

Benefits, harms and costs of screening mammography in women 70 years and over: a systematic review

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BREASTSCREEN AUSTRALIA has provided free mammographic screening for women aged 50–69 years since 1991, but there is at present no national policy on the age at which screening, or regular invitations for screening, should cease.

Breast cancer mortality rises steeply with age (from 21 per 100 000 among women aged 40–49 years to 117, 146 and 197 per 100 000 for women aged 75–79, 80–84 and 85+ years, respectively).¹ However, as older women have a higher risk of death from other causes, the benefits of mammographic screening are increasingly offset by competing causes of death. In addition, older women may experience the immediate downsides of screening (discomfort, anxiety, side effects of tests and treatment), but not live long enough to experience the benefits.

A meta-analysis of trials recruiting women aged 40–74 years of age has shown that mammographic screening decreases breast cancer mortality (relative risk reduction, 23%; 95% CI, 13%–31%),² but only one trial, the Swedish Two County Study, recruited women up to 74 years of age. That study found a (statistically non-significant) relative risk reduction of 21% (relative risk [RR], 0.79; 95% CI, 0.51–1.22) in women over 70 years at recruitment.³ A subsequent analysis of women in the same study aged 65–74 years at recruit-

ABSTRACT

Objective: To assess the (i) benefits, (ii) harms and (iii) costs of continuing mammographic screening for women 70 years and over.

Data sources and synthesis: (i) We conducted a MEDLINE search (1966 – July 2000) for decision-analytic models estimating life-expectancy gains from screening in older women. The five studies meeting the inclusion criteria were critically appraised using standard criteria. We estimated relative benefit from each model's estimate of effectiveness of screening in older women relative to that in women aged 50–69 years using the same model. (ii) With data from BreastScreen Queensland, we constructed balance sheets of the consequences of screening for women in 10-year age groups (40–49 to 80–89 years), and (iii) we used a validated model to estimate the marginal cost-effectiveness of extending screening to women 70 years and over.

Results: For women aged 70–79 years, the relative benefit was estimated as 40%–72%, and 18%–62% with adjustment for the impact of screening on quality of life. For women over 80 years the relative benefit was about a third, and with quality-of-life adjustment only 14%, that in women aged 50–69 years. (ii) Of 10 000 Australian women participating in ongoing screening, about 400 are recalled for further testing, and, depending on age, about 70–112 undergo biopsy and about 19–80 cancers are detected. (iii) Cost-effectiveness estimates for extending the upper age limit for mammographic screening from 69 to 79 years range from \$8119 to \$27 751 per quality-adjusted life-year saved, which compares favourably with extending screening to women aged 40–49 years (estimated at between \$24 000 and \$65 000 per life-year saved).

Conclusions: Women 70 years and over, in consultation with their healthcare providers, may want to decide for themselves whether to continue mammographic screening. Decision-support materials are needed for women in this age group.

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ment found a statistically significant relative risk reduction of 32% (RR, 0.68; 95% CI, 0.51–0.89).⁴ A more

modest relative risk reduction in women aged 70–74 (0.79) compared with women aged 65–69 (0.58) was attributed in part to lower participation by older women in screening (77% v 86%, respectively). These data relate to women first recruited to screening around 70 years of age. As most Australian women aged over 70 who attend for screening have already been screened,⁵ they are unlikely to experience a comparable benefit.

Using a previously published approach to screening evaluation,⁶ we aimed to examine the balance of benefits and harms, and the resource implications, of continuing to screen women past 70 years of age. Because of the paucity of trial data, we reviewed

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decision-analytic models of mammographic screening in older women to assess the benefit of screening.

METHODS

Data sources

“Exploding” a search term retrieves all records with the exact term as well as those with more specific terms in the hierarchy of medical subject headings (MeSH).

The search strategy was [explode mammography] OR [explode breast neoplasms AND explode mass screening] AND [explode decision support techniques OR explode cost-benefit analysis] AND model.mp (MEDLINE looks for that word in the title, abstract or MeSH heading).

