Review Article

# The Singapore National Breast Screening Programme: Principles and Implementation

S C Wang,*MBBS, BSc (Med), FRANZCR

## Abstract

***The Singapore Breast Screening Project (1993-1996) showed that mammographic screening in Singaporean women shifts the size and stage of screen-detected breast cancers downwards and markedly increases the rate of detection of ductal carcinoma in situ, with acceptable recall, needle biopsy and interval cancer rates. Breast cancer is the leading cause of death in Singaporean women. Singapore has one of the highest age-adjusted breast cancer incidences in Asia. Although this is much lower than in the West, for women aged 45-49 years, the breast cancer incidence in Singapore is the same as for women in Australia, Canada or the United States. The latest Singapore Cancer Registry data shows that the age of peak incidence of breast cancer in Singaporean women has risen from 45-49 years in the period 1993-1997 to 50-55 years in the period 1998-1999. This suggests that the age-specific incidence of breast cancer in Singaporean women is shifting more to a pattern usually seen in Western nations. These factors, together with reconfirmed evidence of mortality benefit from breast cancer screening trials, led the Singapore government to establish the first population-based mammographic breast screening programme in Asia, the Singapore National Breast Screening Programme (BreastScreen Singapore). It uses a distributed model of mammography service, with centralised reading and assessment, co-ordinated by the Singapore Health Promotion Board. It is unique in that women co-pay at each step of the screening and assessment process. The programme, launched in January 2002, has adopted international standards of breast screening practice and breast cancer detection. To date, the initial targets for the first year have been met. Several key policies and issues over the programme's implementation are presented.***

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***Key words: Breast cancer detection, Breast cancer in Asian women, Implementation, Screening mammography***

## Introduction

In January 2002, the first population-based national mammographic breast screening programme in Asia, the Singapore National Breast Screening Programme (BreastScreen Singapore), was launched. The programme aims to achieve international standards of breast screening practice and breast cancer detection, as well as to reduce or stabilise the mortality from breast cancer in the country. In the first year, over 34,000 women were screened, with a cancer detection rate of almost 0.4%; 40% of the malignancies detected were ductal carcinoma in situ (BreastScreen Singapore data, unpublished).

This article provides a brief overview of the rationale for the establishment of BreastScreen Singapore and describes the overall structure and implementation of the programme. In addition, the unique financial structure of this programme and its implications are discussed.

## Terminology

Definitions of the technical terms used in this article are provided below:

- *Age-specific incidence (or crude incidence rate)*. The occurrence rate of new cancers per 100,000 women within a specific age range over a specific period. It does not correct for differences in population age distributions.
- *Age-adjusted incidence*. The rate of new cancers per 100,000 women per year ("women-years") over a specific time period adjusted for a reference age distribution (such as the 1970 world population statistics). It permits meaningful comparisons between differing national or regional cancer occurrence rates.
- *Mass or population-based breast screening*. Structured screening with a centralised administration, accreditation and audit system; systematic recruitment and re-screen processes; explicit quality assurance and performance measures and documentation; and systematic and regular reviews and audit processes, with central data collation and analysis. The goal of population-based screening is to increase the detection rate of early breast cancers, thus improving the overall population survival from breast cancer.

* *Associate Professor and Head, Department of Diagnostic Radiology, National University of Singapore*
*Chairman, Quality Assurance, Training and Education Committee*
*BreastScreen Singapore*
*Address for Reprints: Dr Wang Shih-Chang, Department of Diagnostic Imaging, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074.*

- *Opportunistic or sporadic breast screening*. Voluntary screening initiated by the woman, with the goal of excluding carcinoma by all reasonable means. It is not audited or systematically reviewed, has no explicit performance criteria and has not been shown to reduce cancer mortality. Table I lists the differences between mass and sporadic screening.
- *Prevalent round*. The initial round of screening. This will always detect a much higher number of cancers than the baseline incidence rate, because many malignancies which are detectable, but not yet symptomatic, are found. New candidates to the programme are technically in their prevalent round, though in fact many will have had prior screening mammograms.
- *Incident round*. The second and subsequent screening rounds of a programme, where women are invited to re-attend. Apart from interval cancers, incident rounds should detect most cancers at the baseline age-specific incidence rate for that population.

