Effectiveness and cost-effectiveness of screening mammography in women over 70 years of age

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1 Summary

BreastScreen Australia offers screening mammography to women over 40 years of age, with an explicit policy of targeting women in the age range 50-69 years. Women who have been participating in regular screening while in their 60s may continue to be invited to screening well into their 70's. BreastScreen Australia has been in operation now for nearly 10 years so there are increasing numbers of women in this situation. At present there is no national policy on the age at which screening should cease, or the age at which regular invitations should cease. This report examines the balance of benefits and harms, and the resource implications, of continuing to screen women past 70 years of age.

Because of the scarcity of trial data on the effectiveness of screening in older women, we systematically searched for and reviewed decision analytic and cost-effectiveness models of mammographic screening in older women. Six relevant models were found which estimated the benefit of screening as a gain in life expectancy, with or without adjustment for the effect of screening, testing and treatment of breast cancer on quality of life.

Comparison of these models revealed substantial variation in the estimates of benefit. However, the models are consistent in finding only small gains, ranging from less than one day of life up to 20 days of life gained on average per woman screened. To help interpret these results we calculated the benefit of screening among women over 70 years of age relative to the benefit experienced by women aged 50-69 years. These results suggest a mortality benefit of screening mammography in older women, which in women aged 70-79 years ranges from 40% to 72% of the benefit in women aged 50-69 years, and which diminishes with increasing age. With adjustment for the impact on quality of life, the benefit ranges 18% to 62% of that seen in women 50-69 years. For women over 80 years the relative benefit is smaller, ranging from an estimated 32% to 39% without quality of life adjustment, and at an estimated 14% with quality of life adjustment.

There are many possible harms of screening in older women. In particular, because the benefit of mammographic screening is delayed, reduced life expectancy and high competing causes of death in older women mean that older women are likely to experience the downsides of screening [discomfort, anxiety, side-effects of tests and treatment] but may not live long enough to experience the benefit. Diagnosis of low grade cancer, for example DCIS, is particularly likely to result in net harm as it is most unlikely to impact on mortality within the lifespan of older women.

In hypothetical cohorts of 10,000 Australian women participating in on-going screening, approximately 9600 women are reassured they do not have cancer, approximately 400 are recalled for further testing, up to 112 undergo biopsies [depending on age] and up to 80 cancers are detected [depending on age].

Cost-effectiveness estimates of extending the upper age limit for mammography screening from 69 years to 79 years range from $8,119 to $27,751 per Quality Adjusted Life Year Saved. Cost-effectiveness is similar to extending the program to include women aged 40-49 years.

Some groups of older women are more likely to experience benefit from screening than others. Women who are more likely to experience net benefit are those who:

- Are at high risk of death from breast cancer [because of family history, previous breast cancer or presence of other risk factors such as high bone mineral density]
- Are at low risk of death from other causes, such as cardiovascular disease or other cancers
- Perceive themselves to be in good health
- Attach a high value to avoiding death from breast cancer and are not bothered by the prospect of false positive screening test results or of being diagnosed and treated for breast cancer.

Assessment of whether the benefit of continuing screening is likely to outweigh the harms is likely to be highly dependent on the value(s) individual women attach to participation in screening and the consequences of screening. If mammographic screening is extended to women in their 70s and older, at minimum good information materials are needed so that these women can make an informed choice about whether to continue screening.

2. Background and methodological issues

2.1 Introduction

BreastScreen Australia offers screening mammography to women over 40 years of age, with an explicit policy of targeting women in the age range 50-69 years. Women who have been participating in regular screening in their 60s may continue to be invited to screening well into their 70's. BreastScreen Australia has been in operation now for nearly 10 years and there are increasing numbers of women in this situation. At present there is no national policy on the age at which screening should cease, or the age at which regular invitations should be ceased. This report examines the balance of benefits and harms, and the resource implications, of continuing to screen women past 70 years of age.

2.2 Breast cancer incidence and mortality: how much mortality benefit is screening likely to achieve in women over 70?

Breast cancer incidence and mortality

Breast cancer incidence and mortality increase steeply with age. In Australia, in 1996 the age-specific incidence was 112, 247, 293 and 313 per 100,000 women aged 40-44, 50-54, 60-64 and 70-74 years respectively. In women aged 75-84 years the incidence was 306 per 100,000 and declined to 270 per 100,000 in women aged 85+ years[1].

Mortality rates from breast cancer in 1996 were 21, 47, 74, and 92 per 100,000 for women aged 40-44, 50-54, 60-64 and 70-74 years respectively. In women aged over 74 years breast cancer mortality continued to rise to 117, 146 and 197 per 100,000 for women aged 75-79, 80-84 and 85+ years respectively[1]. Therefore, there may be a large benefit to be gained for an individual woman in her 70s by continuing screening because the older she becomes the greater her risk of dying from breast cancer.

Mortality benefits achieved by screening mammography

Breast cancer screening has been shown to decrease mortality from breast cancer in randomized controlled trials which recruited women between the ages of 40 and 74 years, with most women recruited being aged between 45 and 65 years of age. Meta-analysis of the 8 available trials yields a relative risk reduction of 23% [95% confidence interval 13%-31%][2] after 7-12 years of follow-up for women aged 50-74 years at recruitment. A smaller benefit is seen for women aged less than 40-49 years at recruitment; relative risk reduction 15% [95% confidence interval +1% - 29%].

Only the Swedish Two County study recruited women over 70 years of age [70-74 years at recruitment] and found a [non-significant] relative risk reduction of 21% [RR 0.79, 95% confidence interval 0.51-1.22] in this age group[3]. However, analysis of women aged 65-74 years at recruitment gives a statistically significant relative risk reduction of 32% [RR 0.68, 95%CI 0.51-0.89][4]. Chen et al[4] note that the benefit of screening demonstrated in the Two County study for women aged 50-64 years is approximately 1.9 breast cancer deaths averted for every 1,000 women screened. In women in the 65-74 year age group the comparable figure is 2.2 per 1,000. They argue that the more modest relative risk reduction seen in women aged 70-74 [0.79] compared to women aged 65-69 [0.58] is due in part to lower participation by older women in screening [86% in the trial in women 65-69 years and 77% in women 70-74 years]. They conclude that for older women [up to 74 years] who request screening there is still a substantial benefit despite the competing risks from other causes of death.

Observational data

As there are no other experimental data available, observational data [from cohort studies and case-control studies] might be used to estimate the relative risk reduction attributable to mammographic screening in women over 70 years of age. We identified a small number of observational studies of the effectiveness of screening mammography. This comprised five cohort studies, the UK trial of early detection[5] the Breast Cancer Detection Demonstration Project[6], two Finnish studies[7,8], a cohort study in San Francisco[9] and five case-control studies, the DOM project[10], case-control studies in Nijmegen[11,12] and Florence[13], the case-control component of the UK trial of early detection[14] and a small case-control study in North Carolina[15]. Of these, three studies were designed to look at the effect of screening in older women but did not compare results with those observed in younger women[9,11,15]; one study included women over 70 and reported age-specific results for women 50-59 years and women 60-79 years[6] [See Box].

Observational studies that have enrolled older women are generally supportive of a beneficial effect of screening mammography in older women. However, observational studies are likely to be affected by bias, particularly lead time bias, in which screening appears effective because the cancer is detected earlier and therefore survival appears to be increased even in the absence of any benefit from screening. Case-control studies of screening are susceptible to additional biases including selection bias [arising from the methods used to select cases and controls] and measurement error [mainly inaccurate or inappropriate estimates of exposure to screening][16].

Observational studies of the effect of screening mammography in older women

Smith-Bindman et al 2000[9]

Design: Retrospective cohort study

Participants: 690,993 women aged 66-79 years living in San Francisco

Exposure and outcome measures: Women were classified as regularly participating in screening or not according to Medicare records, and the incidence of breast cancer in the groups compared.

Results: In situ, local and regional breast cancer were more common in screened women [RR 3.3, 95% CI 3.1-3.5], whereas metastatic disease was less common [RR 0.57, 95%CI 0.45-0.72].

[Note: no comparative data with younger women were published in this paper]

Van Dijck et al, 1996a[11]

Design: Case-control study

Participants: Women aged over 64 years living in Nijmegen, Netherlands

Exposure and outcome measures: History of regular participation in screening or a history of no screening extracted from computer records of the screening service. Cases were women who had died of breast cancer between 1977 and 1994; 5 age matched controls selected from population for each case.

Results: Rate ratios:

Women 65-92: 0.56 [95%CI 0.28-1.13]

Women 65-74: 0.45 [95%CI 0.20-1.02]

Women 75-92: 1.05 [95%CI 0.27-4.14]

[Note: no comparative data with younger women were published in this paper]

Brown and Hulka 1988[15]

Design: Case-control study

Participants: 309 women aged 60-90 years, resident in North Carolina diagnosed with metastatic cancer of the breast [102] or other organs [207] with diagnoses registered in the Duke Tumor Registry.

