:[20]

1 There is a temporal association between the increase in breast cancer incidence and mammography utilisation. Breast cancer incidence surged in the mid to late 1980s, the time when mammography first became most common and education programs promoting breast self-examination and mammographic screening were first developed.

2 Incidence rates have increased most dramatically for women in age groups targeted for screening. Incidence in unscreened populations have remained relatively constant.

3 Tumours have been detected at an earlier stage and smaller size; the increase in incidence occurred mainly in localised cases and small-sized tumours.[21]

Other factors suspected to contribute to the increased incidence of breast cancer include changes in child-bearing patterns (the full effects of these would be expected to be felt in the future), changing age of menarche and environmental factors such as alcohol consumption, replacement hormone use, diet and

16 NSW Cancer Council, January 1994, op cit, p44.

17 Newcomb, P.A. and Lantz, P.M., 'Recent trends in breast cancer incidence, mortality and mammography', *Breast Cancer Research and Treatment*, 28, 97 - 106, 1993.

18 Kelsey, J. and Horn-Ross, P., 'Breast cancer: magnitude of the problem and descriptive epidemiology', *Epidemiologic Reviews*, 15, 7 - 16, 1993.

19 Hoffman, C., 'Breast cancer incidence, mortality and prospects for control', *Australian Family Physician*, 22, 47 - 52, 1993.

20 Newcomb and Lantz, 1993, op cit, p97.

21 Garfinkel, L., 'Current trends in breast cancer', *CA-A Cancer Journal for Clinicians*, 43, 5-6, 1993.

oestrogen exposure.[22]

Australia

In Australia in 1985 (the latest date for which national data are currently available; data from 1985-1988 are due to be released shortly), there were 5898 cases of breast cancer; 5837 of these were in females, 61 in males. The corresponding figure for the incidence of female breast cancer in 1982 was 5049, for males 68. According to the 1985 data, the lifetime risk of developing breast cancer for males is 1 in 1289, for females 1 in 15.[23] Figures from the same source comparing cancer incidence and mortality across Australia show that NSW had a female rate of breast cancer incidence of 56.8 per 100 000 head of population, Victoria a rate of 61.0, Queensland 65.3, Western Australia 60.6, South Australia 58.5, Tasmania 57.4, ACT 51.3 and Northern Territory 37.7. The overall Australian rate for females was 59.2.

New South Wales

Breast cancer has consistently accounted for 26-28 per cent of female cancer in NSW. From 1973 - 1991, breast cancer was twice as common as any other cancer in NSW women.[24] In 1991 in NSW, there were 2807 new cases of breast cancer reported.[25] This figure represents an increase on the 1990 figure of 2501. 24 of the 1991 cases were males, the remainder (2807) females. 29 of the 1990 cases were males, 2472 females.[26] Allowing for age, women were 125 times as likely to contract breast cancer as men. The number of new cases reported increased with age, reaching a peak in the 55-64 age range:

Table 1: New cases of breast cancer reported in NSW, 1991

Age range	0-44	45-54	55-64	65-69	70-74	75-84	85+
No of cases	469	592	623	355	294	377	97

Over the age of 30, the breast was the most common site of new cancers for

22 Miller, B.A. et al., 'Recent incidence trends for breast cancer in women and the relevance of early detection; an update', *CA-A Cancer Journal for Clinicians*, 43, 27 - 41, 1993.

23 Australian Institute of Health and Welfare and Australasian Association of Cancer Registries, *Cancer in Australia 1983 - 1985*, Cancer Series, Number 1, 1991, p124.

24 NSW Cancer Council, January 1994, op cit, p44.

25 NSW Cancer Council, January 1994, op cit, p44.

26 NSW Cancer Council, December 1992, op cit, pp 44 - 45.

women in NSW.

In the period 1985-89, there were 11 248 new cases of female breast cancer in NSW and 126 new cases of male breast cancer. From 1972-84, migrants from the British Isles had higher relative risks of developing breast cancer when compared to Australian born women. Southern European and Middle East migrants had lower relative risk than Australian born women. There was also a positive association between socioeconomic status and breast cancer risk; better educated women had a higher risk of developing breast cancer.[27] Women from non-English speaking backgrounds had a lower relative risk of developing breast cancer.

Mortality

Breast cancer mortality (age-adjusted) has remained largely unchanged over the past twenty years despite large increases in incidence and earlier diagnosis.[28] In 1988, 2348 deaths from breast cancer were reported in Australian women. This figure represented a rate of around 20.7 per 100 000 women, 18.2 per cent of all female deaths due to cancer and 4.3 per cent of all female deaths.[29] According to the latest figures from the Australian Bureau of Statistics[30] this situation has not changed; breast cancer remains the leading cause of death from cancer in women. In 1991, 2513 women died from breast cancer, a rate of 29 per 100 000 women. Death from breast cancer in 1991 accounted for 4.6 per cent of all female deaths due to cancer.

Deaths due to breast cancer account for the loss of 32 000 woman-years of life annually in Australia;[31] 14 000 -16 000 of these before the age 70, making breast cancer the major cause of premature cancer death.[32]

NSW figures paint a parallel picture. In 1990, 886 females and 4 males died from breast cancer, accounting for 8.1 per cent of all deaths due to cancer and 18.8 per cent of all female cancer deaths. These figures compare with 767 deaths from prostate cancer in males in NSW, representing 7.0 per cent of all deaths due to

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27 NSW Cancer Council, *Cancer Incidence and Mortality by Local Government Area, NSW 1985-89*, May 1993, pp 54-55.

28 The latest NSW Cancer Council data indicates that there has been a 6 per cent increase in breast cancer mortality since 1988. However, the increase in mortality is insubstantial compared to the increase in incidence. In addition, there is evidence that Australian data is demonstrating a lag behind European and Northern American data as there is preliminary evidence that breast cancer mortality may finally be decreasing in the USA (see Newcomb and Lantz, 1993, op cit, p104.

29 Australian Cancer Society, 1993, op cit, p45.

30 Australian Bureau of Statistics, *Women in Australia*, March 1993, p38.

31 Hoffman, C., 1993, op cit, p47.

32 Hurley, S., 'Breast cancer: epidemiology, aetiology and strategies for control', *Australian Cancer Society, Cancer Forum*, 15, 22 - 25, 1991.

cancer and 12.3 per cent of all male cancer deaths.[33] As with breast cancer incidence, the risk of dying from breast cancer also increases with age (see Appendix 1).

Despite the overall constancy of the mortality rate for breast cancer, there have been considerable changes in the age differential mortality rates. In the USA, there has been a slight decline in breast cancer deaths in women younger than 50 (from around 7.0 per 100 000 in 1950 to 6.0/100 000 in 1989). Conversely, there has been a relatively consistent increase in the mortality of women over 50 (from 86.1/100 000 in 1950 to 93.5/100 000 in 1989). Furthermore, there is recent evidence to indicate that the overall mortality rate for breast cancer may have started to decline,[34] in America at least, after remaining stubbornly constant over the past 20 years.

