

Current issues in mammographic breast cancer screening

Mary T Rickard

Mammographic screening for the early detection of breast cancer is widely accepted as the most effective means currently available to reduce breast cancer deaths. However, evidence shows that to maximize benefits and minimize harm, mammographic screening must be of high quality.

In many countries breast cancer is a major health concern and is the leading cause of cancer death in women. Breast cancer detection by mammography has been well researched as a method of early detection and consequent mortality reduction, and is widely used in clinical practice. While its use for women over 50 years of age is generally accepted as effective, some aspects of its use remain controversial, and offer the opportunity for continuing quality improvement and for further research into facets of screening delivery and the natural history of breast cancer and its management.

RANDOMIZED CONTROLLED TRIALS AND OTHER STUDIES

The first randomized controlled trial to examine screening for breast cancer began as the Health Insurance Policy (HIP) study in the US in 1963 (Shapiro et al, 1982). Since then numerous trials and studies have examined the role of mammography in breast cancer screening (Verbeek et al, 1984; Palli et al, 1986; Tabar et al, 1992; Alexander et al, 1994). The conditions of the trials and studies varied, such as the number of mammographic views used, the ages of women examined, and the interval between screens, and not all trials have shown an equal benefit.

However, proof of the effectiveness of mammographic screening in reducing breast cancer mortality in women aged 50 years or more has been strengthened by several meta-analyses of data from multiple trials and studies (Nystrom et al, 1993). These have shown a statistically significant mortality reduction starting at 6–7 years after the commencement of screening of approximately 26–30% for women aged

50–74 years (Fletcher et al, 1993) or 50–69 years (Kerlikowske et al, 1995). Given trial issues, such as less than 100% participation in the study group, and contamination of the control groups by women having mammograms, it is considered likely that the benefit to women who participate in screening is greater than 26–30%.

BENEFITS AND HARMS

Mammographic screening for breast cancer involves examination of a large population of women with the aim of detecting preclinical, early stage breast cancer, thus reducing the mortality of those women diagnosed with breast cancer. The subgroup diagnosed with breast cancer are those women with true-positive results and, depending on several factors including the age group screened, they make up around 0.6% of the screened population (Nystrom et al, 1993). Given that not all women with breast cancer die from the disease, the approximately 50% mortality benefit affects considerably less than 0.3% of the screened population.

To achieve the mortality benefits there are a number of harms or costs imposed on the screened population. The recall rate varies considerably from country to country, but is often around 5%, and 80–90% of the women recalled do not have breast cancer, i.e. false-positive results (Kerlikowske et al, 1993). To exclude breast cancer a number of further examinations are carried out, sometimes including surgery (Figure 1), and these have psychological, physical, social and financial costs (Wright, 1997).

While the costs to the community may be considerable, it can be argued that most women readily accept these costs in order to be reas-

Dr Mary T Rickard is Director/Radiologist, BreastScreen NSW, Central and Eastern Sydney, Royal Prince Alfred Hospital, Camperdown, New South Wales 2050, Australia