Exposure and outcome measures: Screening histories were established from medical and radiology records and compared between those with breast and other cancers.

Results: Only 18 of the 309 women had ever been screened. Adjusted odds ratio 0.73 [0.25-2.14] for women who had ever been screened.

[Note: no comparative data with younger women were published in this paper]

Morrison et al 1988 [BCDDP][6]

Design: Prospective cohort study

Participants: 283,222 women aged 50-74 at recruitment

Exposure and outcome measures: Annual mammography and breast examination for five years; breast cancer mortality after 9 years.

Results: Observed to expected mortality ratio was 0.76 for women 50-59 at entry and 0.74 for women 60-74 at entry.

Given the paucity of trial and observational data available to estimate the benefit of screening in older women, decisional analytic models have been developed to estimate the benefit of screening in this age group and to explore the effect of stopping screening at different ages. The decision analytic approach has the advantage of being able to explore the impact of varying the assumptions used to create the model. For example, the impact of screening on life expectancy can be estimated and then re-calculated with utilities to include the effect of changes in quality of life that might result from attending screening, being recalled and having follow-up tests and treatment. The impact of other factors, such as the effect of discounting future benefits and costs, or of varying mortality rates [for breast cancer and all cause mortality] can also be examined. This report is therefore largely based on the available decision analytic and cost-effectiveness models. The models are described, appraised and summarised in Sections 3 and 4 of this report.

2.3 Impact of declining life expectancy and competing causes of death on benefits of screening for older women

Declining life expectancy complicates the assessment of interventions in elderly people, particularly if the effect of the intervention is delayed [as in mammographic screening] as there is a rapidly increasing chance participants will not be alive to experience the benefit. Therefore, it is more useful to express the benefit of the intervention in terms of its effect on life expectancy rather than as a relative [or absolute] mortality reduction.

Life expectancy is the average remaining lifetime [in years] for persons who survive to that age. Life expectancy varies in different populations and can be calculated from national data sources [census data, mortality data]. As a rough guide, life expectancy for Australian and US women is given in Table 1. The data in Table 1 are Australian routinely collected data [column 2 of Table 1 from ABS 3302.0 1998[17]] and US research data which give life expectancy estimates in

age bands not only for average health women but also for women with mild and severe comorbidity [columns 4-6 of Table 1, from Mandelblatt 1992[18]].

Table 1: Life expectancy [in years] for Australian women, and for US women with and without comorbidity

Age:-	All women [Australia, 1998]*	Age:-	Average health [US women]**	Mild hypertension [US women]**	Congestive Heart Failure [US women]**
69	16.8	65-69	16.9	15.2	9.3
74	13.0	70-74	13.4	12.3	8.1
79	9.7	75-79	10.3	9.6	6.8
84	7.0	80-84	7.7	7.3	5.6
85	6.5	85+	6.6	6.3	5.0
89	4.9				

** ABS Deaths Australia 1998 Catalogue No 3302.0[17] p 69*

*** From Mandelblatt et al, 1992[18]*

As shown in Table 1, people who are below average health have shorter life expectancies. People who report themselves to be in good health generally live longer, and therefore self-reported health status can be a useful predictor of life expectancy[19]. Table 2 shows the association between self-reported health and life expectancy. For example, a 70 year old woman who claims to be in excellent health has the life expectancy of a 65 year old woman. Conversely, a 70 year old woman who reports she is in poor health has a life expectancy, approximately, of a 77 year old woman.

Table 2: Estimated "life expectancy age" based on chronological age and self-reported health status [from East Boston Senior Health Project, cited Welch 1996[19]]

	Self-reported health status			
Age	Excellent	Good	Fair	Poor
65	60	64	66	72
70	65	69	71	77
75	70	74	76	82
80	75	79	81	85+

A closely related concept is that of competing causes of death. To work from the extreme situation, if breast cancer was the only cause of death and screening mammography reduced breast cancer mortality by 30% in women over 70, then it would keep 30% of these women alive for ever. However, breast cancer is only one of many causes of death; all other cancers and cardiovascular disease are responsible for the majority of deaths in elderly women. Therefore, any benefit in terms of reduced risk of death from breast cancer will be reduced in elderly women because of their high probability of dying from heart disease or other cancer before the benefit of screening mammography is achieved.

In summary, declining life expectancy and increasing risk of death from causes other than breast cancer reduce the chances of experiencing a benefit from screening mammography as women grow older. This means it is increasingly likely that the [immediate] harms of screening will outweigh the [delayed] benefits. In other words, there is a much greater risk for the individual elderly woman of experiencing net harm from screening than there is for a younger woman. In particular, we need to pay careful attention to harms arising from the detection and treatment of inconsequential disease.

2.4 Inconsequential disease in elderly women

Inconsequential disease[20] in relation to mammographic screening is breast cancer which is not destined to kill the affected woman because she will die first of another cause.

For example, consider an elderly woman who is screened and has DCIS [ductal carcinoma in situ] detected. Because DCIS progresses slowly (estimated mortality with treatment is 2-3% over 10 years[21]), any anxiety, pain or side effects she suffers as a result of the screen detected DCIS are unlikely to be offset by a mortality benefit within her expected lifespan. This is illustrated by the data in Table 3. These data show that a woman diagnosed with DCIS in her 40s has about an equal chance of dying of breast cancer over the next 8 years [on average] or of dying of something else. However, a woman diagnosed with DCIS in her 70's is about 8 times more likely to die of other causes [largely cardiovascular disease] than of breast cancer. More information about the impact of a diagnosis of DCIS is given in the next section.

To give another example, consider a woman who is diagnosed with invasive breast cancer by screening but who is very soon after killed by something else [perhaps a stroke, a hip fracture or a heart attack]. This is likely for elderly women because of their high risk of death from cardiovascular disease and other cancers. As for the woman with DCIS, any anxiety, pain or side effects she suffers from tests and treatment for her screen detected breast cancer are harms of screening which are not offset by any benefit.

Table 3: Age specific DCIS diagnosis and causes of death

Age at DCIS diagnosis	DCIS cases	Breast cancer death	Cardiovascular death	Other causes of death	All causes of death
40-49	1567	30	6	37	73
50-59	1743	21	20	92	133
60-69	1933	43	86	177	306
70-79	1829	51	302	428	781
Total	7072	145	414	734	1293
US data. From Ernster et al 2000[21]. All cases between 1978 and 1989 with follow-up to 1995; median length of follow-up 99 months					

In short, because elderly women are at high risk of death from another cause before the benefit of screening mammography can be experienced, harms from the detection of inconsequential disease, particularly DCIS, are likely to be very important when weighing up the benefits and harms of screening in this age group.

2.5 Anxiety, pain and side effects of tests and treatment

Screening attendance and abnormal mammography generate anxiety for women who participate in screening. The anxiety of screening attendance is generally short-lived, whereas the anxiety of being recalled for further tests can persist for months[22,23,24].

Elderly women are less likely to be recalled for further imaging or for biopsy after screening mammography than younger women. Kerlikowske et al[25] report that 1.4% of women over 70, having second round mammography screening, receive an abnormal mammogram report. This compares with 2.0%, 1.9% and 2.0% of women having second round mammography who are aged 40-49, 50-59 and 60-69 years respectively[26].

Because the incidence of breast cancer is higher in women in this age group, relatively more women aged over 70 whose mammogram is abnormal have breast cancer. Thus in older women the positive predictive value of screening mammography is higher and the false positive rate is a little lower than in younger women. Kerlikowske[25] estimates the positive predictive value at 7%, 16%, 7% and 22% [each estimate with wide confidence intervals] for women aged 40-49, 50-59, 60-69 and 70-79 years respectively attending second screening mammography[26].

Local Australian data[27,28] show recall rates are around 3-4% for women attending subsequent screening rounds and may decline slightly with age [Table 4]. Positive predictive values clearly improve with age.

Table 4: Recall rates and PPV for asymptomatic women attending subsequent screening rounds

	Recall rate* [VIC]	Recall rate* [QLD]	PPV** [VIC]	PPV*** [QLD]
40-49	4.8%	4.3	5.7%	3.6%
50-59	4.5%	4.1	8.3%	6.4%
60-69	4.2%	3.9	12.8%	10.5%
70-79	3.7%	3.9	15.3%	14.9%
80+	2.7%	3.9	20.0%	18.8%

** assessment recommended because of abnormal mammography only/all screened*

*** cancers detected among asymptomatic women / assessment recommmended for abnormal mammography*

**** all cancers detected / all recommended for assessment*

As for younger women, a proportion of older women who have breast cancer detected by screening will have DCIS. Like invasive cancer, the incidence of DCIS increases with age although DCIS as a proportion of all cancers detected tends to go down with age [Tables 5a and 5b].