Survival

Age-specific survival rates for breast cancer have increased only marginally since the 1970s.[35] Data from the American National Cancer Institute (see table below) show that whilst there was some increase in five-year survival times between 1960 and 1988, most of this increase occurred prior to 1977. In addition, the five-year survival rate for black American women is significantly lower than for white American women:

Table 2: Five-year Relative Survival Rates for a range of cancers in Whites and Blacks in the USA 1960-1988[36]

	1960-63		1970-73		1974-76		1977-79		1983-88	
Site	**W**	**B**	**W**	**B**	**W**	**B**	**W**	**B**	**W**	**B**
Colon	43	34	49	37	50	46	53	48	59	48
Lung	8	5	10	7	12	11	14	11	13	11
Skin melanoma	60	-	68	-	80	69	82	52	83	68
Breast	63	46	68	51	75	63	75	63	79	62
Cervix	58	47	64	61	69	63	69	62	68	55
Prostate	50	35	63	55	68	58	72	62	78	63

Note: W is whites; B is blacks.

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33 Australian Bureau of Statistics, *State of Health in NSW*, NSW Department of Health, Sydney, October 1993, p23.

34 Newcomb and Lantz, 1993, op cit, pp 97 - 106.

35 Kelsey and Horn-Ross, 1993, op cit, p8.

36 Boring, C. et al., 'Cancer statistics, 1993', *CA-A Cancer Journal for Clinicians*, 43, 7 - 26, 1993.

Age-specific five-year survival rates for breast cancer also show differences between black and white Americans:

Table 3: Five-year survival rate for breast cancer[37]

Age-group	Whites	Blacks
<35	70.5	55.6
35-44	78.3	61.5
45-54	79.5	61.9
55-64	79.0	62.4
65-74	81.2	66.9
>75	79.3	58.6

Explanations for the difference in five-year survival rates for breast cancer between black and white Americans focus on the fact that black women present for treatment at a much later stage of disease than white women; a fact that warrants careful consideration when designing screening or educational programs. Other factors such as lifestyle and educational level probably also play a role.[38]

The overall five year survival rate for breast cancer in Australia is around 70.0 per cent.[39] This rate is on a par with the United States. Currently calculated survival rates are supposed to have not yet revealed the full impact of mammography and large-scale screening as these were only commenced on a comprehensive scale in the late 1980s. Five-year survival rates vary in accordance with the size of the tumour and its stage of development at detection. Patients with tumours less than 2cm and no lymph node or axilla involvement have a five year survival rate of approximately 90 per cent. Conversely, patients with lymph node involvement may have survival rates as low as 20 per cent. Five year survival rate also depends on the type of carcinoma and the oestrogen status of the carcinoma; 70 per cent of those tumours sensitive to oestrogen will regress with chemotherapy. Disseminated recurrence and thus mortality from breast cancer continues to occur many years after the diagnosis.[40]

37 Kelsey and Horn-Ross, 1993, op cit, p8.

38 Boring, C. et al., 1993, op cit.

39 Hoffman, C., 1993, op cit, p47.

40 Secondary cancers have been reported in sites remote from the original tumour up to thirty years after original diagnosis. One study with 40-50 year follow-up reported estimated cure rates of 53 per cent with localised tumours, 19 per cent with lymph node involvement and 32 per cent overall (Hoffman, C., 1993, op cit, p47).

6 Cause of Breast Cancer

Despite years of scientific endeavour, the basic cause of breast cancer remains unknown. There are some risk factors which have been established as being associated with increased incidence of breast cancer. It should be emphasised, however, that about 80 per cent of women presenting with breast cancer between ages 30-54 and 70 per cent of women aged 55-84 had diagnoses which could be attributed to one or more risk factors.[41] Thus around three quarters of women with breast cancer have no established risk factors.

Risk factors

Established major risk factors for developing breast cancer include: age, family history of breast cancer, prior breast cancer, benign breast disease, endogenous endocrine[42] factors such as age at menarche (onset of menstruation), age at birth of first child and age at menopause, and radiation exposure. Proposed or unresolved risk factors include exogenous hormone exposure such as oral contraceptive use and oestrogen replacement therapy and environmental factors including diet.[43]

Age

No single factor is as important as age in determining a woman's risk of developing breast cancer. As mentioned previously, the relative risk of developing breast cancer increases with age. Women in their 20s and 30s do develop breast cancer, but breast cancer is relatively uncommon before menopause. According to American data, the risk that a 30-year-old women will have breast cancer is 7 per cent that of a 60-year-old woman. By 35, the ratio begins to change with the average 35-year-old having 20 per cent the risk of a 60-year-old of developing breast cancer. In addition, from age 35, the constellation of other risk factors (see below for details) may in fact increase the risk of an individual woman to above that of the average 60-year-old.[44]

Family history

After age, a family history of breast cancer in either the maternal or paternal line most increases the risk of a woman developing breast cancer. Most cancers (around 80 per cent), however, occur in women with no family history of breast cancer. The relative risk of developing breast cancer increases most substantially

41 Henderson, I., 1993, op cit, p2138.

42 Endocrine factors are those controlled primarily by hormonal function. Reproduction and growth are two examples of human physiology mediated primarily by hormones.

43 Henderson, I., 1993, op cit, p2128 and Hoffman, C., 1993, op cit, p50.

44 Henderson, I., 1993, op cit, p2127.

in line with the number of affected first degree relatives; mother, sister, daughter, father, brother or son. Breast cancer in one first degree relative is associated with a two-fold increase in risk. Breast cancer in two or more first degree relatives increases the risk further, perhaps even four to six fold. Bilateral breast cancer in a first degree relative increases this risk further; a woman with a sister who has had bilateral breast cancer before age 50 has a lifetime cumulative risk of developing breast cancer which is greater than 50 per cent. This risk would increase further if the sister was affected before age 40.[45]

Prospective epidemiologic studies indicate that approximately 8 per cent of women in the general population have at least one first degree relative with breast cancer. Nearly 14 per cent of patients with breast cancer report a family history of the disease; family history is thus an important factor in breast cancer risk.[46]

Two general modes of inheritance of susceptibility to breast cancer have been identified. The first involves direct inheritance of a gene/genes/genetic defect which increases risk. The second involves familiar aggregation of inherited susceptibility which is modified by environmental factors.

At least half of so-called genetic breast cancer cases are thought to involve the BCRA1 (Breast Cancer 1) gene. This gene was first implicated in 1990 in association with a specific genetic defect on chromosome 17 which increases the risk of breast cancer, ovarian cancer and perhaps other cancers.[47] Recently, scientists have shown that women who carry the BCRA1 gene have an 87 per cent chance of developing breast cancer and a 44 per cent chance of developing ovarian cancer by age 70.[48] Screening tests enabling detection of this gene in women at risk (ie. those with a strong family history of breast cancer) should soon be available, although any such testing would need to be combined with organised and comprehensive counselling as there are no studies of survival rates in women who undergo procedures such as prophylactic double mastectomy.