The search strategy was applied to MEDLINE 1966 to July 2000, and 44

articles were retrieved. All abstracts were reviewed and the relevant articles obtained in full. (This search was repeated in January 2002, and an additional 13 citations were retrieved; none met the inclusion criteria.)

We also contacted the authors of all models published since 1995 to locate any other published models, and reviewed the reference lists of all the articles describing models.

Inclusion criteria

Included were articles reporting decision-analytic or cost-effectiveness models of screening mammography, which provided age-specific results for women 70 years and over (and for younger women for comparison) and presented the results as estimated gains in life expectancy per woman screened, either with or without quality-of-life adjustment.

Critical appraisal

The included articles were critically appraised according to criteria outlined by Richardson and Detsky,⁷ with modification to include the suggestion of Justice et al⁸ — 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.

Estimating relative benefits

The models varied widely in their methods, assumptions, results and presentation. To provide a common outcome, we calculated the relative life-expectancy benefit (and relative quality-adjusted life-expectancy benefit when available). This was done by establishing a base benefit predicted by the model for younger women (generally

1: Critical appraisal of decision-analytic models estimating life-expectancy gains from mammographic screening in older women (tinted entries indicate criterion is met)

Study	Were important strategies included?	Was the potential impact of uncertainty in the evidence determined?	How strong is the evidence?	Do the probabilities fit the Australian population?	Do the utilities* reflect the values of older Australian women?
Rich and Black 2000	Yes — compares screening from 50 years to end of life with no screening	No sensitivity analyses done	Assumes relative risk reduction is the same as in trials of women under 70	Probably, but incidence and mortality rates are higher in the US than in Australia. Model not tested in any other population	No adjustment for quality of life
Kerlikowske et al 1999	Yes — compares stopping screening at 69 years with stopping at 79 years	Sensitivity analyses were done for varying discount rates, [†] relative risk reductions and breast cancer mortality rates	Assumes range of relative risk reduction from 22% to 32%	Probably, but incidence and mortality rates are higher in the US than in Australia. Model not tested in any other population	Unknown — uses utilities only for two states: life after treatment and life with metastatic disease
Kattlove et al 1995	Yes — compares biennial screening from 40 to 74 years with no screening	No sensitivity analyses done	Assumes relative risk reductions from Swedish Two County Study	Not known	No adjustment for quality of life
Mandelblatt et al 1992	Yes — compares screening for women 65 years or more with no screening	Sensitivity analyses for adverse impact on quality of life, breast cancer incidence, perioperative death, sensitivity and specificity of mammography and stage distribution of detected cancers	Assumes US breast cancer stage distribution and stage-specific survival data	Not tested in other populations	Probably — utility data for impact of screening on women with negative and positive results of screening, but based on US women aged 50–74 years
Eddy 1989	Yes — compares screening for women 40–75 years with no screening	Only sensitivity analysis was inclusion of 5% discounting	Assumes US stage and survival data plus trial data	Model applied to UK and Malmö trial data and predicted greater than observed declines in mortality (model assumes annual screening and 100% compliance)	No adjustment for quality of life

* Weights used to adjust life-expectancy gains for impact on quality of life. † The discount rate is an adjustment which gives more weight to present, rather than future, costs and benefits. It takes into account, among other things, the general preference for immediate benefits, and delayed costs.