Table 5a): DCIS as a percentage of all cancers diagnosed by age in women attending subsequent screening rounds

	40-49	50-59	60-69	70-79	80+
QLD	18%	21%	19%	18%	15%
VIC	32%	19%	18%	15%	~ *
** none detected*					

Table 5b) DCIS and invasive cancer detection rates per 1,000 women attending subsequent screening rounds [VIC data]

	40-49	50-59	60-69	70-79	80+
Invasive cancer	2.4	3.3	4.6	5.4	7.2
DCIS	1.1	0.8	1.0	0.9	~ *
** none detected*					

Mortality from DCIS is largely unknown: it has been estimated at 1.9% for screen detected DCIS and 3.5% for clinically detected DCIS over 10 years[21]. According to US Surveillance Epidemiology and End Results program data, there was a 300% increase in DCIS diagnosis between 1983 and 1992, co-incident with the introduction of mammographic screening in the US, with the greatest increase being seen in women over 50 years of age. As with invasive breast cancer, DCIS is commonly treated by mastectomy with apparently little variation by age, in the US at least, as shown in Table 6.

Table 6: Age-specific estimated numbers of DCIS newly diagnosed and treated by mastectomy in the United States, 1992 [SEER data, cited Ernster 1996[29]]

Age	Estimated N. DCIS	% Treated by mastectomy
30-39	1030	47.1
40-49	4920	45.6
50-59	5234	46.1
60-69	5971	42.4
70+	6130	41.3

The harms of screening will be compounded for elderly women who have screen detected cancers if there is increased morbidity and mortality associated with treatment for older people.

The main harms of treatment can be expected to relate to peri-operative mortality and morbidity, and any side effects of radiotherapy and chemotherapy.

Mortality rates for mastectomy are reported as 1.5% for women over 75 years [mean aged 81 years] and 0.5% for women under 75 [mean age 57 years] based on a large, representative 1990 sample[30]. [More recent or local estimates were not found in MEDLINE]. A review published in 1994 gives estimates of peri-operative mortality from mastectomy from 8 studies, all in elderly women, ranging from 0.2% to 4.5%[31]. SEER data [1967-1973] included in this review were 0.9% for 30 day postoperative mortality for women over 75 years, compared to 0.4% for all women.

Substantial post-operative morbidity has also been reported for between 7% and 20% of elderly women undergoing mastectomy. The major complications are reported to be related to the wound [eg infection, infection and necrosis requiring grafting[32]], and to neurologic and cardiovascular complications. Hunt et al report that operative morbidity is not significantly different in elderly compared to younger patients undergoing breast surgery, and that unlike abdominal and thoracic surgery post-operative pneumonitis and cardiovascular complications are rare following mastectomy. There are also complications of breast conserving surgery. There is a tendency for elderly women not to be offered post-operative radiotherapy, which results in higher local recurrence rates[31]. Finally, there are complications of axillary dissection; major complications, such are vascular or nerve damage in the axilla, are reported to be rare[31] but lymphoedema is common [reported range of occurrence after axillary dissection is 1.5-62.5% according to Morrow 1994[31]]. In a quality of life study, Velanovich[33] estimated that lymphoedema occurs in about 8% of women undergoing axillary lymph node dissection and results in major detrimental quality of life effects.

In terms of emotional and psychological effects, Fallowfield et al[34] report that women undergoing both mastectomy and breast conserving therapy have problems with anxiety and depression. They found that approximately 29% of women undergoing either mastectomy or lumpectomy were anxious 12 months later and approximately 20% were depressed. Wenzel et al [1999][35] found that older women [over 50 years of age compared to women aged less than 50 years of age at diagnosis] reported significantly less quality of life distruption; significant differences were seen in emotional well-being, breast cancer concern, depression and disease specific intrusive thought. Unfortunately they do not report the mean age or age range of the over 50 years age group.

Perioperative mortality and morbidity will become a smaller source of harm to the extent that a higher number of older women are offered [and choose] less aggressive surgery such as lumpectomy[36] or elect medical therapy such as tamoxifen only[37]. Limited treatment approaches such as lumpectomy with local irradiation and/ or tamoxifen are claimed to be well tolerated by the elderly[31,36,37].

2.6 Participation in screening by older women

As noted earlier the participation rates for women over 70 were lower than for younger women in the trials of mammographic screening. Age-specific attendance rates in the Two County study[38] are shown in Table 6.

Table 6: Attendance rates in the Two County Study[38]

Age	Estimated N. DCIS	% Treated by mastectomy
30-39	1030	47.1
40-49	4920	45.6
50-59	5234	46.1
60-69	5971	42.4
70+	6130	41.3

Other studies have also reported lower rates of attendance for older women. Smith-Bindman et al[9] report screening participation [defined as one screening mammogram in a two year period] as 50%, 48%, and 40% for women aged 66-69, 70-74 and 75-79 years respectively[9]. Likewise van Dijck et al[12] report rates of participation in second and subsequent screening rounds of the Nijmegen screening program of 67%, 55%, 39% and 15% for women aged 50-64, 65-69, 70-74 and 75+ years respectively[12]. Similar results have been reported in the UK[39].

Local, recent data are available and show a similar pattern. Participation rates [defined as women having one or more screening mammogram between Jan 97 and Dec 98 over the target population] were 10.6%, 56.5% and 28% for women aged 40-49, 50-69, and 70-79 years respectively in Victoria[27]. Comparable Queensland data are 28.5%, 52.4% and 29.4%[28].

3. Methods

As outlined in Section 2, there are few estimates of the effect of screening mammography available from either trials or observational studies. Therefore we decided to explore the available decision analytic models and cost-effectiveness models which have estimated the effects of mammographic screening in older women.

3.1 Literature review

Computerised searching

We conducted a systematic review of decision analysis and cost-effectiveness models examining the effectiveness of mammographic screening on mortality or life expectancy among elderly women.

The search strategy was as follows:
Exp mammography OR [exp breast neoplasms AND exp mass screening] AND
[Exp decision support techniques OR exp cost-benefit analysis] AND model.mp

The search strategy was applied to MEDLINE 1966 to present and was last conducted in January 2002.

This strategy retrieved 57 papers. Abstracts of all papers were reviewed and those that appeared relevant were obtained in full.

Other searching

In addition we

- Contacted the authors of all models published since 1995 [Black, Kerlikowske and Boer] and asked them whether they knew of any other published models. No new models were obtained in this way.
- Reviewed the reference lists of all the papers describing models.

3.2 Inclusion criteria

Inclusion criteria were:

- decision analytic or cost-effectiveness model of screening mammography
- model provides age-specific results for women over 69 years of age (and in younger women for comparison)
- results presented as gains in average life expectancy [with or without quality of life adjustment].

Applying these criteria reduced the accumulated papers to five models which are listed in Table 7.

Table 7: Models included in this review

Author[s]	Type of model	Age group studied
1. Rich & Black, 2000[40]	Decision analysis	65+
2. Kerlikowske et al, 1999[25]	Decision analysis and cost-effectiveness analysis	Up to 79
3. Kattlove H et al, 1995[41]	Cost-effectiveness analysis	Up to 74
4. Mandelblatt et al, 1992[18]	Decision analysis	65+
5. Eddy, 1989[42]	Decision analysis and cost-effectiveness analysis	Up to 75

A number of other models were found which we could not use because they did not provide benefits in terms of age-specific life expectancy gain per woman[41,42,43,44,45,46], or they did not provide data on women over 70 years of age[47], or they did not provide data on women under 70 years of age which we could use to calculate a relative benefit[48].

Other literature retrieved

In addition to this search for decision analytic and cost-effectiveness models we searched MEDLINE for information about observational studies of screening mammography in older women, breast cancer management and treatment by age, post-operative morbidity and mortality from mastectomy, screening harms in older women, and quality of life associated with breast cancer detection and treatment in older women.

Local data

For life expectancy data we contacted the Australian Bureau of Statistics for age specific life expectancy data for Australian women.

For local screening data we contacted all Australian state and territory co-ordination units and requested statistical reports. BreastScreen Queensland agreed to perform additional analyses for the balance sheets.

3.3 Critical appraisal

The papers identified in Table 7 were critically appraised according to the criteria outlined in Richardson et al[49] Users guides to the medical literature VII How to use a clinical decision analysis A: Are the results valid? The criteria were slightly modified, in particular to include the suggestion of Justice et al[50] that models should be assessed for their transportability between populations and that if valid, they should accurately predict events in populations other than the one in which the model was developed.

3.4 Calculation methods for estimates of impact on life expectancy

After reviewing the models it became clear that they varied widely in their methods, estimates of life expectancy benefit, and presentation of benefit. To provide a useful common outcome we decided to calculate the relative life expectancy benefit [and relative quality adjusted life expectancy benefit when available]. This was done by establishing a base benefit as the benefit predicted by the model for younger women [generally women aged 50-69 years]. The base benefit was obtained from either the paper reporting the model or from previous publications using the same model or modeling approach. The base benefit was calculated as the average benefit per 5 years or per 10 years [depending on the presentation of results] for women aged 50-69 years. In other words, we assumed a constant benefit over this age interval. Then the benefit seen in 5 and/or 10 year age brackets for older women was expressed as a percentage of the base benefit. In addition, we calculated the relative benefit for women aged 40-49 years [as a percentage of the same base benefit for women aged 50-69 years] for comparison. Details of the calculations are given in Appendix 2.