## Why Breast Screening in Singapore?

### *Breast Cancer in Singapore*

Breast cancer is the leading cause of death for women in Singapore. From an age-adjusted incidence of 20 per 100,000 in 1968-1972, it has doubled in the last 30 years to 46.1 per 100,000 in 1993-1997, a rise of 3.4% per annum.[1]

TABLE I: DIFFERENCES BETWEEN POPULATION AND OPPORTUNISTIC SCREENING

| Factor | Population | Opportunistic |
|---|---|---|
| Goal of screening | Reduce mortality | Detect cancer |
| Two-view mammograms | Yes | Yes |
| Quality assurance programme | National | Site-specific |
| Site accreditation | Yes | No |
| Co-ordinated invitation process | Yes | No |
| Specific entry criteria | Yes | No |
| Standardised re-screen interval | Yes | No |
| Subsidised or free screening | Yes | No |
| Subsidised or free recall | Yes | No |
| Number of readers | 2 with consensus 3rd | 1 |
| Formal reader accreditation | Yes | No |
| Audited reader performance | Yes | No |
| Audited cancer detection rate | Yes | No |
| Audited cancer miss rate | Yes | No |
| Multidisciplinary review and routine radiological-pathological concordance checks | Yes | No |
| Regular case review and CME | Yes | Sometimes |
| Evidence-based use of ultrasound | Yes | No |
| Proven mortality reduction | Yes | No |

Since then, it has increased further to 53.1 per 100,000 in 1998-1999.[2] Although this is the highest national age-adjusted incidence of breast cancer in Asia, it is half of that seen in Australian or Canadian women. It is, however, similar to the rate for Chinese women in the United States (US), which in turn is much higher than that for Chinese women in China. Breast cancer incidence statistics for various Asian and Western nations are shown in Figure 1. Overall, Singaporean women have the same breast cancer incidence as their US Chinese counterparts, increased greatly from traditionally low values such as are seen in China today. Japanese and Filipina women have a much higher breast cancer incidence than women in their countries of ethnic origin.

The age-specific rate of breast cancer in Singapore rises sharply from <20 per 100,000 women at 30 years of age to a plateau that starts at 166 per 100,000 between 45-49 years old, which peaks at 185 per 100,000 women at 50-55 years of age and levels off to a rate of 158 per 100,000 at the age of 80.[2] The shape of this curve, up to the age of 45-49 years old, follows that seen in Western women and then diverges; in the US, Canada and Australia, progressively increasing cancer incidence up to about 80 years of age is the norm, while for older Singaporean women the incidence peaks at 55 years old. Nevertheless, for Singaporean women aged 45-49 years old, the breast cancer incidence is similar to that in the same age cohort in Australia (1992-1996, 187.5 per 100,000),[10] Canada (1992, 170 per 100,000),[5] and the USA (1992-1996, 198.6 per 100,000).[4] It should be noted that the peak incidence of 185 per 100,000 was previously seen in the 45-49 years old cohort; it has shifted as these women have aged since the previous analysis.

These curves are compared in Figure 2. It should be noted from this figure that for the age range 45-49 years, Singaporean women have an age-specific breast cancer incidence as high as women of the same age from any Western country. Where they differ is that older Singaporean women have a much lower incidence than in Western nations. Hence, after the age of 60, the incidence of breast cancer actually declines. This is similar to the pattern in Korea, though the incidence is much greater in Singapore at every age. Note that the US Asian age-specific curve is intermediate between the Singapore incidence curve and the curves seen in Australia, Canada and US Whites; it is not inconceivable to speculate that the overall breast cancer incidence curve in Singapore will approximate the US Asian curve in the coming decades as these women age.