Breast cancer occurring in women with a family history of the disease does NOT have a worse prognosis than breast cancer occurring in other women. In fact, some studies suggest that there might even be better prognosis in these patients when all genetic and familial factors are considered.[49] Women with a family history of breast cancer do, however, tend to develop the disease at an earlier age.

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45 Hoffman, C., 1993, op cit, p49.

46 Vogel, V. et al., 'Clinical management of women at increased risk for breast cancer', *Breast Cancer Research and Treatment*, 28, 195 - 210, 1993.

47 Cowley, G., 'Family Matters', *Bulletin*, pp 58 - 63, December 7, 1993; Henderson, I., 1993, op cit, pp 2127 - 2128; Thompson, L., 'The Breast Cancer Gene: a woman's dilemma', *Time (Australia)*, p26, January 17, 1994.

48 Lancet, March 18 1994.

49 Henderson, I., 1993, op cit, p2128.

Prior breast cancer

A diagnosis of breast cancer, even after surgical removal of the cancer, increases the risk of subsequent breast cancer development. This risk is estimated at 0.5 - 1 per cent per year for the other breast when the diagnosis is of an invasive cancer. A similar risk is estimated for in situ carcinomas and for the ipsilateral (original) breast tissue if a complete mastectomy was not carried out.[50] There is, however, a dearth of studies in this area and current opinion is that the increased risk is neither sufficient argument for initially performing radical mastectomy nor for bilateral prophylactic mastectomy. It should also be pointed out that the development of two breast cancers, whether concomitantly or sequentially, does not necessarily mean a worse prognosis as survival rates for breast cancer are determined primarily by the size and type of cancer.

Benign breast disease

Benign breast disease has been regarded as a risk factor for breast cancer for many years. Recent evidence, however, has shown that it is not the number of biopsies for benign breast cancer that a women undergoes which is associated with increased risk for breast cancer, but whether the biopsy indicates proliferative changes or atypical hyperplasia.[51] Around 50 per cent of all patients who have biopsies show proliferative changes; the risk for these patients is moderate (around 2). However, the risk for the approximately 7 per cent of patients who show proliferative changes with atypical hyperplasia is more significant - around 4.4 - and if these patients have a family history of breast cancer the risk may be as high as 8.9.[52]

Endogenous hormone factors

There has been considerable research examining the role of hormones and women's reproductive cycle in relation to risk for developing breast cancer. Unfortunately the findings are of no real comfort to the twentieth century woman who desires to pursue a career before having a family somewhat later in her reproductive history. Well recognised hormonally related risk factors for breast cancer include early menarche (onset of menstruation before age 12), late menopause (after 55), longer menses (more than 30 years), older age at time of first full term pregnancy and having fewer children.[53]

Early menarche is a relatively weak risk factor; women who menstruate before age

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50 Henderson, I., 1993, op cit, p2129.

51 Hoffman, C., 1993, op cit, p49.

52 Henderson, I., 1993, op cit, p2130. The relative risk for all patients who have biopsies is around 1.5, the risk for patients with nonproliferative changes around 0.9 and the risk for patients with atypical hyperplasia but no family history about 3.5.

53 Hurley, S., 1993, op cit, p22.

12 have a relative risk of 1.5.[54] The time at which a woman establishes a regular ovulatory cycle may be more important. The relative risk of breast cancer occurring in a woman who has a regular ovulatory cycle before age 13 is almost four times that of a woman who first menstruates after 13 and who takes approximately five years to establish regular ovulation.[55] Late menopause is also a relatively minor risk factor (relative risk around 2). However, total duration of menstruation is a more substantial risk factor; women who menstruate for more than 30 years are at substantially higher risk. It should be emphasised, however, that no study has examined the effects of artificially induced early menopause on breast cancer risk and the risks associated with either long menses or late menopause may be outweighed by the adverse effects of early menopause.

Both the number of pregnancies a woman has and her age at the time of first full-term pregnancy are also important determinants of relative risk. A woman whose age at first birth was less than 19 has approximately 50 per cent of the risk of a nulliparous (woman who has not born a child) woman. Women whose first full-term birth was between 30 - 34 have approximately the same risk as a nulliparous woman and women who first give birth after 35 have an increased risk when compared to nulliparous women.[56]

Reasons for these observations are unclear. It is obvious that these factors are becoming increasingly important as women delay the birth of their first child in order to pursue careers. There is some evidence to suggest that pregnancy permanently changes a woman's hormonal (endocrine) function. However, this does not explain the protective factor incurred by an early first birth and negated by a first pregnancy after 34. Studies do indicate that the time between menarche and first pregnancy is crucial for the occurrence of events related to risk of developing breast cancer. Furthermore, it has been suggested that the number of ovulatory cycles before a first pregnancy determine a woman's lifetime risk of developing breast cancer. This hypothesis has not yet been convincingly proved. It does, however, provide an explanation of the increase in breast cancer incidence experienced only by girls and young women exposed to atomic bomb blasts in Japan.[57]

Radiation exposure

There is growing evidence that there is a relationship between radiation exposure and breast cancer development. Japanese women and girls exposed to the atomic bomb blast, women treated with radiotherapy for mastitis and patients who had multiple fluoroscopies for tuberculosis have been shown to suffer an increased incidence of breast cancer.[58] Radiation exposure seems to have a ten year

[54] Hoffman, C., 1993, op cit, p49; Hurley, S., 1991, op cit, p22.

[55] Henderson, I., 1993, op cit, p2131.

[56] Henderson, I., 1993, op cit, p2131.

[57] Henderson, I., 1993, op cit, p2131; Hurley, S., 1991, op cit, p22.

[58] Hurley, S., 1991, op cit, pp 22 - 23.

latency period and also seems to most affect women aged less than 35.

Exogenous and environmental factors

A large number of other factors have been investigated in relation to breast cancer, including a high fat diet, high socioeconomic status, alcohol consumption, oral contraceptive use, oestrogen replacement therapy and pesticide exposure. The evidence in relation to many of these factors is equivocal. However, the most important and contemporary of these will be discussed briefly.