3.5 Estimates of consequences of screening for balance sheets

Data for the balance sheets were supplied by BreastScreen Queensland. Actual numbers of women who were screened, recalled, tested and diagnosed with cancer were supplied and were converted to rates per 10,000 women screened. All data are for asymptomatic women attending subsequent screening rounds. Data for women undergoing open biopsy include all women having open biopsy and may include some women having open biopsy as treatment.

4. Results

4.1 Critical appraisal of models of effectiveness of screening in women over 70

A summary of the critical appraisal is presented in Table 8. Bold typeface in Table 8 indicates the study met the relevant criterion.

In terms of methodological approach the models fall broadly into two groups: models which use an estimated relative risk reduction for screening in older women [Rich and Black[40], Kerlikowske[25] and Kattlove[41]] and models which use changes in stage distribution achieved by screening to model the impact on disease progression and mortality [Mandelblatt[18] and Eddy[42]].

Only two models included adjustment for the impact on quality of life caused by screening attendance, investigation in those who test positive and treatment for those who do have cancer. In one model [Kerlikowske[25]] quality of life adjustment was made only for those health states occurring after diagnosis of breast cancer [that is impact of diagnosis and initial treatment and impact of metastatic disease]. In the model by Mandelblatt[18] more extensive adjustment was done by including utilities for women who screened negative (for anxiety and discomfort of undergoing mammography) and women who experienced a false positive result (for anxiety, inconvenience and discomfort of biopsy).

Table 8: Critical appraisal of models [bold indicates criteria is met]

Study	Were all important strategies included?	Was an explicit and sensible process used to obtain probabilities?	Were the utilities obtained from credible sources?	Was the potential impact of uncertainty in the evidence determined?	How strong is the evidence?	Could the uncertainty in the evidence change the results?	Do the probabilities fit the Australian population?	Do the utilities reflect the values of Australian elderly women?
Rich & Black 2000[40]	**Screening from 50 versus no screening**	**Used US vital statistics and SEER cancer registry data to calculate life expectancies**	No quality of life adjustment.	No sensitivity analyses and no 95% confidence limits	**Assumes RRR is the same as in trials of women under 70**	Yes. Including harms is likely to affect the results	**Probably but incidence and mortality rates are higher in the US than in Australia.** Model not tested in any other population	Not applicable
Kerlik-owske et al 1999[25]	**Stop screening at 69 versus stop at 79 years**	**As for Rich and Black**	**Yes**	**Sensitivity analyses were done for varying discount rates, relative risk reductions and breast cancer mortality rates**	**Assumes range of RRR from 22% - 32%.**	Yes. Even before quality adjustment, number of days gained is small.	**As for Rich and Black**	Unknown. Uses utilities only for 2 states: life after treatment and life with metastatic disease
Katt-love et al 1995[41]	**Biennial screening to 74 years**	Data sources unclear	No quality of life adjustment	No sensitivity analyses done	**Used RRR from 2 County trial**	Yes	Not known	None used
Mandel-blatt et al 1992[18]	**Extending screening past 65 years compared to no screening for women with and without co-morbid conditions**	**Stage shift model based on US data**	**Yes**	**Yes Sensitivity analyses for quality of life, incidence, peri-operative death, sensitivity/ specificity of test, and stage distribution**	**Stage distribution and stage specific survival data.**	Yes	Not tested in other populations or trials	Unknown. Utility data based on US women aged 50-74 years
Eddy 1989[42]	**Screening for women over 40 versus no screening**	**Stage shift model based on SEER, BCDDP and HIP data**	**No quality of life adjustment**	**Only sensitivity analysis was inclusion of discounting of 5%**	**Based on stage and survival data + trial data**	Yes	Model applied to UK and Malmo trial data and predicted greater than observed declines in mortality [model assumes annual screening, 100% compliance and life time follow-up]	No utilities used

4.2 Relative effects of screening in women over 70 on life expectancy and quality adjusted life expectancy

Tables of the inputs and results of each study can be found in Appendices 1 and 2. The key results are presented in Table 9a) and Table 9b). Because the estimated life expectancy benefit varied widely between studies the relative benefit is shown. For example, for the Rich and Black model, if we regard women in the base group [women 50-69 years] as experiencing 100% benefit from mammographic screening, then women 70-74 years will experience about three quarters of that benefit, and women 75-79 years will experience about half the benefit. In Table 9b) similar information is presented for quality adjusted life expectancy where available. For example, from Kerlikowske's study we estimate that women aged 69-79 years will experience about 40% of the benefit experienced by women 50-69 years old, but when quality of life adjustment is made we estimate that older women experience only about 18% of the benefit experienced by the younger women.

From Tables 9a) and 9b) it seems likely that there is a mortality benefit of screening mammography in older women, which in women aged 70-79 years is approximately one-third to two-thirds that seen in women aged 50-69 years, and which diminishes with increasing age. For women aged approximately 70-79 years the relative benefit ranges from an estimated 40% to 72% without quality of life adjustment, and from an estimated 18% to 62% with quality of life adjustment. For women over 80 years the relative benefit is smaller, ranging from an estimated 32% to 39% without quality of life adjustment, and is estimated at 14% with quality of life adjustment.

The relative effects of screening mammography for women in the 50-69 and 70+ age group are compared with the relative effect in the 40-49 year age group in Table 10. Unfortunately such data were only available from two studies[25,42], and only one[25] provides quality adjusted data.

Table 9a) Summary of relative effects of screening in women over 70 – based on life expectancy gains without quality adjustment

	Rich & Black[40]	Kerlikowske[25]	Kattlove[41]	Mandelblatt[18]	Eddy[42]
Base group	50-69 year olds	50-69 year olds	50-69 year olds	65-69 year olds	55-65 year olds
Age-specific relative benefits compared to base group*	70-74 75% 75-79 54% 80-84 39% 85+ 25%	69-79 40%	70-74 33%	70-74 83% 75-79 61% 80-84 45% 85+ 32%	65-75 78-90%
Average relative benefit* for 69-79 age group	65%	40%	NA	72%	NA
Average relative benefit* for 80-89 age group**	32%	NA	NA	39%	NA
Outcome used	Life expectancy without discounting	Life expectancy with 3% discounting	Life expectancy without discounting	Life expectancy without discounting	Life expectancy with 5% discounting

Table 9b) Summary of relative effects of screening in women over 70 –*with quality adjustment*

	Rich & Black[40]	Kerlikowske[25]	Kattlove[41]	Mandelblatt[18]	Eddy[42]
Base group	50-69 year olds	50-69 year olds	50-69 year olds	65-69 year olds	55-65 year olds
Relative benefit*	NA	69-79 18%	NA	70-74 76% 75-79 48% 80-84 24% 85+ 4%	NA
Average relative benefit* 69-79	NA	18%	NA	62%	NA
Average relative benefit* for 80-89*	NA	NA	NA	14%	NA
Measure	NA	Quality adjusted life expectancy with 3% discounting	NA	Quality adjusted life expectancy without Discounting	NA

Table 10: Relative benefits of screening women in older age groups compared with women in the 40-49 year age group

Kerlikowske[25]			Eddy[42]	
Age group	Without quality adjustment	With quality adjustment	Age group	
40-49	42%	37%	40-49	67-80%
50-69	100%	100%	55-65	100%
70-79	40%	18%	65-75	78-90%

4.3 Combining estimated life expectancy benefits with local screening data to display the benefits and harm of screening: balance sheets for screening mammography in older women

The benefits and harms of screening for older Australian women are summarised and compared with the benefits and harms expected for Australian women aged 50-69 years in Balance sheet 1. Comparable data for women aged 40-49 years are provided in balance sheet 2.

As noted in Section 3.2 [Methods] the data for the balance sheets are from BreastScreen Queensland. We note that there is some variability in state and territory BreastScreen services; for example, recall rates, numbers and types of assessment procedures and cancer detection rates all differ to some extent in different services. A detailed comparison of state and territory data is beyond the scope of this report. However these variations should be acknowledged and readers should be aware that the data in the balance sheets are illustrative rather than precise estimates.