While the cause of this sharp peak in breast cancer incidence in Singaporean women is unknown, it is likely that the environmental, lifestyle, reproductive and dietary factors that accompanied Singapore's rapid modernisation over the last 35 years have had some part to play. It is conceivable that the breast cancer incidence in women who

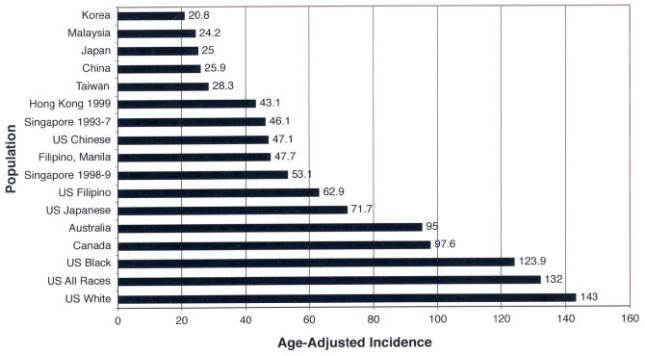


*Fig. 1. Age-adjusted incidence of breast cancer in women from various populations up to 1999. World data unless listed below, 1988-1992.[3] US data, 1992-1999 for Whites, Blacks and all races.[4] Canada data, 1992-1995.[5] Australian data, 1992-1996.[6] Singapore data, Singapore Cancer Registry. Hong Kong Data, Hong Kong Cancer Registry. Taiwan data, 1996.[7] Malaysia data, 1997.[8] Korean data, 1993-1997.[9]*

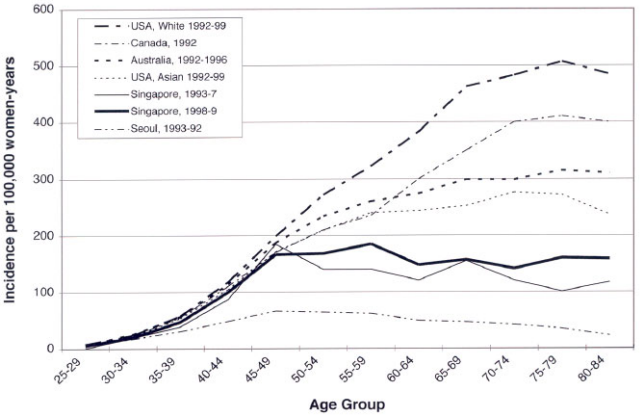


*Fig. 2. Age-specific incidence of breast cancer in Singaporean women in 1998-1999[2] compared to Singaporean women 1993-1997,[1] US Whites and Asians,[4] Canadian,[5] Australian[6] and Korean women.[9]*

grew up during this period of rapid modernisation will continue to rise as this cohort ages; the age of peak breast cancer incidence and its magnitude are expected to rise progressively in the coming decades.

### *Breast Screening in Singapore–Before the Programme*

In Singapore, sporadic screening has been the norm for the last 20 years. In our centre, women undergoing such screening typically have about a 20% chance of having additional views and/or ultrasound of the breast performed, usually at additional cost. The motivation for such practice is not to miss any cancer, regardless of the cost. Yet there is no evidence that improved survival will be the result of such practices.

One justification for this imaging usage is the widely held belief that mammography is not effective for breast cancer detection in Asian women. Yet there is good evidence from the Singapore Breast Screening Project that mammography is just as effective at early cancer detection in Asian women as it is in Western women.[11]

There are several alternatives to mammography for detection of breast cancer. However, none of them has any proven impact on survival. Intensive and well-taught breast self-examination has recently been shown to confer no mortality benefit.[12] Similarly, though ultrasound, magnetic resonance (MR) imaging and scintimammography can all detect mammographically occult cancers, none has been shown to affect survival.