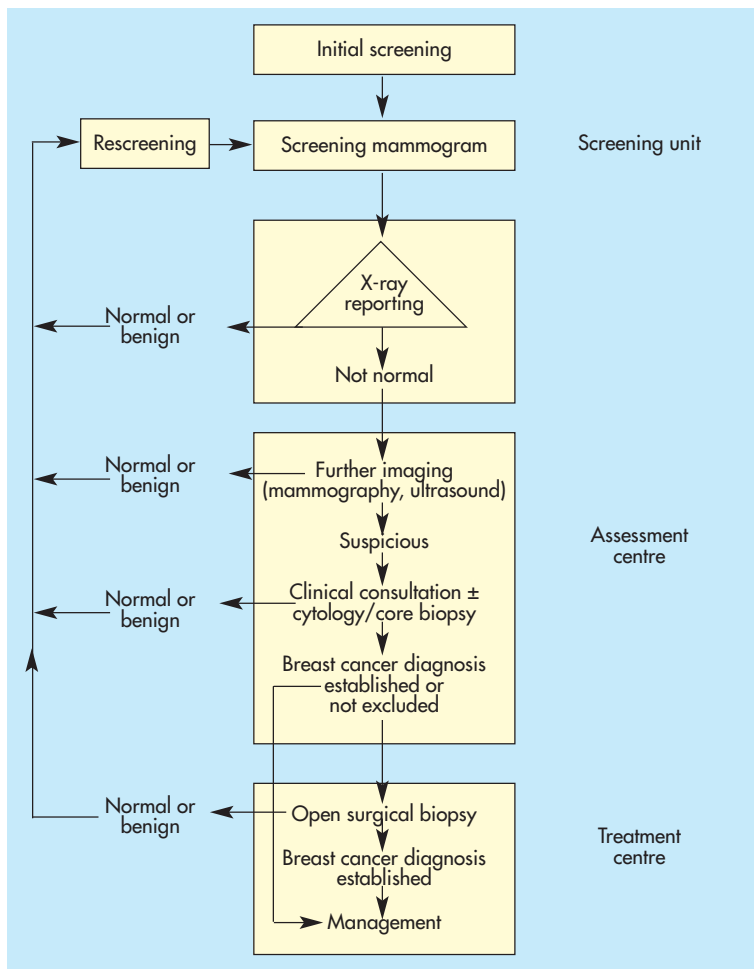


Figure 1. Treatment algorithm for mammographic breast cancer screening.

sured that they do not have breast cancer. In fact reassurance is the main reason why most women participate in mammographic screening services. In the majority of cases the negative results of screening are accurate, i.e. true negatives, and are appropriately reassuring. However, for approximately 10% of breast cancer patients (around 0.06% of the screened population), the results are falsely negative, and

these women are inappropriately advised that breast cancer is not present (Tabar et al, 1987). This may lead to a delay in clinical (interval) cancer diagnosis.

Clearly the better the overall quality of the service, the higher the true-positive and true-negative rates, and the lower the false-positive and false-negative rates (Table 1). An optimal screen service design, high standards of clinical care, and continuing quality improvement are clearly issues for clinical services.

A negative effect of screening is that of 'lead time', and this affects those women with cancers that are diagnosed at screening but that still result in death. This group of women die from their disease at the same time that they would have without screening, and yet know about their disease for several years longer (the lead time) (Miller, 1991).

Over-diagnosis and over-treatment are also 'harms' of mammographic screening (Peeters et al, 1989). A certain number of cancers diagnosed by screening are likely to have never become clinically apparent or lethal (over-diagnosis). Their diagnosis by screening leads to unnecessary treatment (over-treatment). The magnitude of this problem appears to be small but may be rising with the increasing emphasis on diagnosis of small foci of ductal carcinoma in situ (Emster et al, 1996).

Radiation exposure from mammographic screening is not generally believed to be significant. The dosages used are small and the hypothetical risks of breast cancer induction and mortality are considered equivalent to those of other minor risks, such as smoking (Feig, 1995). More controversial issues include the risk of radiation to genetically susceptible individuals, such as those with the ataxia telangiectasia gene (Swift et al, 1991), or the risk posed by compression to the normal or cancer-containing breast (Jatoi, 1997).

TABLE 1. Benefits and harms associated with major outcomes of mammographic screening

Outcome (approximate % of screened population)	Benefits	Harms
True positives (0.6%)	Early diagnosis Mortality reduction	Longer time with a diagnosis of breast cancer Over-diagnosis and over-treatment
False positives (5.4%)	Reassurance, but this is delayed	Additional tests Anxiety
True negatives (94.0%)	Reassurance	Radiation exposure Financial costs
False negatives (0.06%)	Possible increased awareness of breast cancer	False reassurance Possible delay in clinical breast cancer diagnosis

Financial costs involved in screening have been well examined. The cost effectiveness of screening, including the costs per quality adjusted life year, generally compare favourably with other medical practices (Lindfors and Rosenquist, 1995). Based on the Swedish Overview Analysis, the cost per life saved for women aged 50–59 years was estimated at \$183 000, and for women aged 60–69 years at \$146 000 (Kattlove et al, 1995). The issue of appropriate spending is important given limited health resources and competing health interests.

SCREENING WOMEN AGED 40–49 YEARS OF AGE

One of the most controversial current issues in mammographic screening is whether or not it should be recommended for women aged 40–49 years (Jatoi, 1997; Kopans, 1997). The randomized controlled trials and other studies carried out to evaluate screening were not designed to specifically examine this subset of women, and generally the number of women in this age group included in the trials and studies is low.

However, recent examination of the data by meta-analysis has shown a 15% mortality reduction (95% confidence interval 0.71–1.01) at 13 years follow-up (Organising Committee and Collaborators, 1996). Therefore compared with women aged 50 years or more at the commencement of screening, the degree of benefit is ‘less certain’, ‘not as great’ or ‘delayed’. There is much discussion in the literature as to the reasons for the differences. Based on these findings, some of the arguments for and against screening this age group are presented below.