Balance sheet 1: Consequences of screening for women over 50 years [per subsequent screening round]

No. of women having…..	50-69 years	70-79 years	80+ years
Screening mammogram	10,000	10,000	10,000
Recall for assessment	418	409	401
Imaging tests [mammography and/or ultrasound]	417	407	401
Biopsy*:-	85	112	87
Fine needle biopsy	47	61	44
Core biopsy	41	50	36
Open biopsy	33	43	36
Cancer detected:			
All:-	37	65	80
Invasive	29	54	66
DCIS	8	11	15
Benefit			
Relative life expectancy	Base rate set at 100%	40-72%	32-39%
Relative quality adjusted life expectancy	Base rate set at 100%	18-62%	14%

** Number of women undergoing biopsy of any kind. The sum of individual biopsy procedures is greater because some women have more than one biopsy.*

Balance sheet 2: Consequences of screening for women under 50 years [per subsequent screening round]

No. of women having…..	40-49
Screening mammogram	10,000
Recalled for assessment	451
Imaging tests	450
Biopsy*:	70
Fine needle biopsy	44
Core biopsy	30
Open biopsy	22
Cancer detected:	
All :-	19
Invasive	16
DCIS	3
Relative life expectancy benefit base set to 50-69 years: Kerlikowske[25] base set to 55-65: Eddy[42]	 42% 67-80%
Relative quality adjusted life expectancy benefit base set to 50-69 years: Kerlikowske[25]	 37%

** Number of women undergoing biopsy of any kind. The sum of individual biopsy procedures is greater because some women have more than one biopsy.*

4.4 Cost-effectiveness of screening mammography in women over 70

Cost-effectiveness estimates for extending mammography screening to women aged 70-79 years has been calculated using QALY (Quality Adjusted Life Years) estimates based on the Dutch MISCAN model[43]. This model includes estimates of health effects and social costs of the primary process of screening, changes in diagnostic procedures, primary therapies, follow up treatment, metastatic disease, terminal illness and breast cancer mortality when a two yearly screening program is carried during a period of 27 years, after which time the maximum impact of screening on mortality is reached. The model

assumptions which are specifically relevant for screening in older women are summarised in Appendix 1.

Two variants of the cost-effectiveness model are presented, an *optimistic model*, which assumes no further increase in preclinical duration (sojurn time) after the age of 65. The *pessimistic variant* assumes a further increase in preclinical duration with age which is extrapolated from the trend in younger age groups[43].

The QALYs in the model are discounted at an annual rate of 5% and costs have been converted from Euro dollars to Australian dollars. The conversion of Dutch cost per QALY estimates to Australian currency provide ballpark estimate of the marginal cost-effectiveness [see Box for a description of marginal analysis] of extending biennial screening for women aged 50 to 69 years to 50 to 79 years. Patterns of health service utilisation and health costs are likely to be different between countries but this is unlikely to have a substantial impact on the direction and magnitude of the cost-effectiveness ratios.

Sorting out average, incremental and marginal costs and benefits

The most common question confronting decision-makers is typically 'how much more or less of something should we do'? Translating this question to resource allocation in breast cancer screening, the question becomes 'what are the costs and benefits of extending breast cancer screening to women aged 70 to 79 years'? It is a matter of ***changes*** in the scale of an activity. These ***changes*** are described as incremental or marginal. As Drummond[51] notes, the terms are often used interchangeably in the literature, but they infer different scales of change.

An ***average cost effectiveness ratio*** is calculated by dividing the total cost of screening by a measure of the total effectiveness (such as life years saved), without regard to its alternatives.

The term ' ***incremental'*** is used to describe the ***difference*** (in cost and/or effect) between screening and not screening. An ***incremental cost-effectiveness ratio*** is estimated by calculating the ***additional (or difference in)*** costs and benefits of a screening program compared to a situation without screening (for women aged 70 to 79 years).

The term '***margin***' refers to the addition costs or benefits of producing one extra unit of output, or as Drummond[46] suggests, to the *next logical batch of output*. For example, the current upper limit for screening women for breast cancer may be 69 years. We may want to know the ***marginal cost-effectiveness*** of extending screening to include women aged 70 to 79 years.

Table 11. The Marginal Cost per QALY (discounted at 5%) of extending mammography screening from 50 years of age to older women.[a]

Screening extended to women aged	Optimistic model Cost per QALY	Pessimistic Model Cost per QALY
73 years	$6,788	$18,374
75 years	$7,342	$20,754
77 years	$7,708	$23,620
79 years	$8,119	$27,751

[a] The base case, from which all comparisons are made, is assumed to be two yearly screening, starting at age 50 years and ending with the last invitation to screen at age 68. No base year has been assumed by Boer for the cost per QALY calculations.

From Table 11, we can say that the marginal cost effectiveness of extending the upper age limit for mammography screening from 69 years to 79 years, ranges from $8,119 to $27,751 per Quality Adjusted Life Year Saved. The range between these two point estimates

represents an assumption as to whether there is no further increase in preclinical duration after the age of 65 (optimistic model) and there a further increase in preclinical duration after the age of 65 (pessimistic model).

Table 12. The Marginal Cost per QALY (discounted at 5%) of extending mammography screening between age groups in women aged between 70 to 79 years

Age Group Screened	Optimistic model Cost per QALY	Pessimistic Model Cost per QALY
70 to 73 years	$7,156	$19,894
73 to 75 years	$8,817	$27,338
75 to 77 years	$9,174	$37,080
77 to 79 years	$10,565	$63,9581

The marginal cost-effectiveness of extending screening within the over 70 age group varies by a factor of between 3 to 6 fold in moving from the optimistic to pessimistic cost-effectiveness model. This reflects greater uncertainty about the size of the cost and the benefits as the upper age limit for screening approaches 80 years.

4.5 Resource implications of extending the screening program to women over 70

In section 4.3 the benefits and harms of screening for older Australian women were compared with the benefits and harms expected for Australian women aged 50-69 years.

In this section, the financial costs of the consequences of screening for women over 60 years (per subsequent screening round) are summarised. As was the case with the benefit and harm data, the financial information are illustrative rather than precise estimates.

The cost data used in the balance sheet summary are taken from two sources; a previous report for the NBCC on the 'cost of diagnostic investigations for women presenting with breast symptoms'[52] and unpublished cost data from the Central and Eastern BreastScreen program.

Table 13: Unit Cost data

Procedure	Unit Cost $	Source
Screening mammogram	90	NBCC report: Screening women aged 40-49 years
Recall for assessment Diagnostic Management 'A' Diagnostic Management 'B'	 108.35 per pt 61.35 per pt	NBCC report: Costs of diagnostic investigations
Imaging tests Mammography Ultrasounds	 40.41 76.26	NBCC report: Costs of diagnostic investigations
Fine needle biopsy	118.93	NBCC report: Costs of diagnostic investigations
Core Biopsy	153	Unpublished data: BreastScreen
Open Biopsy	1,338	AN-DRG V4

A = *Women who have symptoms indicative of a malignancy and require surgical intervention*

B = *Women who have symptoms that are not indicative of a malignancy and who are managed conservatively*

Financial Balance Sheet 1: Costs of screening for hypothetical cohorts of 10,000 women over 50 years of age [per subsequent screening round]

	50-69 $	70-79 $	80+ $
Screening mammogram	900,000	900,000	900,000
Recall for assessment	3,575 a 23,620 b	4,659 22,454	3,900 22,393
Imaging tests [mammography and or ultrasounds]	38,539	37,615	37,060
Fine needle biopsy	5,590	7,255	5,232
Core Biopsy	6,273	7,650	5,508
Open Biopsy	44,154	57,534	48,168
Total Cost	1,021,751	1,037,167	1,022,261
Cost per screenee	102.18	103.71	102.23

A =*Women who have symptoms indicative of a malignancy and require surgical intervention*

B = *Women who have symptoms that are not indicative of a malignancy and who are managed conservatively*

Financial Balance Sheet 2: Costs of screening for a hypothetical cohort of 10,000 women under 50 years [per subsequent screening round]

	40-49 **$**
Screening mammogram	900,000
Recall for assessment	2,383 [a] 26,319 [b]
Imaging tests [mammography and or ultrasounds]	41,589
Fine needle biopsy	5,233
Core Biopsy	4,590
Open Biopsy	29,436
Total Cost	1,009,551
Cost per screenee	100.95

As the results in the two financial balance sheets show, there is very little difference in the average cost of screening and diagnostic assessment by age group. The slightly higher cost per screenee in the 70-79 year age group reflects the higher rates of biopsy in this age group when compared to the 50-69 year age group.

5. Discussion

5.1 Impact of risk on balance of benefits and harms of screening in women over 70 who have a family history of breast cancer

Age-specific estimates of risk associated with a family history indicate that women over 50 years of age with a family history have approximately twice the risk of women the same age without a family history[53]. These data [based on a systematic review of 52 case-control studies and 22 cohort studies] are reproduced in Table 14.

Table 14: Pooled estimates of risk [95% CI] by age of subject and age of affected relative

Family history category	Subject age	
	< 50 years	>50 years
Any first-degree relative diagnosed:		
<50 years	3.3 [2.8-3.9]	1.8 [1.6-2.0]
> 50 years	1.8 [1.5-2.2]	1.7 [1.5-2.0]
Mother diagnosed:		
< 50 years	2.5 [1.6-3.8]	1.7 [1.1-2.6]
> 50 years	1.6 [1.1-2.3]	1.7 [1.2-2.4]
Sister diagnosed:		
< 50 years	3.3 [2.1-4.5]	1.8 [1.2-2.4]
> 50 years	3.0 [1.4-4.6]	[1.1-2.7]
Second degree relative	1.7 [1.4-2.0]	1.6 [1.3-2.0]

Therefore it is likely that the benefit of screening for older women with a family history will be about 1.5 to 2 times greater than that shown in the balance sheets, depending on the closeness and age of diagnosis of the affected relative[s].