Oestrogen

The association between risk of developing breast cancer and various aspects of the female reproductive cycle have prompted investigations into endogenous oestrogens in breast cancer. Oral contraceptives and hormone replacement therapy have been the major targets of research. Unfortunately, the results of studies into both types of preparations have produced contradictory and equivocal results.[59]

Post-menopausal oestrogen therapy

Oestrogen used in post-menopausal hormone therapy has become one of the most widely used drugs amongst American women (around 32 per cent usage amongst women aged 50 - 65 years) and there are indications that Australian usage will be of a similar order. Early case-control studies showed a clear increase in breast cancer risk, other studies indicated no increase and still others a decreased risk.[60] Methodological factors contributing to difficulties encountered by researchers include the high association between socioeconomic status and ethnic group and both risk of developing breast cancer and post-menopausal oestrogen use. Women of high socioeconomic status are more likely to use hormone replacement therapy and to develop breast cancer. The validity of exposure estimations and recall bias also are factors potentially obscuring the results of studies. The results of prospective studies have shown relative risk values from 0.4 to 1.7 for women who had ever used oestrogen post-menopausal, 1.3 to 2.5 for women currently using oestrogen and 0.9 to 1.4 for women who had used oestrogen in the past.[61] Results concerning duration of use are also inconclusive; some studies indicate no effect of duration of use, others an increase of relative risk with increased duration of use. A meta-analysis[62] of case-control studies assessing risk after post-

[59] Brinton, L.A. and Schairer, C., 'Estrogen replacement therapy and breast cancer risk', *Epidemiologic Reviews*, 15, 66 - 79, 1993.

[60] Henderson, I., 1993, op cit, p2131.

[61] Brinton and Schairer, 1993, op cit, p69.

[62] A meta-analysis of other studies involves combining studies and analysing their findings on the basis of the results published. Thus, such an analysis does not use the original raw data and is limited by the reliability and detail of the results published in the studies included in the

menopausal oestrogen use reported the following relative risk ratios:

Table 4: Relative risk of developing breast cancer in women after post-menopausal oestrogen use[63]

Group	Relative risk
All women, any use	1.0
> 15 years exposure	1.3
Family history of breast cancer	3.4
No family history of breast cancer	1.5
Nulliparous	1.5
Parous	1.3
Benign breast disease	1.7
No benign breast disease	1.4
Age at first pregnancy	
<20	1.1
20-30	1.1
>30	1.7

There has also been no conclusive evidence that there is a dose-response relationship between oestrogen use and breast cancer development risk.[64] Higher doses of oestrogen do not seem to be associated with an increased risk. The use of post-menopausal oestrogen replacement therapy has been shown to increase the risk of endometrial cancer. However, interspersing progestins with the oestrogen returned the risk to normal. There is some concern that progestins may also increase the risk of breast cancer.[65]

As a result of these studies, there appears to be a clinical view that oestrogens should be avoided in women with a past history of breast cancer. However, there is no conclusive evidence to support this strategy. Indeed, recent evidence suggests that the converse may be true. Survival rates for women given tamoxifen which has both anti-oestrogen and oestrogen like effects, or diethylstilboestrol (a non-steroidal oestrogen-like compound) were equivalent and greater than placebo in a recent clinical trial. Overall, in view of the documented beneficial effects of

analysis.

63 Henderson, I., 1993, op cit, p2132.

64 Brinton and Schairer, 1993, op cit, p71.

65 Henderson, I., 1993, op cit, p2133.

hormone replacement therapy, especially in relation to heart disease and osteoporosis, in post-menopausal women, it would seem premature to discard oestrogens on the basis of the somewhat inconclusive and confusing data currently available concerning increased breast cancer risk.[66]

Oral contraceptive use

The association between oral contraceptive use and breast cancer has received as much attention as that between oestrogen replacement therapy and breast cancer risk. The results are also conflicting and inconclusive. Some studies suggested an increased risk for women who had taken oral contraceptives for four or more years before age 25 or their first full-term pregnancy.[67] Other, more recent studies have been less conclusive; the meta-analysis shown below illustrates the conflicting and often contradictory nature of the data.

Table 5: Relative risk of developing breast cancer in women who have used oral contraceptives[68]

	Relative risk
All cases, all ages	
Case control studies (n=27)	1.06
Duration of use ≥ 10 years	1.14
Cohort studies (n=5)	1.06
Cases occurring in woman aged ≤ 45 years	
Any use	1.17
Duration of use ≥ 10 years	1.46
Before first full-term pregnancy	
Duration of use ≤ 1 year	1.07
Duration of use ≥ 4 years	1.72
Duration of use ≥ 4 years after 1980	1.73

66 Bluming, A., 'Hormone replacement therapy: benefits and risks for the general postmenopausal population and for women with a history of previously treated breast cancer', *Seminars in Oncology*, 20, 662 - 674, 1993.

67 Hurley, S., 1991,op cit, p23.

68 Henderson, I., 1993,op cit, p2134.

Overall, the data seem to indicate that risks of developing breast cancer associated with oral contraceptive use are small. The proviso seems to be that prolonged use of oral contraceptives in young women before their first full-term pregnancy should be considered to contribute a significantly increased risk and patterns of use should be monitored accordingly.

Environmental factors

Dietary fat

There is compelling evidence, largely resulting from ethnic incidence studies,that environmental factors are important in the development of breast cancer. Meta-analysis of twelve case-control studies has suggested that dietary factors account for 24 per cent of breast cancer incidence in post-menopausal women and 16 per cent in pre-menopausal women.[69] Dietary fat has received particular attention. However, even in this area, the research has provided conflicting results. Laboratory studies suggest that rats fed a high fat diet have a higher risk of mammary cancer. Other studies indicate that a low-calorie diet even with a high fat content is protective compared to a high fat diet. In addition, clinical studies indicate that women with the highest fat intake have the lowest risk of breast cancer. International correlation studies also provide conflicting results; Japanese and Chinese women who have the lowest breast cancer incidence around the world also have low fat diets. At this stage resolution of this issue seems unlikely, particularly since the chances of a successful clinical trial of Western women adhering to substantial dietary fat restrictions for a prolonged period seem small.

Alcohol

Concern has also been expressed about the relationship between alcohol consumption and risk of developing breast cancer. This relationship has been investigated in more than twenty cohort and case-control studies, most of which show increased risk for drinkers versus non-drinkers, and a dose-response relationship.[70] A meta-analysis of four cohort studies has also shown a strong correlation between increased relative risk of developing breast cancer and increased daily consumption of alcohol. In addition, there is evidence that the alcohol a woman consumes before age 30 is most important in determining breast cancer risk.[71] Overall, relative risk is put at approximately 1.5 for drinkers versus non-drinkers. It should be noted, however, that there is great potential for other factors such as diet and lifestyle to influence the results of studies comparing non-drinkers with heavy drinkers and thus caution should be exercised when interpreting this finding.

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69 Henderson, I., 1993, op cit, p2136.