2: Summary of available relative life-expectancy benefits and quality-adjusted relative life-expectancy benefits of screening women 70 years and over

		Relative benefit (RB)/quality-adjusted relative benefit (QARB)				Average relative benefit per decade		
		70–74 y	75–79 y	80–84 y	≥ 85 y	40–49 y	70–79 y	80–89 y
Rich and Black (base group: 50–69 y)*	RB	75%	54%	39%	25%		65%	32%
Kerlikowske et al (base group: 50–69 y)*	RB		40% [†]			42%	40%	
	QARB		18% [†]			37%	18%	
Kattlove et al (base group: 50–69 y)*	RB	33% [‡]				0		
Mandelblatt et al (base group: 65–69 y)*	RB	83%	61%	45%	32%		72%	39%
	QARB	76%	48%	24%	4%		62%	14%
Eddy (base group: 55–65 y)*	RB	78%–90% [§]				67%–80%	78%–90% [§]	

* Benefit for base group is regarded as 100%. † Estimate for women aged 69–79 years. ‡ Estimate for women aged 70–74 years. § Estimate for women aged 65–75 years.

women aged 50–69 years). The base benefit — the average benefit per five or per 10 years (depending on data presentation) for women aged 50–69 years — was obtained from the article reporting the model or from previous publications with the same model or modelling approach. The relative life-expectancy benefit (and/or relative quality-adjusted life-expectancy benefit), estimated in 5- and/or 10-year age groups for older women, was then expressed as a percentage of the base benefit. For comparison, if data were available, we calculated the relative benefit for women aged 40–49 years (as a percentage of the same base benefit).

Estimating the harms

To quantify the harms of screening, we contacted all Australian State and Territory breast-screening coordination units and requested statistical reports. BreastScreen Queensland provided actual numbers of women screened (82 731 women aged 40–85+ years screened in 1998), recalled, tested and diagnosed with cancer. These data were converted to age-specific rates per 10 000 women screened. All data in the balance sheets 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.

Resource implications

Our estimates of the cost-effectiveness of extending mammographic screening to women aged 70–79 years were calculated from the costs per quality-adjusted life-year (QALY) provided by Boer et al using the MISCAN model (MICrosimulation SCReening ANALysis).^{9,10} This model is the most comprehensive of the cost-effectiveness models available, and estimates, for a two-yearly screening program, 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. The MISCAN model provides two variants: an optimistic model (which assumes no further increase in preclinical duration¹⁰ after the age of 65) and a pessimistic variant (which assumes a further increase in preclinical duration, with age

extrapolated from the trend in younger age groups). The QALYs are discounted at an annual rate of 5%, and costs have been converted from euros to Australian dollars.

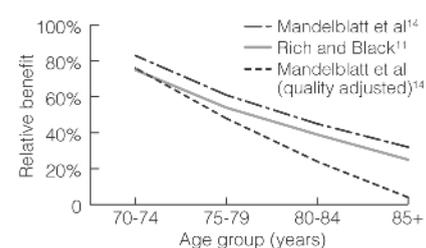
RESULTS

Estimating the benefit

Five models met the inclusion criteria.^{11–15} A summary of the critical appraisal is given in Box 1. The models broadly fell into two groups: those that used an estimated relative risk reduction for screening in older women,^{11–13} and those that used changes in the distribution of cancer stages at detection achieved by screening to model the impact on disease progression and mortality.^{14,15} Thus, the models incorporated a wide range of assumptions about the effect of screening on mortality or stage distribution, baseline risk of mortality from breast cancer, stage-specific survival rates, test sensitivity and specificity, frequency of diagnosis of ductal carcinoma in situ (DCIS), attendance rates and discount rates for benefits and costs.

Only two of the models^{12,14} included adjustment for the impact on quality of life caused by screening. In one study¹² the quality-of-life adjustment was limited to health states after diagnosis of breast cancer (ie, impact of diagnosis and initial treatment and impact of

3: Impact of age on relative life-expectancy benefit according to different models



4: Balance sheet of the consequences of screening for women over 40 years (per subsequent screening round)

	40–49 y	50–69 y	70–79 y	≥ 80+ y
Number of screening mammograms	10 000	10 000	10 000	10 000
Number of women recalled for imaging tests	450	417	407	401
Number of women proceeding to biopsy*	70	85	112	87
Fine needle biopsy	44	47	61	44
Core biopsy	30	41	50	36
Open biopsy	22	33	43	36
Number of cancers detected	19	37	65	80
Invasive	16	29	54	66
Ductal carcinoma in situ	3	8	11	15
Relative life-expectancy benefit	42%–80%	100%	40%–72%	32%–39%
Relative quality-adjusted life-expectancy benefit	37%	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.