5.2 Impact of co-morbidity on balance of benefits and harms of screening in women over 70

Women with a family history of breast cancer will, on average, experience a greater benefit from screening because of their greater risk of dying of breast cancer. Conversely, women who are at low risk of dying of breast cancer will, on average, experience less benefit from screening.

There are many ways of being at lower risk of death from breast cancer. One is by having a relatively high risk of death from another cause. Therefore we would expect that women with major comorbidities, such as a diagnosis of other invasive cancer or of cardiovascular disease, are less likely to experience benefit from mammographic screening.

This theoretical approach has some empirical support from a US study in which the impact of comorbidity on three year survival among women with breast cancer was assessed[54]. Women with 3 or more of 7 selected comorbid conditions* had a 20 times higher rate of death from causes other than breast cancer than women with no comorbid conditions. Women with one or two serious comorbid conditions had approximately 3 and 7 fold increases respectively in their risk of death from causes other than breast cancer. They conclude that among women with serious comorbid conditions early diagnosis of breast cancer confers no survival advantage. [*Comorbid conditions included were myocardial infarction, other types of heart disease, diabetes, other cancer, respiratory, gallbladder and liver disease. A further 11 comorbid conditions were assessed but were not independently associated with increased mortality and so were not included in the analysis.]

Other groups of women at relatively low risk of breast cancer death can also be identified. These include women with low bone mineral density; women in the lowest quartile of bone mineral density at the age of approximately 65 years have about a forty percent reduction in breast cancer risk[25].

5.3 Participation and comorbidity

Because of the relationship between comorbidity and risk of breast cancer death, and between increasing age and reducing participation in screening, we hypothesize that those who are least likely to participate in screening are in fact those least likely to benefit from screening. It therefore seems likely that allowing women over 70 to decide for themselves whether they feel well enough to attend screening may be a good proxy for individuals, and the program as a whole, to decide whether screening is worthwhile.

Women over 70 who are most likely to benefit from continuing to be screened are those who:

- Are at high risk of death from breast cancer [because of family history, previous breast cancer or presence of other risk factors such as high bone mineral density]
- Are at low risk of death from other causes, such as cardiovascular disease or other cancers
- Perceive themselves to be in good health
- Attach a high value to avoiding death from breast cancer and are not bothered by the prospect of false positive screening test results or of being diagnosed and treated for breast cancer

5.4 Values, preferences and consumer information

This analysis has shown that there probably is a benefit of mammographic screening for women over 70 that is approximately one-third to two thirds that seen in women 50-69 years of age. The benefit is less when adjusted for quality of life. Therefore women who are likely to be bothered by screening attendance, who will be made anxious by follow-up investigations and who will not easily tolerate treatment for breast cancer, or who have serious co-morbid conditions, will experience less benefit from screening. Conversely women at high risk of breast cancer death for whatever reason, or

who are not bothered by the prospect of screening, testing and treatment, have much more chance of experiencing net benefit from screening.

These considerations are highly individual and emphasise the need for informed, individual decision making. Choices will vary between women depending on their assessment of their individual risks, personalities, values and preferences.

Options for best helping elderly women deal with this decision include:

- Beginning a process of community informed consent[55] for continuing screening past 70 years of age. At minimum this would include community research to explore the values older women attach to screening and its consequences. This process has already been undertaken for women aged 40-49 years[56] and could be repeated with older women. The process could be extended by comparable work for women 50-69 years so that good age-specific utility data are available. This is important because it seems likely that the values women place on mammographic screening and its consequences may vary widely with age.
- Developing good consumer information materials, possibly including a decision aid, for women over 70 to help them understand the potential benefits and harms of screening and to clarify their own preferences in relation to those benefits and harms.
- Educating health professionals about the benefits and harms of mammographic screening for women of different ages so that they are in a position to help their patients clarify whether they wish to begin and continue screening.

5.5 Does extending mammographic screening to women over 70 represent value for money?

From an economic point of view, the central question is whether extending mammography screening represents value for money. This is a value judgement based on the relative (***marginal***) cost of achieving the health gain. One approach to answering this question is to compare the relative cost effectiveness of extending mammography screening for older women with an extension in the lower age range, to include women aged 40-49 years. Unfortunately, the data from the Boer report cannot be compared with Australian estimates of screening women aged 40-49 years. Nonetheless, we would expect the marginal cost of screening women from 40 to 49 years of age to be similar to screening older women because the additional benefit is about the same, the consequences of screening are similar, and costs should not differ by age.

6. Recommendations

Policy decisions about the age at which women should cease screening mammography should:

1. Be based on the available evidence which shows a probable mortality benefit. We estimate the size of the mortality benefit is in the range 40% to 72% of the benefit seen in women aged 50-69 years.
2. Recognise that the benefit will be greater for women who:
    - Are at high risk of death from breast cancer [because of family history, previous breast cancer or presence of other risk factors such as high bone mineral density]
    - Are at low risk of death from other causes, such as cardiovascular disease or other cancers
    - Perceive themselves to be in good health
    - Attach a high value to avoiding death from breast cancer and are not bothered by the prospect of false positive screening test results or of being diagnosed and treated for breast cancer.
3. Recognise that women who are at low risk of death from breast cancer, who have other major co-morbid conditions or who perceive themselves to be in poor health, or who are likely to be bothered and made anxious by screening, testing and treatment, are unlikely to benefit and may suffer harm as a result of screening.
4. Recognise that there are real and important harms of screening and accept that for many older women a choice to discontinue screening at around 70 years of age may be a good and rational choice.

5. Consider the development of supportive consumer information materials or a decision aid to help women choose when to cease screening.

6. Consider the development of supportive training or education for health practitioners to help them assist women in choosing when to cease screening.

Policy decisions about the age at which women should cease screening mammography could be better informed by:

1. A project to measure attitudes to the benefits and harms of screening mammography in women over 70 years, similar to that undertaken by Cockburn and Pit[51] in women 40-49 years. This could be extended to assess community consent for policies of screening mammography for women 40-49 years, 50-69 years and over 70 years.

2. A project measuring the utilities that Australian women aged 40 years and over attach to the full range of health states which can follow screening mammography. It is likely that these utilities will vary by age and will be extremely useful as, to our knowledge, relevant age-specific utility data have not been collected previously.

3. Using the utilities [obtained in the project described above] to rerun a model of screening mammography [such as that developed by Rich and Black[40]] to assess quantitatively the age-specific benefits of screening mammography using local incidence, mortality and utility data.

References

1. Australian Institute of Health and Welfare (1998). Breast cancer screening in Australia 1996-1997. Canberra, Australian Institute of Health and Welfare.

2. Kerlikowske K, Grady D, Rubin SM, Sandrock C, Ernster VL (1995). "Efficacy of screening mammography. A meta-analysis." JAMA **273**: 149-154.

3. Tabar L, Fagerberg G, Chen HH, Duffy SW, Smart CR, Gad A, Smith RA (1995). "Efficacy of breast cancer screening by age." Cancer **75**: 2507-2517.

4. Chen HH, Tabar L, Fagerberg G, Duffy SW (1995). "Effect of breast cancer screening after age 65." J Med Screening **2**: 10-14.

5. UK Trial of Early Detection of Breast Cancer Group (1999). "16-year mortality from breast cancer in the UK trial of early detection of breast cancer." Lancet **353**: 1909-1914.

6. Morrison AS, Brisson J, Khalid N (1988). "Breast cancer incidence and mortality in the Breast Cancer Detection Demonstration Project". J Natl Cancer Inst **80**:1540-1547.

7. Hakama M, Pukkala E, Heikkila M, Kallio M (1997). "Effectiveness of the public health policy for breast cancer screening in Finland: population based cohort study." BMJ **314**: 864-867.

8. Klemi PJ, Joensuu H, Toikkanen S, Tuominen J, Rasanen O, Tyrkko J, Parvinen I (1992). "Aggressiveness of breast cancers found with and without screening." BMJ **304**: 467-469.

9. Smith-Bindman R, Kerlikowske K, Gebretsadik T, Newman J (2000). "Is screening mammography effective in elderly women?" American Journal of Medicine **108**: 112-119.

10. Collette HJA, Day N, Rombach JJ, de Waard F (1984). "Evaluation of screening for breast cancer in a non-randomised study (the DOM Project) by means of a case-control study." Lancet **i**: 1224-1225.

11. van Dijck JAAM, Verbeek ALM, Beex LVAM, Hendriks JHCL, Holland R (1996a). "Mammographic screening after the age of 65 years: Evidence for a reduction in breast cancer mortality." Int J Cancer **66**: 727-731.