70 Hurley, S., 1991, op cit, p23.

71 Henderson, I., 1993, op cit, p2136.

Environmental pollutants

One of the most controversial questions in relation to environmental exposure and risk of developing breast cancer concerns pollutants, particularly the organochloride pesticide DDT. DDT is now banned in Australia and in many western countries. However, DDT is highly fat soluble and thus may accumulate in a number of body tissues, including the breasts, testes and brain, all of which have an high fat content. Recent evidence that women with breast cancer have higher than normal blood levels of DDE, a metabolite of DDT,[72] has given substance to the so-called xenoestrogen hypothesis: the idea that the rise in breast cancer incidence might be explained by increasing environmental levels of fat-soluble synthetic chemicals that mimic or amplify the effects of oestrogen. Laboratory studies have shown that some pollutants such as DDT and PCBs[73] do mimic the actions of oestrogen in activating the oestrogen receptor and promoting breast cell division, as occurs at puberty and also with tumour formation.[74] In addition, there is growing concern regarding the role of carcinogenic dietary contaminants. Since the 1960s there has been recognition that carcinogenic organochlorine pesticides such as aldrin, dieldrin, chlordane and heptachlor accumulate in animal and human fat. Such substances have also been shown to induce breast cancer in rodents.[75] Oestrogens used as growth hormone supplements in feedlot animals have also come under fire as a possible cause of the increased incidence of breast cancer.[76] To date, the most persuasive evidence has come from the study mentioned above showing that women with increased blood levels of DDE had four times the risk of developing breast cancer compared to women with lowest DDE levels. However, many scientists argue that the evidence for a role in breast cancer for DDT or any other environmental pollutant is too preliminary to justify any action. Furthermore, they argue that the laboratory studies have only shown that DDE and other substances bind to oestrogen receptor, not that they induce the same biological effects in humans. It is also the case that women manufacture far greater concentrations of oestrogen themselves than they could ever absorb from environmental contaminants, and the evidence from the oral contraceptive and oestrogen post-menopausal replacement therapy studies show only a small increased risk of developing breast cancer.[77] The National Cancer Institute in the U.S.A. has commissioned a study examining the cancer risk of farmers and their spouses, as this group are most likely to have experienced extensive occupational exposure to environmental pollutants. Other researchers will continue to examine the role of environmental pollutants in mimicking oestrogen physiologically in the hope that they might find an answer. However, the issue remains a contentious one and is

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72 Beardsley, T., 'A war not won', *Scientific American*, January 1994, pp 118 - 126.

73 PCBs were used in a wide range of applications including pain and electrical transformers. PCBs were never manufactured in Australia and their importation is now banned. Gradual phasing out of the use of these substances is currently taking place.

74 Watson, T., 'Breast cancer's deadly masquerade ?', *U.S. News & World Report, February 7, 1994*, pp 59 - 60.

75 Epstein, S., 'Breast cancer and the environment', *The Ecologist*, 23, 192 - 193, 1993.

76 Epstein, S., 1993, op cit, p192.

77 Watson, T., 1993, op cit, p60.

likely to require many more years of scientific endeavour before resolution.

The issue of the role of environmental pollutants in breast cancer is of particular interest to women's groups who feel that, of the risk factors identified to date, it is one possible contributing risk factor that women would be able to change without compromising their quality of life and lifestyle.

7 Breast Cancer in Men[78]

Breast cancer is relatively rare in men and the problem has not received much media or research attention. The cancer usually presents in the form of a lump or nipple discharge. Most male breast cancers are in situ cancers and are histologically indistinguishable from female in situ breast cancers. Around 87 per cent of male breast cancers respond to oestrogen (compared to about 60 per cent of female cancers).[79]

The incidence of breast cancer in males is around 100 times lower than in females. Incidence increases sharply after 35 years of age with the median age for detection about 67 years. Mortality also increases with age although there has not been any increase in either incidence or mortality rates over the last twenty to thirty years as there has been with female breast cancer.[80]

The strongest risk factor for developing breast cancer in men is Klinefelter's syndrome, a condition resulting from the inheritance of an extra X chromosome. Sufferers have approximately 20 times the risk of developing breast cancer than men with one X chromosome and around one fifth of the risk of women. However, Klinefelter's syndrome accounts for only a small proportion of breast cancers in men. Other risk factors identified in case control studies of breast cancer in men include undescended testes, congenital inguinal hernia, mumps as an adult and a range of other unverified factors. Family history also seems to play a role in breast cancer risk in men with similar relative risk ratios observed between the two sexes when first degree relatives are affected.[81]

In the absence of hormonal factors known to affect the risk of women developing breast cancer (eg. age at first pregnancy, length of menses), the investigation of breast cancer in men may well provide information as to previously undetected aspects of breast cancer aetiology.

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[78] For a comprehensive review of breast cancer in men see Thomas, D., 'Breast Cancer in Men', *Epidemiologic Reviews*, 15, 220 - 231, 1993.

[79] Thomas, D., op cit, 1993, p220.

[80] Thomas, D., 1993, op cit, pp 221 - 222.

[81] Thomas, D., 1993, op cit, pp 222 - 227.

8 Control of Breast Cancer

Mortality from breast cancer may be reduced by prevention of the disease, earlier diagnosis and better treatment or by absolute cure.

Treatment of breast cancer

Despite many years of effort, there is no universal panacea for cancer and no absolutely successful and reliable means of treating breast cancer. Medical research has made significant advances. Notably, in association with earlier detection of breast cancer have come improvements in treatment such that women do not necessarily face the prospect of losing their breast once diagnosed.

Surgery remains the mainstay of breast cancer treatment. Over the past twenty years there has been a move away from radical mastectomy towards more conservatives procedures such as simple mastectomy and lumpectomy. This shift has not, however, changed mortality or survival rates. A number of randomised clinical trials have shown that more conservative surgical procedures result in equivalent mortality and survival rates to radical surgery[82] and thus potential for survival improvement must be sought elsewhere. Reports from some Australian sources indicate that breast conservation is possible in some 45 per cent of cases.[83]

Small in situ and small invasive cancers without lymph node involvement seem to have proven to be the most successful candidates for conservative surgery.[84] Many practitioners recommend the addition of radiotherapy to breast conservation surgery; "After breast conserving operations the incidence of further malignancy in the breast is between 30 and 40 per cent, without radiotherapy. Radiotherapy will reduce this incidence to around five per cent."[85] International studies indicate that survival rates associated with conservative procedures with or without radiotherapy are equivalent to that obtained with radical mastectomy.[86]

Whilst more conservative surgery has not altered survival rate it has dramatically improved the treatment options for women as the potential for their breast to be conserved may have an enormous positive psychological benefit. Unfortunately, breast conservation is not always possible; a large lump in a small breast may

82 Fisher, B. et al., 'Ten year results of a randomised clinical trial comparing radical mastectomy and total mastectomy with or without radiation', *New England Journal of Medicine*, 312, 674 - 681, 1985; Fisher, B. et al., 'Eight year results of a randomised clinical trial comparing total mastectomy and lumpectomy with or without radiation in the treatment of breast cancer', *New England Journal of Medicine*, 320, 822 - 828, 1989.