† Rates are based on raw data from 18 458, 51 612, 11 290 and 1371 women aged 40–49, 50–69, 70–79 and 80 years and over, respectively.

metastatic disease). In the other,¹⁴ there was also adjustment for a decrement in quality of life for women who were screened but did not have cancer (for anxiety and discomfort from the mammogram for screen-negative women; and anxiety, inconvenience and discomfort of biopsy for women with a false-positive result).

Estimates of relative benefits

Relative life-expectancy benefits (and quality-adjusted relative life-expectancy benefits) of screening in women over 70 compared with women aged 50–69 years are shown in Box 2. For example, for the Rich and Black model,¹¹ if we regard women in the base group (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 (Box 2). When available, similar information is presented for quality-adjusted life expectancy. For example, from the model by Kerlikowske et al,¹² 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,

women 70–79 years experience only about 18% of the benefit experienced by younger women.

Thus, the life-expectancy benefit of screening mammography in older women appears to diminish with increasing age (Box 1). For women aged 70–79 years, the relative benefit ranges from an estimated 40% to 72% without quality-of-life adjustment, and from an estimated 18%–62% with quality-of-life adjustment. For women over 80 years,

5: The marginal cost per quality-adjusted life-year (QALY) (discounted at 5%) of mammographic screening beyond 69 years

Extending screening to:	Marginal cost per QALY	
	Optimistic model*	Pessimistic model†
73 years	\$6788	\$18 374
75 years	\$7342	\$20 754
77 years	\$7708	\$23 620
79 years	\$8119	\$27 751

* Assumes no further increase in preclinical duration¹⁰ after the age of 65 years.

† Assumes a further increase in preclinical duration with age extrapolated from the trend in younger age groups.

the relative benefit, estimated as 32%–39%, is further reduced when quality-of-life adjustment is made (14%). Relative effects of screening mammography for women in the 40–49-years age group were provided by only three studies,^{12,13,15} and only one^{12,16} included a quality-of-life-adjusted estimate.

Estimates of harms

The consequences of mammographic screening for older Australian women are summarised and compared with the consequences for younger Australian women in the balance sheet given in Box 4.

Of 10 000 Australian women undergoing a second or subsequent screening mammography, about 9600 women in each age group will be reassured that they do not have breast cancer and about 400 will be recalled for further tests. Of these, depending on age, about 70–112 women will undergo breast biopsy and 19–80 cancers will be detected. About 15%–20% of these cancers in each age group will be DCIS.

Resource implications

Box 5 shows the marginal cost effectiveness of extending the upper age limit for mammographic screening from 69 years to 79 years. Estimates range from \$8119 (optimistic model) to \$27 751 (pessimistic model) per QALY saved.

DISCUSSION

The benefit of screening women 70–79 years is about 40%–72% of that achieved in women 50–69 years, and declines further with increasing age and when quality-of-life adjustment is made. Extending screening to women 70–79 years is relatively cost-effective (similar to that of extending screening to women 40–49 years of age).

Impact of risk on benefits v harms

Age is the strongest risk factor for breast cancer, as indicated by the increasing number of cancers detected across age groups (Box 4). However, this increased risk, and therefore potential increased benefit, is mitigated by the reducing

relative benefit from screening with age (Boxes 2, 3, 4).

Women who are at higher risk (family history or previous personal history of breast cancer) also have more to gain from screening. Conversely, women at low risk (eg, women who have low bone mineral density¹² or a high risk of death from other causes) stand to benefit less from screening.^{14,17} Thus, those women least likely to participate in screening are, in fact, those least likely to benefit from screening. Therefore, whether women perceive themselves as in sufficiently good health to attend screening may be a good proxy for deciding whether screening is worthwhile.