12. van Dijck JAAM, Verbeek ALM., Hendriks JHCL, Holland R, Mravunac M (1996b). "Mammographic screening after the age of 65 years: early outcomes in the Nijmegen programme." British Journal of Cancer **74**: 1838-1842.

13. Palli D, Rosselli del Turco M., Buiatti E, et al (1986). "A case-control study of the efficacy of a non-randomised breast cancer screening program in Florence (Italy)." Int J Cancer **38**: 501-504.

14. Moss SM, Summerley M, Thomas BT, Ellman R, Chamberlain JOP (1992). "A case-control evaluation of the effect of breast cancer screening in the United Kingdom trial of early detection of breast cancer." Journal of Epidemiology & Community Health **46**: 362-364.

15. Brown JT, Hulka BS (1988). "Screening mammography in the elderly: a case-control study. J Gen Intern Med **3**:126-131.

16. Morrison, A. (1992). "Efficacy of screening for breast cancer in older women." Journal of Gerontology **47**(Special Issue): 80-84.

17. Australian Bureau of Satistics. (1998). Life tables. Canberra, Australian Bureau of Statistics**:** 67-69.

18. Mandelblatt JS, Wheat M, Monane M, Moshief RD, Hollenberg JP, Tang J (1992). "Breast cancer screening for elderly women with and without comorbid conditions." Annals of Internal Medicine **116**: 722-730.

19. Welch HG, Albertsen PC, Nease RF, Bubolz TA, Wasson JH (1996). "Estimating treatment benefits for the elderly: the effect of competing risks." Ann Intern Med **124**: 577-584.

20. Barratt A, I. L., Glasziou P, Cumming RG, Raffle A, Hicks N, Muir Gray JA, Guyatt GH (1999). "Users' guides to the medical literature. XVII. How to use guidelines and recommendations about screening." JAMA **281**: 2029-2034.

21. Ernster VL, Barclay J, Kerlikowske K, Wilkie H, Ballard-Barbash R (2000). "Mortality among women with ductal carcinoma in situ of the breast in the population-based surveillance, epidemiology and end results program." Archives of Internal Medicine **160**: 953-958.

22. Brett J, Austoker J, Ong G (1998). "Do women who undergo further investigation for breast screening suffer adverse psychological consequences? A multi-centre follow-up study comparing different breast screeing result groups five months after their last breast screening appointment." J Pub Health Med **20**: 396-403.

23. Lerman C, Trock B, Rimer BK, Boyce A, Jepson C, Engstrom PF (1991). "Psychological and behavioral implications of abnormal mammograms." Ann Intern Med **114**: 657-661.

24. Cockburn J, Stapls M, Hurley SF, De Luise T (1994). "Psychological consequences of screening mammography." Journal of Medical Screening **1**: 7-12.

25. Kerlikowske K, Salzmann P, Phillips KA, Cauley JA, Cummings SR (1999). "Continuing screening mammography in women aged 70 to 79 years. Impact on life expectancy and cost-effectiveness." JAMA **282**: 2156-2163.

26. Kerlikowske K, Grady D, Barclay J, Sickles EA, Eaton A, Ernster V (1993). "Positive predictive value of screening mammography by age and family history of breast cancer." JAMA **270**: 2444-2450.

27. BreastScreen Victoria (2000). 1998 Annual Statistical Report. Carlton South, BreastScreen Victoria.

28. BreastScreen Queensland (2000). 1998 Annual Statistical Report. Brisbane, Queensland Health.

29. Ernster VL, Barclay J, Kerlikowske K, Grady D, Henderson IC (1996). "Incidence of and treatment for ductal carcinoma in situ of the breast." JAMA **275**: 913-918.

30. Busch E, Kemeny M., Fremgen A, Osteen RT, Winchester DP, Clive RE (1996). "Patterns of breast cancer care in the elderly." Cancer **78**: 101-111.

31. Morrow, M. (1994). "Breast disease in elderly women." Surgical Clinics of North America **74**: 145-161.

32. Hunt KE, Fry D, Bland KI (1980). "Breast carcinoma in the elderly patient: An assessment of operative risk, morbidity and mortality." American Journal of Surgery **140**: 339-342.

33. Valenovich V, Szymanski W. (1999). "Quality of life of breast cancer patients with lymphedema." Am J Surg **177**: 184-188.

34. Fallowfield LJ, Hall A, Maguire GP, Baum M (1990). "Psychological outcomes of different treatment policies in women with early breast cancer outside a clinical trial." Br Med J **301**: 575-580.

35. Wenzel LB, Fairclough DL, Brady MJ, Cella D, Garratt KM, Kluhsman BC, Crane LA, Marcus AC (1999). "Age-related differences in the quality of life of breast carcinoma patients after treatment". Cancer **86**:1768-1774.

36. Wazer DE, Erban JK, Robert NJ, Smith TJ, Marchant DJ, Schmid C, DiPetrillo T, Schmidt-Ullrich R (1994). "Breast conservation in elderly women for clinically negative axillary lymph nodes without axillary dissection." Cancer **74**: 878-883.

37. Horobin JM, Preece P, Dewar JA, Wood RAB, Cuschieri A (1991). "Long-term follow-up of elderly patients with locoregional breast cancer treatment with tamoxifen only." Br J Surg **78**: 213-217.

38. Tabar L, Fagerberg G, Duffy SW, Day NE, Gad A, Grontoft O (1992). "Update of the Swedish two-county program of mammographic screening for breast cancer." Breast Imaging: Current Status and Future Directions **30**: 187-210.

39. Taylor DH, McPherson K, Parbhoo S, Perry N (1996). "Response of women aged 65-74 to invitation for screening for breast cancer by mammography: a pilot study in London, UK." Journal of Epidemiology and Community Health **50**: 77-80.

40. Rich JS, Black WC. (2000). "When should we stop screening?" Eff Clin Pract **3**: 78-84.

41. Kattlove H, Liberati A, Keeler E, Brook RH (1995). "Benefits and costs of screening and treatment for early breast cancer. Development of a basic benefit package." JAMA **273**: 142-148.

42. Eddy, D. (1989). "Screening for breast cancer." Ann Intern Med **111**: 389-399.

43. Boer, R. (1999). In search of the best upper age limit for breast cancer screening. In Doctoral thesis "From Evidence to decision support in cancer screening. Applications of Miscan Models." University of Erasmus, Rotterdam.

44. Jansen J, Zoetelief, J. (1997) "Optomisation of mammographic breast cancer screening using a computer simulation model." European Journal of Radiology **24**: 137-144

45. Rosenquist C J, Lindfors K K. (1998) "Screening Mammography Beginning at Age 40 Years: A reappraisal of Cost-Effectiveness." Cancer **82**(11): 2235-2240

46. Okuba I, Glick H, Frumkin H, Eisenberg J. (1991) "Cost-effectiveness Analysis of Mass Screening for Breast Cancer in Japan." Cancer **67**: 2021-2028

47. Norum J. (1999) "Breast cancer screening by mammography in Norway. Is it cost effective?" Annals of Oncology **10**: 197-203

48. Leivo T, Sinton H, Tuominen R, Hakama M, Pukkala E, Heinonen O-P. (1999). "The cost-effectiveness of nationwide breast carcinoma screening in Finland, 1987-1992." Cancer **86**(4): 638-646

49. Brown, M. (1992). "Economic considerations in breast cancer screening of older women." Journal of Gerontology **47**(Special Issue): 51-58.

50. Szeto K, Devlin, N. (1996) "The cost effectiveness of mammography screening: evidence from a microstimulation model for New Zealand." Health Policy **38**: 101-115

51. Messecar D. (2000) "Mammography Screening for Older Women With and Without Cognitive Impairment." Journal of Gerontological Nursing April 2000: 14-24

52. Richardson WS, Detsky AS. (1995). "Users' guides to the medical literature. VII. How to use a clinical decision analysis. A. Are the results of the study valid?" JAMA **273**: 1292-1295.

53. Justice A, Covinsky K, Berlin JA (1999). "Assessing the generalizability of prognostic information." Ann Intern Med **130**: 515-524.

54. Drummond MF, Obrien B, Stoddardt GL, Torrance GW. (1997) Methods for the Economic Evaluation of Health Care Programmes. New York: Oxford University Press.

55. Salkeld G and Easter S. (1998) "The cost of diagnostic investigations for women presenting with breast symptoms." The NHMRC National Breast Cancer Centre, Sydney.

56. Pharoah PDP, Day N, Duffy S, Easton DF, Ponder BAJ (1997). "Family history and the risk of breast cancer: A systematic review and meta-analysis." Int J Cancer **71**: 800-809.

57. Satariano WA, Ragland DR. (1994). "The effect of comorbidity on 3-year survival of women with primary breast cancer." Ann Intern Med **120**: 104-110.

58. Irwig L, Glasziou P. (2000). "Informed consent for screening by community sampling." Effective Clinical Practice **3**: 47-50.

59. Cockburn J, Pit S. (1998). Perceptions of screening mammography amongst women aged 40-49. Canberra, NHMRC National Breast Cancer Centre.