Benefit ‘less certain’

Against: The data are ‘not supportive’ of any proven benefit, and there is no scientific basis for recommending screening of women 40–49 years.

For: The data are ‘weak’ because of the insufficient numbers involved in trials and studies. Because younger women have lesser incidences of breast cancer, larger numbers are required to prove a (small) change in mortality.

Benefit ‘not as great’

Against: If one accepts the lesser benefit as being real, then the mortality reduction remains insufficient to outweigh the negative effects (psychological, physical, social and financial) of screening.

For: The trials/studies were not designed to maximize the potential benefit to younger

women whose cancers are often difficult to see mammographically. The benefit could be increased by better screening quality, and as younger women have more potential years of life to be gained from early diagnosis and effective treatment, mammographic screening is worthwhile (Rosenquist and Lindfors, 1994).

Benefit ‘delayed’

Against: The trial results are based on age at entry, and a reduction in mortality is not seen until approximately 13 years after entry. Statistical analysis supports the argument that most or all the benefit is related to cancers diagnosed over the age of 50 years (de Koning et al, 1995).

For: The biology of breast cancer in younger women indicates that they are less lethal than those in older women. Therefore the results support screening women in their 40s as it takes longer to show an effect on mortality (Adami et al, 1986; Henderson, 1992).

What can be concluded from these results?

Among the arguments against screening younger women is the increased harm caused in this age group compared with the older age groups. There are relatively more false-positive and false-negative diagnoses per true cancer diagnosis, greater financial costs per cancer diagnosis, and possibly more risk from radiation exposure and overdiagnosis and overtreatment.

However, if one accepts the value of screening in this age group, then there is an argument for optimizing the procedure to maximize early detection. This can be done by ensuring double view rather than single view mammography is employed, shortening the screening interval to 12–18 months, and perhaps lowering the ‘threshold’ for intervention in this group.

OPTIMIZATION OF SCREENING SERVICES

Despite the controversies related to mammographic screening, the scientific evidence has been sufficient to lead to the establishment of many mammographic screening services worldwide. For those working in these services, the challenge is to optimize screening and ensure that:

- Comprehensive and appropriate information is available to women and their medical advisers
- An acceptable and accessible service is offered
- Uptake or compliance with the service is maximized

- The radiography and radiology aspects of the service are of high quality
- Assessment of screen-detected abnormalities is carried out in a multidisciplinary environment
- Screening and assessment services are linked to quality breast cancer treatment services
- Women attending mammography screening services, especially those diagnosed with breast cancer, are given support and counselling as needed
- The mammography screening service is well administered, monitored and evaluated
- Comprehensive ongoing education is given to all mammography screening staff.

Such measures ensure that the potential benefits of mammography screening are realized.

CONCLUSIONS

Breast cancer is a major modern medical problem and yet, despite decades of research and improvements in breast cancer treatment, the only currently effective means of reducing mortality from this disease is mammographic screening. Many countries around the world have therefore established mammographic screening services, even though there is ongoing debate regarding benefits and harms. Continuing research into all aspects of breast cancer is a priority. Until a better alternative to mammography screening becomes available, it is important for those involved in mammographic screening practice to maximize benefits and minimize harms by striving for optimal service quality.

HM

KEY POINTS

- Scientific evidence indicates that mammographic screening reduces mortality from breast cancer in women aged 50–69 years by approximately 30%.
- The benefit of mammographic screening for women aged 40–49 years remains controversial, although meta-analyses indicate a likely 15% mortality reduction.
- Benefits of mammography screening include mortality reduction for women with true-positive breast cancer diagnoses, and reassurance for those with true-negative normal results.
- Harms of mammography screening include anxiety and further testing for women with false-positive results, and inappropriate reassurance for those with false-negative results.
- Mammography screening services must aim to maximize benefits by offering a comprehensive and integrated service with high-quality radiography, radiology, multidisciplinary clinical assessment and treatment, and support.
- Ongoing monitoring and evaluation of mammography screening trials and services, and research into breast cancer remains of vital importance.