### *Evidence for Mammographic Screening Stage Shift*

A key concept that underpins population-based screening with mammography is that the detection of smaller and pre-invasive breast cancer is highly desirable, as it greatly improves the likelihood of long-term survival. Even in the absence of mammographic screening, women with stage 0 or stage I disease have an almost 100% 5-year survival rate, while those with stage II, III and IV cancers have progressively lower 5-year survival rates.[13] Thus, one of the goals of a population-based programme is to shift the stage of diagnosis, as this is a surrogate for eventual mortality reduction. Indeed, without this stage shift, any reduction in mortality is highly unlikely.

There is no dispute that screening leads to a significant downward shift in the size and stage of screen-detected breast cancers compared to unscreened women; this has been repeatedly shown by various breast screening programmes, whether randomised or case-controlled. Furthermore, screening markedly increases the rate of detection of DCIS,[11,14,15] which has extremely high curative rates with appropriate treatment. The Singapore Breast Screening Project showed this "left-shift" in cancer size and stage for Singaporean women undergoing mammography.[11]

### *Mortality Reduction*

Mammographic breast screening has been shown to reduce breast cancer mortality in a number of trials. The Swedish Two-County trial of mammographic screening[16] has shown a significant reduction in breast cancer mortality in the group invited to screening [relative risk (RR), 0.71] up to 31 December 1996. The Edinburgh breast screening trial also showed a relative risk reduction in death of 0.71 [95% confidence interval (CI), 0.53 to 0.95] for women enrolled in the screening arm at 14 years follow-up.[17] Similar mortality reductions have been reported in the Stockholm trial[18] and the United Kingdom (UK) Trial of Early Detection of Breast Cancer.[19]

A 1996 review of the Swedish screening trials estimated the reduction of breast cancer-related mortality to be 24% for the whole group (40 to 74 years old at randomisation).[20] Another 1996 review of 4 of the Swedish breast screening

trials found that there was no significant difference in mortality between the screened and unscreened populations, *except for breast cancer mortality*,[21] implying that screening mammography was the main cause of improvement in breast cancer-related survival for the screened women.

*Controversies*

The near universal acceptance of the benefits of screening mammography was dealt a blow in 2000. Gøtzsche and Olsen[22] concluded that all the Scandinavian trials (except the Malmö trial) were biased because of slight imbalances in the baseline population. This review regarded the fact that national mortality rates had not significantly changed over the trial periods to be evidence of lack of effect of breast cancer screening. It rejected breast cancer specific mortality as a valid outcome measure because of possible assignment bias, and rejected all data from these trials despite a relative RR of 0.75 (95% CI, 0.67 to 0.83) for breast cancer specific mortality seen in the screened group. The two trials assessed to be unbiased (the Canadian NBSS and Malmö trials) showed no effect of screening on breast cancer or total mortality.

There were various contrasting and strongly worded responses to this review:

1. It was supported by a few naysayers, who have consistently opposed breast screening because of the resources that have to be devoted to it,[23-25] and who wanted breast screening programmes to either be terminated[26] or to never start in the first place.[27]
2. The conclusions of this review were strongly rebutted in letters from several international experts.[28-35] They pointed out that mass screening trials using a regional randomisation methodology cannot perfectly match the control and screening groups, that breast cancer mortality should not be discarded as an outcome measure, and that Gøtzsche and Olsen dismissed the relevant trials without sufficient grounds.
3. In 2002, a detailed re-analysis of the Swedish trials[36] directly addressed most of the issues raised by Gøtszche and Olsen, including analysis of some of the original trial data which had not been available previously. This review also added data from the continuation of the Malmö trial (MMST II). At the median follow-up time of 15.8 years after enrollment, there was a significant reduction in breast cancer mortality (RR, 0.79; 95% CI, 0.70 to 0.89) in the screened women. The authors concluded that the recent criticism against the Swedish randomised controlled trials (RCTs) was misleading and unfounded, and that screening *did* confer a survival advantage.