8. Appendices

Appendix 1: Inputs and assumptions of models

Rich and Black	
Assessment of benefit	
Estimate of effect	30% relative risk reduction [does not specify annual or biennial
Lead time [preclinical duration]	Not Applicable
BrCa incidence data	Not Applicable
BrCa mortality data	SEER data from cancer registries around US 1994-1996
All cause mortality data	National Center for Health Statistics for same regions as SEER cancer registry data
Assessment of harms	**Not done**
DCIS incidence	
DCIS mortality	
Utilities for diagnostic and treatment states	
Assumptions	
Duration of mortality benefit	5 years after screening stops
Discounting	No
Attendance rates	
Sensitivity analyses	None

Kerlikowske et al	
Assessment of benefit	
Estimate of effect	27% relative risk reduction for biennial screening
Lead time [preclinical duration]	Not Applicable
BrCa incidence data	1994 SEER data
BrCa mortality data	1984 SEER data 10 year mortality rate 32%
All cause mortality data	Vital statistics in US, 1991
Assessment of harms	
DCIS incidence	Approx 1/1000 per year in screened women and about 1/10,000 per year in unscreened women
DCIS mortality	1.9% over 10 years in screened and 3.4% over 10 years in unscreened women
Utilities for diagnostic and treatment states	Life after treatment: 1
Assumptions	
Duration of mortality benefit	5 years after screening stops
Discounting	Benefits and costs 3% pa
Attendance rates	
Sensitivity analyses	
Utilities	Life after Rx 0.8, 0.9 Life with metastases 0.3
Discount rates	0,5,10,15%
RRR	22%, 32%
BrCa mortality	25% over 10 years

Kattlove	
Assessment of benefit	
Estimate of effect	30% relative risk reduction [biennial screening]
Lead time [preclinical duration]	Not Applicable
BrCa incidence data	Not Applicable
BrCa mortality data	US data source not specified
All cause mortality data	US data source not specified
Assessment of harms	**Not done**
DCIS incidence	
DCIS mortality	
Utilities for diagnostic and treatment states	
Assumptions	
Duration of mortality benefit	Unclear
Discounting	No
Attendance rates	
Sensitivity analyses	None

Mandelblatt	
Assessment of benefit	
Estimate of effect	Early diagnosis assumed to shift stage distribution based on stage distribution in BCDDP and Two
Lead time [preclinical duration]	?
BrCa incidence data	SEER data – stratified by race [all races / black]
BrCa mortality data	Age and stage specific survival data from NCI based on SEER data 1975-1984
All cause mortality data	See below
Comorbid conditions	Used excess disease specific mortality data for mild hypertension and congestive heart failure [based on
Assessment of harms	
DCIS incidence	Not addressed
DCIS mortality	Not addressed
Utilities for diagnostic and treatment states	Utilities for local, regional and distant cancer and for screening attendance and false positive result
Assumptions	
Duration of mortality benefit	Not stated
Discounting	No
Attendance rates	
Sensitivity analyses	Quality of life [base case has no QoL adjustment], incidence rates, perioperative death rate, sensitivity &

Eddy	
Assessment of benefit	
Estimate of effect	Screening assumed to shift stage distribution and [optionally] to alter stage specific survival as follows:
Lead time [preclinical duration]	Assumed 1 year
BrCa incidence data	US data sources [not specified]
BrCa mortality data	US data sources [not specified]
All cause mortality data	US data sources [not specified]
Assessment of harms	
DCIS incidence	Not addressed
DCIS mortality	Not addressed
Utilities for diagnostic and treatment states	None used
Assumptions	
Duration of mortality benefit	Not stated
Discounting	Not in base case
Attendance rates	Assumed 100%
Sensitivity analyses	5% discounting of life expectancy benefit and costs
	25% attendance

Appendix 2: Results and estimates of relative benefits of models

Rich and Black		
Life expectancy gain	Days of life "lost" by [or days of life gained by continuing for life instead of stopping screening at 69 years 13.9 74 years 8.5 79 years 4.6 84 years 1.8	
Quality adjusted gain in life expectancy	Not done	
Other measure of benefit/ effect: % maximum potential benefit achieved [MBA] by stopping at	69 years 68% 74 years 80% 79 years 89% 84 years 96% 97 years 100%	
Cost-effectiveness estimate	Not done	
Relative gains from screening women 70 to 97 compared to a base of women 50-69	50-69 100% 70-74 75% 75-79 54% 80-84 39% 85+ 25%	Data According to model maximum benefit [screening from 50-97] is 42.7 days. Therefore benefit of screening 50-69 = 42.7-13.9 = 28.8 days or 7.2 days on average for each 5 year age bracket 50-54,55-59,60-64,65-69 or 14.4 days per decade. Gains for each subsequent age increment are: 70-74 5.4 3.9 2.8 1.8 Therefore relative gain for 70-74 year olds is 5.4/7.2 =75% etc.

Kerlikowske **Life expectancy gain** [increase in days] achieved by stopping at 79 [rather than 69]	2.4	
Quality adjusted life expectancy gain [increase in days] achieved by stopping at 79 years [rather than 69]	1.05 [midpoint of range -0.1-2.2]	
Other estimates of benefit / effect: Deaths averted per 10,000 women screened to 79 [rather than 69]	10.8	
Life years saved per 10,000 women screened to 79 [rather than 69]	67.7	
BrCa deaths averted 10,000 women screened to 79 [rather than 69]	17	
Cost-effectiveness estimate Cost per life year saved per 10,000 women screened to 79 [rather than 69]	$73,855	
Relative gain from screening women 69-79 compared with a base of women 50-69	50-69 100% 40% Quality adjusted relative gain: 50-69 100% 69-79 18%	Data Life expectancy gain from Salzman, Kerlikowske and Phillips is 12 days [not quality adjusted] for women 50-69 years, or on average, 6 days for each 10 year age bracket 50-59,60-69; and 11.8 quality adjusted days or 5.9 days on average per 10 year age bracket. Therefore relative gain for 69-79 year olds is 2.4/6 = 40%. For quality adjusted data, relative gain is 1.05/5.9 =18%. Note extending screening to women 40-49 years extended life expectancy gain by 2.5 days.

Kattlove		
Life expectancy gain [days] 50-59 60-69 70-74	 11.7 9.8 1.8	
Quality adjusted life expectancy gain	**Not done**	
Other	**Not done**	
Cost-effectiveness estimate [costs per life year gained] 50-59 60-69 70-74	 8,280 9,890 35,900	
Relative gain from screening screening women over 70 compared to base of women 50-69 years 50-69 70-74	 100% 33%	Data: estimate 5.4 days gained on average per 5 year age bracket in women 50-69 [11.7+9.8 /4]. Relative gain 70-74 year olds is 1.8/5.4 = 33%.

Mandelblatt			
Life expectancy gain [days]	Average health	Mild hypertension	Congestive heart failure
65-69	2.17	1.93	1.09
70-74	1.80	1.61	0.98
75-79	1.32	1.20	0.77
80-84	0.98	0.91	0.64
85+	0.69	0.65	0.49
Quality adjusted life expectancy gain [days]			
65-69	1.44	1.22	0.43
70-74	1.10	0.93	0.33
75-79	0.69	0.57	0.16
80-84	0.34	0.27	0.01
85+	0.05	0.01	-0.15
Other	Not done		
Cost-effectiveness estimate	Not done		

Relative gain from screening women aged 70+ compared to base of women 65-69	65-69 100% 70-74 83% 75-79 61% 80-84 45% 85+ 32%	Data Base group gain is 2.17 days. Therefore relative gain for women 70-74 is 1.8/2.17 = 83% etc.
	65-69 100% 70-74 76% 75-79 48% 80-84 24% 85+ 3.5%	Quality adjusted life expectancy gain for average health women
	65-69 100% 70-74 76% 75-79 47% 80-84 22% 85+ 0.8%	Quality adjusted life expectancy gain for women with mild hypertension
	65-69 100% 70-74 77% 75-79 37% 80-84 2.3% 85+ 0	Quality adjusted life expectancy gain for women with congestive heart failure

Eddy		
Life expectancy gain [days] a) gain from screening by breast physical examination [BPE] for 10 years from 65-75 years of age a) marginal gain of adding mammography to BPE c) BPE + mammography	10-18 [5-9 with 5% discounting] 5-18 [2-9 with 5% discounting] 15-36 [7-18 with 5% discounting]	
Quality adjusted life expectancy gain	Not done	
Other		
Cost-effectiveness Cost of adding a year of life by screening [with both PBE and mammography] women 65-75 years	$25,395-$92,412 [5% discounting included]	
Relative gain from screening women 65-75 compared to base of women 55-65	55-65 100% 65-75 78%-90%	Data [increase in life expectancy of BPE + mammo with 5% discounting, days] Women 40-50 Women 55-65 Women 65-75 6-16 9-20 7-18 Relative gain for 65-75 year olds is 7/9 =78% - 18/20 = 90%.