83 Malycha, P., 'Treatment options for breast cancer', *Australian Family Physician*, 22, 35 - 39, 1993.

84 Malycha, P., 1993, op cit, p35.

85 Malycha, P., 1993, op cit, p38.

86 Hoffman, C., 1993, op cit, p50.

prevent a good cosmetic result; conversely, large breasts may be surgically more suitable for conservative surgery but the accompanying radiotherapy may prove more troublesome. In addition, there is the problem for women in rural or poorly serviced areas that access to post-operative radiotherapy facilities is so limited as to necessitate a significant delay in their return home after surgery and thus these women may opt for a mastectomy to overcome the need for radiotherapy.[87] As a result of recent claims that there is a lack of treatment facilities serving Western Sydney, the New South Wales government has ordered a review of radiotherapy services.[88] One other problem is the anecdotal report that less well-informed doctors, particularly in remote areas, do not know or recognise the equivalent success rates associated with more conservative surgical procedures and do not offer their patients this option.

Adjuvant therapy[89], particularly the use of systemic cytotoxics or hormonal drugs such as tamoxifen[90], has proved effective in reducing mortality, although the gains have been small. More than 100 randomised trials of various substances have been reported. A relatively recent overview of these trials concluded that adjuvant systemic therapy can delay breast cancer recurrences and improve survival.[91] However, the gains are small; tamoxifen therapy in women aged 50 and over was associated with an improvement in five-year survival from 67.7 per cent to 73.3 per cent.[92] Questions concerning the cost-effectiveness and benefits of such small gains abound therefore, and scientists continue to actively pursue more successful therapies.

Primary Prevention

It would obviously be preferable to prevent breast cancer from ever occurring. Indeed, the international variances in breast cancer incidence suggest that there should be great potential for implementing a primary prevention program based on

87 Malycha, 1993, op cit, p38.

88 Cook, D., 'Shake-up for breast cancer treatment', *The Sydney Morning Herald*, 17 March 1994, p5.

89 Adjuvant therapy is usually chemical therapy given *in addition to*, rather than instead of, radiotherapy and/or surgery. It is not the prime treatment but an important accompaniment.

90 Tamoxifen is the most commonly used endocrine agent in breast cancer treatment. It has demonstrated an overall positive response rate in 30 to 35 per cent of patients and is well tolerated with few side effects, a relatively uncommon occurrence in cancer chemotherapy. Tamoxifen has both oestrogen like and anti-oestrogen effects. It is no more successful than high dose oestrogen treatment in breast cancer therapy, however, it has markedly fewer side effects. The most worrisome side effect associated with tamoxifen use is an increased risk of endometrial cancer. The exact mechanism of action of tamoxifen is unknown (Eden, J., 'Oestrogen and the breast. 1. Myths about oestrogen and breast cancer', *The Medical Journal of Australia*, 157, 175 - 177, 1992).

91 Early Breast Cancer Trialists' Collaborative Group, 'Effects of adjuvant tamoxifen and of cytotoxic therapy on mortality in early breast cancer', *New England Journal of Medicine*, 319, 1681 - 1692, 1988.

92 Hurley, S., 1991, op cit, p24.

the differences so observed. The reality is, however, that understanding of the aetiology of breast cancer is still far from sufficient to enable even the most basic of primary prevention programs. In addition, the identified risk factors - long menses, late first pregnancies, oral contraceptive use - are such that any modification of their impact would require a total change in the life and lifestyle of the average woman in industrialised countries. Dietary modification may prove useful in the long term, but the evidence is still less than persuasive currently. There is interest in the concept of preventative chemotherapy for women at greatest risk of developing breast cancer and a large clinical trial examining the potential of tamoxifen in this capacity is under way. The difficulties faced by this trial are enormous, as recruiting and follow-up of sufficient numbers of potentially high risk women will require many years, especially since statistical estimates indicate that at least 16 000 women and 10 years follow-up will be required to even come close to indicating whether tamoxifen will be useful prophylactically![93]

Breast cancer may be avoided by prophylactic mastectomy and some women with a strong family history of breast cancer or with benign breast disease have apparently taken this step.[94] However, as mentioned there have been no thorough investigations of the long term effects of this strategy and it is certainly not one which will ever become a general means of control. In the absence of suitable and effective means of primary prevention, secondary prevention, or early detection is the next most viable alternative and one which has demonstrated a reasonably high degree of success.

Secondary Prevention

In the face of an absence of means to prevent breast cancer, other strategies have been examined in worldwide efforts to reduce mortality from this disease. One of the most widely implemented methods is to improve detection of breast cancer so that treatment can be implemented earlier in the natural history of the disease. Three general methods have been investigated - breast self-examination (BSE), clinical examination of the breast (CE) by a qualified practitioner (nurse or doctor) and mammography.

Breast self-examination and clinical examination

Neither breast self-examination nor clinical examination have been examined in clinical trials as extensively as mammography. However, studies have indicated that patients who practice breast self-examination and attend regular clinical examinations may have better prognosis that patients who don't.[95] However, despite evidence that the incidence of axillary lymph node involvement and tumour size greater than 2 cm was lower in patients who practised breast self-examination

93 Henderson, I., 1993, op cit, p2137; Hurley, S., 1991, op cit, p23.

94 Cowley, G., 1993, op cit, p58; Hurley, S., 1991, op cit, p23.

95 Hill, D. et al., 'Breast self-examination: is it beneficial?', *British Medical Journal*, 297, 271 - 275, 1988.

compared to those who did not,[96] no difference in survival rate has been demonstrated between the two groups in other studies.[97] A World Health Organization study involving 90 000 women has also shown that the average tumour size in women who practised breast self-examination was 1.3 cm less than in women who did not.[98] There do not appear to have been any trials examining the efficacy of clinical breast examination in improving tumour detection.

Overall, medical acceptance of breast self-examination as a useful technique to improve breast cancer detection is good. The American Cancer Society recommends that all females aged 20 and over should practise breast self-examination monthly, all females aged 20 - 40 should have a clinical breast examination every three years and those over 40 every year.[99] The Society also recommends that all females aged 40 - 49 have a mammography every one to two years and all women 50 or over every year. Australian authorities recommend that all women over the age of 35 should be encouraged to practice breast self-examination on a monthly basis.[100] There are concerns, however, that breast self-examination may contribute to the 'overtreatment' of breast lumps in women, particularly those aged less than 35. The WHO has not endorsed breast self-examination as an effective means of reducing breast cancer mortality, partly because of these concerns and also because of the lack of studies on acceptability of, and compliance with long term breast self-examination programs.[101] Data from NSW and Australian studies provide some evidence that concerns about compliance and awareness of the usefulness of breast self-examination and, indeed clinical examination and mammography, are justified:

96 Hill, D., 1988, op cit, p271.

97 UK Trial of Early Detection of Breast Cancer Group, 'First results on mortality reduction in the UK Trial of Early Detection of Breast Cancer', *Lancet*, ii, 411 - 416, 1988.