Furthermore, previously reported evidence of contamination (i.e., the use of mammography) in the control groups in the Canadian[37] and Malmö trials[34] were ignored by Gøtzsche and Olsen. A recent review by Demissie et al[38] performed statistical adjustment for this effect. They showed that the reported summary risk estimates of RCTs (RR, 0.76; 95% CI, 0.69 to 0.83) were similar to that from case-control studies (RR, 0.44; 95% CI, 0.38 to 0.50) after the adjustment. In other words, the efficacy of mammography in women >50 years old is probably *greater* than the effectiveness reported by RCTs.[38]

The triallists from the Swedish Two-County trial have recently used an alternative approach to determine the survival benefit from service (as distinct from trial) screening in two Swedish counties.[39] Breast carcinoma-specific mortality was compared across three periods: 1968-1977, prior to screening mammography; 1978-1987, the period of the Two-County RCT; and service screening from 1988-1996, with a correction for self-selection bias to prevent overestimation of the benefit of screening. The breast carcinoma mortality for women aged 40 to 69 years who were actually screened during the service screening period, adjusted for selection bias, was reduced by 48% (RR, 0.52; 95% CI, 0.43 to 0.63) compared to the period when no screening was performed. Again, this implies that service screening should actually have a *higher* survival benefit for screened women than has been reported in RCTs. Finally, a recent report from the Malmö triallists using a similar approach directly contradicts the assessment that the Malmö trial shows no benefit from screening; the age-adjusted breast cancer mortality for Malmö trial participants was significantly decreased by 43%, compared to 12% for the rest of Sweden ($P$ <0.001).[40]

While the effect of screening on mortality in Western populations has been confirmed, it remains controversial in Asia as there is no comparable trial data. A recent review from Hong Kong confirms the validity of the mortality reduction shown by previous trials, but argues, using only estimates of recall and biopsy rates, that the false positive rates for screening in Asian women would be too high and that the cost would be unacceptable for the anticipated yield.[41] Surprisingly, the authors claim that the sensitivity and specificity of screening mammography in Chinese women would be less than in Western women. This was despite the fact that the Singapore Breast Screening Project had already debunked this myth and that a recent study of mammographic screening from Hong Kong had shown figures for cancer detection comparable to the Singapore Project.[42]

After careful consideration of the controversial reviews and their replies, all the existing breast screening programmes have continued unabated. In this climate, BreastScreen Singapore was launched in January 2002.

## A Breast Screening Programme for Singapore

### *Plan to Control Breast Cancer*

In September 1998, the Workgroup On Breast Cancer was set up to study the feasibility of a Breast Cancer Screening Programme, to work out a public education plan on breast cancer education and to regularly update the government's Committee on Women's Health. This workgroup achieved a number of goals:

- Development of a standardised breast "health message" for Singaporean women.
- Strengthening of public education about breast cancer and screening to Singapore women in the target groups.
- Publication of Guidelines for Quality Control in Mammography through the Academy of Medicine, Singapore. These became the foundation for BreastScreen Singapore's mammography accreditation guidelines.

The Workgroup also drafted "The Plan to Reduce Breast Cancer in Singapore", which proposed 3 major initiatives, all of which were accepted and announced by the Ministry of Health:

- Mammography units would be installed in all government polyclinics in Singapore.
- All women aged 50 to 64 years would be eligible for 50% subsidised funding for screening mammography at these units.
- Improved community awareness of breast cancer screening would be raised through an intensive health education programme.

There were 2 major deficiencies in this proposal. First, there was no explicit mechanism to ensure consistent and high quality breast assessment. Second, there were no recommendations for professional training and development, accreditation standards, audits, review of processes or data collection crucial to the delivery of a high-quality screening service. In short, the proposal could deliver more and cheaper mammography without any processes to ensure that this was of a high quality, or any way of determining whether it was beneficial in the long run.