Impact of values and preferences

Few quality-of-life-adjusted estimates were available. In the MISCAN model, which assesses cost-effectiveness,^{9,10} quality-of-life adjustment was done by including utilities (the weights used to adjust life-expectancy gains for impact on quality of life) for 16 health states arising from screening, which included screening attendance and attendance for follow-up of positive test results, as well as health states arising from the detection and treatment of breast cancer. However, we were unable to use this model in the assessment of benefit, as it does not provide outcomes in terms of life-expectancy gains per woman.

The two models providing information on average life expectancy with quality-of-life adjustment^{12,14} are consistent in showing that the benefit of screening is reduced when quality-of-life adjustment is made. Thus, 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 a diagnosis of breast cancer and treatment are less likely to benefit from screening. Women who are diagnosed with DCIS are particularly likely to experience net harm if they are bothered by testing and treatment for cancer, as it is unlikely that DCIS would impact on their lifespan.¹⁸

In particular, the adverse effects of treatment need to be considered. Based on a large, representative 1990 sample, mortality rates for mastectomy are reported as 1.5% for women over 75

years (mean age, 81 years) and 0.5% for women under 75 (mean age, 57 years).¹⁹ Substantial postoperative morbidity has also been reported for between 7% and 20% of elderly women undergoing mastectomy.^{20,21} On the other hand, in terms of emotional and psychological effects, older women (over 50 years of age at diagnosis) may experience significantly less quality-of-life disruption (including emotional well-being, breast cancer concern, depression and disease-specific intrusive thought) than younger women.²² In short, more information about the impact of screening on quality of life in older women is urgently needed. Further, women's views about the balance of the benefits versus the adverse impacts of screening on quality of life are important when a decision to continue screening (or not) is made (Box 6).

Impact of uncertainty

There is clearly great uncertainty in the estimates of benefit from screening. The diversity of results of the models

indicates the impact of differing assumptions and methods. Only with randomised trials can the likely effect size be quantified without bias. In recognition of the inherent uncertainty, we have presented range-of-benefit estimates. Further, there are known State-to-State variations in the delivery of screening services.^{5,23} Nevertheless, decisions need to be made and the estimates provided here give some indication of the likely effects of screening mammography in older women.

Impact of costs

The conversion of costs per QALY estimates from Dutch data (given in euros) to Australian dollars provides a rough estimate of the relative efficiency (marginal cost-effectiveness) of extending biennial screening for women from ages 50–69 years to 50–79 years.^{9,10} Patterns of health service use and health costs are likely to be different between countries, but this is unlikely to have a substantial impact on cost-effectiveness ratios.

From an economic point of view, the central question is whether extending mammographic screening represents value for money. This is a value judgement based on the relative (marginal) cost of achieving health gain. One approach to answering this question is to compare the relative cost effectiveness of extending mammographic screening (from the current 50–69 years) to include women aged 40–49 years. In a previous study, we calculated (using the MISCAN model) the marginal cost of screening women from 40 years of age as between \$24 000 and \$65 000 per life-year gained.²⁴ Although these cost-effectiveness ratios are not adjusted for “quality of life”, the results show that extending screening to women aged 70–79 years is probably at least as cost-effective as extending screening to women aged 40–49 years.

6: Should breast screening continue beyond age 69?

Women may want to decide for themselves whether to continue screening. The choices women make are likely to vary, depending on how each woman values the possible benefits and risks. In making their decision, women and their healthcare providers should take into account that women are more likely to experience a benefit from screening if they:

- 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), or
- Are at low risk of death from other causes, such as cardiovascular disease or other cancers, or
- Perceive themselves to be in good health, or
- 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.

These considerations are highly individual and emphasise the need for informed choice, which could be facilitated by decision-support materials for women in this age group.

COMPETING INTERESTS

None declared

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