98 Australian Cancer Society, 1993, op cit, p47.

99 American Cancer Society, 'Recommendations on Breast Self-Examination, Clinical Breast Examination and Mammography', *CA-A Cancer Journal for Clinicians*, 42, 44 - 45, 1992.

100 Australian Cancer Society, 1993, op cit, p47.

101 Australian Cancer Society, 1993, op cit, p46.

Table 6: Frequency of breast self-examination (BSE), clinical breast examination (CE) and mammography in Australian women[102]

National Health Survey 1989-90						
	Age-group					
	18-24	25-34	35-44	45-54	55-64	Total
BSE	48.8*	61.7	68.7	68.4	67.0	62.9
CE	47.1	73.4	78.9	78.9	74.1	70.8
Mammography						
in last 3 years	2.6	6.4	16.7	25.4	19.5	13.2
not tested ever	65.5	72.5	63.4	52.4	53.7	63.0
not heard of	31.2	18.1	14.8	14.7	18.2	19.2

* percentage of respondents replying in the affirmative; over five million women participated in the survey.

More detailed analysis of the data in terms of age, marital status, child-bearing status, ethnic background and place of residence provides further insights concerning those women most likely not to carry out breast self-examination or attend regular clinical examinations or screening mammography. This information is contained in the table following:

[102] Australian Bureau of Statistics, March 1993, op cit, p62.

Table 7: Frequency of breast self-examination (BSE), clinical breast examination (CE) and mammography in Australian women, separated by age, marital status, motherhood and ethnic background[103]

Group of Women									
	All	Women without children		Women with children		60-64	Non-English speaking background	Urban	Other
		18-24 not married	18-34 married	Married	Single				
BSE	62.9	46.3	60.6	66.4	60.4	65.6	55.6	61.0	67.3
CE	70.8	42.4	70.1	77.0	72.1	72.8	59.6	70.5	71.6
Mammography < 3 years ago	13.2	2.2	4.4	11.5	10.2	18.2	12.5	13.7	12.0

The results of these surveys indicate that younger women are less likely to practice BSE or have CE or a mammography and also that a significant number of Australian women of all ages are not even aware of what a mammography is let alone how it may help save their lives. Of further concern is the relatively lower proportion of women from non-English speaking backgrounds who practice BSE and attend a regular clinical examination. NSW data provide similar insights:

Table 8: Frequency of breast self-examination (BSE), clinical breast examination (CE) and mammography in NSW women[104]

National Health Survey 1989-90, NSW Respondents				
	Age group			
	18-39	40-49	50-64	Total
BSE	61	71	68	65
CE	66	81	77	72
Mammography	11	35	34	21

[103] Australian Bureau of Statistics, March 1993, op cit, pp 61-62; 82.

[104] Australian Bureau of Statistics and NSW Department of Health, 1993, op cit, pp 65 - 67.

Overall, only 28 per cent of women in NSW aged 40 - 49 and only 23 per cent of those age 50 - 64 had had a mammography in the last three years. There were also variations across health areas and regions.

Obviously from this data a lot needs to be done in terms of improving the awareness of all Australian women concerning the importance of practicing breast self-examination and having regular clinical examinations. It should be noted, however, that the results of this survey pre-date much of the recent activity publicising breast self-examination and also the National Screening program for Breast Cancer. It could be expected therefore that a significant proportion of women who had not heard of mammography and who did not practise breast self-examination in 1989-90 might have changed their habits or knowledge since.

Mammography

There have been a number of extensive trials examining the efficacy of mammography in reducing breast cancer mortality. The results of these trials have been very encouraging; two studies - one in America and one in Sweden - demonstrated approximately 30 per cent reduction in breast cancer mortality at eight to ten year follow-up.[105] Other studies have not demonstrated such convincing mortality reductions[106], however, meta-analysis of a number of studies suggests that mammography does have a worthwhile role to play in reducing breast cancer mortality,[107] particularly for women over the age of 50.[108] As a result of international studies, Australia implemented a series of pilot screening programs during 1984-89. The Breast Cancer Screening Evaluation Steering Committee of the Australian Health Ministers Advisory Council recommended in 1990 that a National Early Detection Program for breast cancer, based on mammography, be implemented. The Commonwealth Government acted upon this recommendation and the National Program was phased in in late 1990.[109]

Questions still remain, however, concerning the cost-effectiveness of a mammographic screening program, the women who should be targeted for screening and the relative health care burden. The Australian Cancer Society supports the screening of women aged over 50 years, but not for women aged 40 - 49. Currently, in NSW, women over the age of 40 are entitled to a free mammogram annually, although the screening program does specifically target older women. A detailed analysis of the cost-effectiveness of mammographic screening in Australia concluded that "screening for women aged 50 to 69 every two to three years is reasonable value for money. For women aged 40 to 49 the mortality and

105 Australian Cancer Society, 1993, op cit, pp 47 - 49.

106 Hoffman, C., 1993, op cit, p50.

107 Carter, R. et al., 'Cost-effectiveness of mammographic screening in Australia', *Australian Journal of Public Health*, 17, 42 - 50, 1993.

108 Australian Cancer Society, 1993, op cit, p50.

109 Australian Cancer Society, 1993, op cit, p50; Hurley, S., 1993, op cit, p24.

cost-effectiveness is less clear"[110]. The same study concluded that screening for women over 50 was more cost-effective than for women aged under 50. Reasons for this difference lie both within the incidence of breast cancer and the nature of mammography. Those most at risk from developing breast cancer are post-menopausal women, aged 50 - 65. In addition, the breast tissue of younger women is more fibrous and dense than that of older women making mammography less accurate; ultrasonagraphy is preferred in women under 30.[111]

In the bigger picture, however, mammography is relatively cost effective and beneficial. If a comparison is made of the cost/utility effectiveness of mammography on a two yearly basis for women aged over 40 (assuming a baseline of no current screening) compared to other programs, the results suggest that mammography is certainly within the standards of other health programs and may in fact be more cost effective:

Table 9: Comparison of cost per life year of various medical and hospital procedures[112]

Program	Adjusted cost per life year (1988-1989 $ prices)
AIDS treatment with zidovudine	130 000
Hospital dialysis	47 789
Cervical cancer screening	30 782
Breast cancer screening	6 600 - 11 000
Nondrug blood pressure clinic	5 000
Neonatal intensive care, babies < 801g	3 600 - 4 600
Kidney transplant	4 596
Neonatal intensive care, babies 1000 - 1500g	1 200 - 3 000
Sydney Quit Smoking Campaign	16

110 Carter, R., 1993, op cit, p42.

111 Parkyn, R., 'Discovering a breast lump. Management plans and pitfalls', *Australian Family Physician*, 22, 43 - 46, 1993.