- Adami HO, Malker B, Holmberg L, Persson I, Stone B (1986) The relationship between survival and age at diagnosis in breast cancer. *N Engl J Med* **315**: 559–63
- Alexander FE, Anderson TJ, Brown HK et al (1994) The Edinburgh randomized trial of breast cancer screening: results after 10 years of follow up. *Br J Cancer* **70**: 542–8
- de Koning HJ, Boer R, Warmerdam PG, Beemsterboer PM, van der Maas PJ (1995) Quantitative interpretations of age-specific mortality reductions from the Swedish breast cancer screening trials. *J Natl Cancer Inst* **87**: 1217–23
- Emster VL, Barclay J, Kerlikowske K et al (1996) Incidence of and treatment for ductal carcinoma in situ of the breast. *JAMA* **275**: 913–18
- Feig SA (1995) Mammographic screening of women aged 40–49 years. Benefit, risk and cost considerations. *Cancer* **76**: 2097–106
- Fletcher SW, Black W, Harris R, Rimer BK, Shapiro S (1993) Report of the international workshop on screening for breast cancer. *J Natl Cancer Inst* **85**: 1644–56
- Henderson IC (1992) Biologic variations of tumors. *Cancer* **69**: 1888–95
- Jatoi I (1997) The case against mammographic screening for women in their forties. In: Jatoi I, ed. *Breast Cancer Screening*. Landes Bioscience, Texas: 35–49
- Kattlove H, Liberati A, Keeler E, Brook RH (1995) Benefits and costs of screening and treatment for early breast cancer. *JAMA* **273**(2): 142–8
- Kerlikowske K, Grady D, Barclay J et al (1993) Positive predictive value of screening mammography by age and family history of breast cancer. *JAMA* **270**: 2444–50
- Kerlikowske K, Grady D, Rubin SM et al (1995) Efficacy of screening mammography: a meta-analysis. *JAMA* **273**: 149–54
- Kopans DB (1997) The case in favor of mammographic screening for women in their forties. In: Jatoi I, ed. *Breast Cancer Screening*. Landes Bioscience, Texas: 9–34
- Lindfors KK, Rosenquist CJ (1995) The cost-effectiveness of mammographic screening strategies. *JAMA* **274**: 881–4
- Miller AB (1991) Screening and detection. In: Bland KI, Copeland EM, eds. *The Breast: Comprehensive Management of Benign and Malignant Diseases*. WB Saunders, Philadelphia: 419–25
- Nystrom L, Rutqvist LE, Wall S et al (1993) Breast cancer screening with mammography: overview of Swedish randomized trials. *Lancet* **341**: 973–8
- Palli D, del Turco MR, Buiatti E et al (1986) A case control study of the efficacy of a non-randomized breast cancer screening program in Florence (Italy). *Int J Cancer* **38**: 501–4
- Peeters PHM, Verbeek ALM, Straatman H et al (1989) Evaluation of overdiagnosis of breast cancer in screening with mammography: results of the Nijmegen programme. *Int J Epidemiol* **18**: 295–9
- Organizing Committee and Collaborators (1996) Breast cancer screening with mammography in women aged 40–49 years. Report of the Organizing Committee and Collaborators, Falun Meeting, Falun, Sweden. *Int J Cancer* **68**: 693–9
- Rosenquist CJ, Lindfors KK (1994) Screening mammography in women aged 40–49 years: analysis of cost-effectiveness. *Radiology* **191**: 647–50
- Shapiro S, Vanet W, Strax P et al (1982) Ten of fourteen-year effect of screening on breast cancer mortality. *J Natl Cancer Inst* **69**: 349–55
- Swift M, Morrell D, Massey RB et al (1991) Incidence of cancer in 161 families affected by ataxia-telangiectasia. *N Engl J Med* **325**: 1831–6
- Tabar L, Fagerberg G, Day NE et al (1987) What is the optimum interval between mammographic screening examinations — an analysis based on the latest results of the Swedish two-county breast cancer screening trial. *Br J Cancer* **55**: 547–51
- Tabar L, Fagerberg G, Duffy SW et al (1992) Update of the Swedish two-county program of mammographic screening for breast cancer. *Radiol Clin N Am* **30**: 187–210
- Verbeek ALM, Hendriks JHCL, Holland R et al (1984) Reduction of breast cancer mortality through mass screening with modern mammography: first results of the Nijmegen project 1975–1981. *Lancet* **i**: 1222–4
- Wright CJ (1997) Screening mammography: balancing the harm, the cost and the benefit. In: Jatoi I, ed. *Breast Cancer Screening*. Landes Bioscience, Texas: 65–80