112 Carter, R., 1993, op cit, p49.

There is also evidence to suggest that problems such as the lower compliance of women from non-English speaking backgrounds may be successfully tackled via community health programs, such as the Women's Health Nurse program, which are already up and running.[113]

[113] A recent study of a Sydney Area Health Service showed that there was a significant increase in the number of non-English background speaking women who practiced breast self-examination and had a mammography after their initial visit (Barclay, L. et al., 'A study of the service provided by the Women's Health Nurses in a Sydney Area Health Service', *Australian Family Physician*, 22, 2016 - 2023, 1993).

9 Research and Funding for Breast Cancer in Australia

There has been much media attention recently to the relative lack of research funding for breast cancer in comparison to other diseases.

Federal government funding for medical research via the National Health and Medical Research Council program allocated around $1.4 million for breast cancer research this year. This amount compared with $16 million for heart disease, $12 million for AIDS, $5 million for asthma and $2 million for mental health research.[114]

Premier John Fahey recently announced the allocation of $1.5 million for the establishment of a Breast Cancer Institute in NSW. In addition, the NSW Cancer Council has allocated $1.4 million over a five year period for breast cancer research, a large proportion of which supports breast cancer research at the Garvan Institute in Sydney.

The National Screening Program, which is funded by combined Federal, State and Territory resources, costs approximately $64 million. The NSW Health Department formally assigned responsibility for the implementation of the NSW program to the NSW Cancer Council in November 1992. Funds are transferred to the Cancer Council on a monthly basis for this project. Since this time, three new Screening and Assessment services have been established and the two established services expanded. The existing services are located in the Hunter region, Central Eastern Sydney, Western Sydney, Northern Sydney, North Coast and New England. Planning is also underway for the establishment of further services in Southern Sydney and South West Rural NSW.[115]

Concern has been expressed recently regarding the comparative lack of research funding for breast cancer in relation to other diseases, especially when the relatively high mortality figures associated with breast cancer are considered. Whilst it is true that more Australian women die each year of breast cancer than cases are diagnosed of AIDS, it is difficult to make comparisons regarding research funding for these diseases on such a global basis. Of more salience perhaps are comparisons looking at the cost of a disease in terms of years of potential life lost. On that basis, it could be argued that AIDS is at least as destructive as breast cancer and more destructive than heart disease.[116] It is also the case that other diseases such as prostate cancer are equally as virulent as breast cancer and are allocated substantially less funding.[117]

It should also be remembered that "no one can possibly know which research funds will save lives because no one can predict where or when breakthroughs

[114] National Health and Medical Research Council, Research Funding Grants 1994-95.

[115] NSW Cancer Council, *Annual Report 1992 - 1993*, pp 30 -31.

[116] Nulty, P., 'Where all that AIDS money is going', *Fortune*, February 7, 1994, pp 91 - 92.

[117] Senator Graham Richardson, *AM*, Tuesday 22 February 1994.

might come ..."[118] The critical problem is not the lack of specific funds for breast cancer research but the overall lack of medical research funding in Australia and the relative lack of priority given by all Australian governments to redressing this problem. The consequences of this deficiency do not just limit medical research capacity in all areas including breast cancer, but also impact upon the health of all Australians and the economic future of our country.

10 Conclusion

Breast cancer is a significant public health problem which potentially will impact upon the lives of all Australians. There is currently no means of preventing breast cancer and treatment relies upon early detection for greatest success. All Australian women should be encouraged to take responsibility for protecting themselves against breast cancer mortality by performing regular monthly breast self-examination, having regular clinical breast examinations and, if over the age of 50, having a yearly or two yearly screening mammogram. It is to be hoped that in the very near future advances in medical science will provide a means to prevent or completely cure breast cancer. In the meantime, physicians, patients and the community need to ensure that all that can be done is done to improve the care and prognosis of breast cancer sufferers.

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[118] Nulty, P., 1994, op cit, p92.

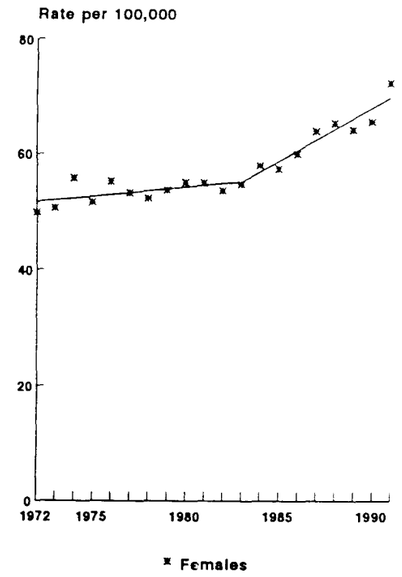
Appendix 1

Breast Cancer Incidence and Mortality in NSW 1991

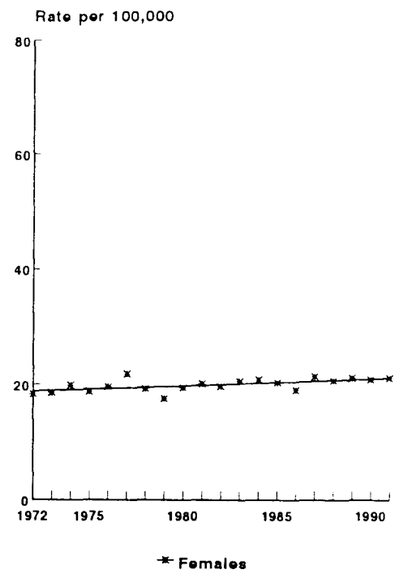
from Cancer Council *Cancer in New South Wales Incidence and Mortality 1991*

BREAST CANCER

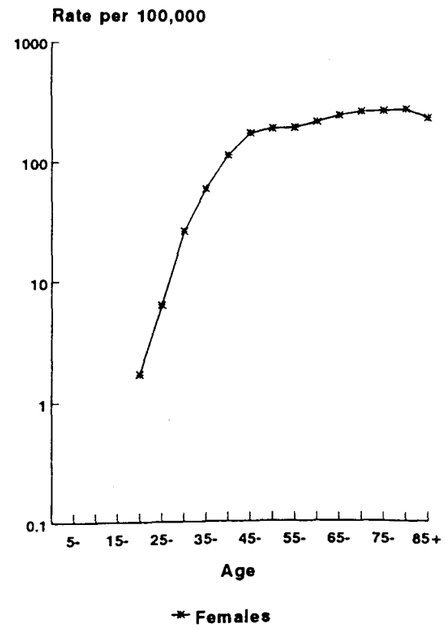
Age-standardised incidence, NSW



Age-standardised mortality, NSW



Age-specific incidence, NSW, 1989-91



Age-specific mortality, NSW, 1989-91