The accuracy of screening mammography is highly dependent on the quality and consistency of the screening mammograms, for which there are stringent technical requirements. This area received the greatest blame for the poor results of the Canadian Breast Screening Study: most mammograms were performed at general radiology practices around the country without formal training, quality assurance and audited feedback.[43]

The various trials of breast screening have shown that accurate detection and diagnosis also requires more than just the provision of mammography. Accurate assessment using explicit and well-established criteria for needle biopsy can markedly reduce the rate of negative open surgical breast biopsies. Historically, the ratio of benign to malignant breast lesions at open biopsy in Singapore is estimated to be between 10:1 and 16:1 (T S Iau, G S Hong, 2002, personal communication). However, through expert and structured breast assessment, dedicated assessment centres can reduce the benign-to-malignant surgical biopsy ratio to about 1:1 in the prevalent round,[44] and can reach as low as 1:3[45] or 1:5 (M Rickard, 2002, personal communication) in the incident rounds.

### *The National Committee on Cancer Care (NCCC) Report*

In mid-2000, the NCCC formed a subcommittee to critique the above plan, review the evidence for breast screening and determine whether a formal breast screening programme within Singapore was warranted. The subcommittee concluded that the weight of evidence was in favour of breast screening in Singapore, but that the costs and resources required were significant. It recommended establishment of dedicated breast screening and assessment centres with dedicated staff external to the existing institutions, with full funding of screening to the point of final diagnosis. These recommendations were modelled after the Australian or UK breast screening programmes.

### *Creating the Breast Screening Programme*

The steering committee for the National Breast Screening Programme was formed in mid-2001, under the auspices of the newly formed Health Promotion Board (HPB), to oversee the development of the programme. The Committee was informed that:

- The programme was to be the first of a series of cancer screening programmes to be implemented.
- The programme was to have an accelerated timeline for launch by January 2002, with progressive expansion of the programme till the end of 2008.
- Full evaluation of the success of the programme would occur after 2008, but interim evaluation of the programme's progress would be monitored annually.
- The Ministry had decided on a distributed model for the screening mammograms, using the already announced subsidised polyclinic-based mammography units, with a few designated hospital-based reading and assessment centres.
- Initially, there would be 2 designated breast screening assessment centres, one for each health cluster in Singapore. More such centres would be set up as the demand increased.
- There would be no start-up government funding for the establishment of polyclinic screening centres or hospital assessment centres; funding would have to be obtained

through the existing funding mechanisms.
- Women would co-pay for breast screening, recall assessment and any diagnostic biopsies through the existing health system subsidies.
- The Ministry of Health's funding commitment was to the planning, co-ordination and implementation of breast screening programme management through the HPB.

The HPB, in turn, created 3 committees for:

- Quality assurance, accreditation and training, which became the key medical advisory and implementation working group for the programme.
- Development of a centralised, integrated database for screening registration, reading results and assessment outcomes, with linkage to the National Cancer Registry.
- Development of publicity and education programmes on breast screening for the public and general practitioners.

*Key Policy Issues*

The first problem was to coin an appropriate name for the Programme. An internal competition resulted in "BreastScreen Singapore" being adopted, based on the name of the Australian programme. Other key policy issues for the programme are discussed below:

*Status of Women*

Women attending breast screening should, by definition, be asymptomatic and well. Women with admitted breast symptoms, such as a palpable mass, are encouraged to seek a specialist opinion instead of attending the programme, though not all admit to such symptoms until after screening has been performed. A process to ensure such women are recalled for assessment and clinical examination is in place.

Thus, until a diagnosis of breast cancer is made, the participants are not patients, but clients. If a diagnosis of breast cancer is established, they leave the programme until they have shown at least 5 years of disease-free survival, after which they can rejoin the programme.

However, for the purposes of billing and reimbursement within the assessment centres, all clients are registered as patients in order to use the existing funding mechanisms and accounting infrastructures.

*Eligibility for Screening*

Pooled data from several trials have suggested a survival benefit for women who were screened under the age of 50. Proponents of breast screening had also argued that screening should occur from the age of 40 onwards.[43] In 1997, an analysis of women aged 40-49 years from 4 of the Swedish trials showed a 23% reduction in breast cancer mortality, using a screening interval of 18 to 24 months.[46] However, in a 1999 review, the Two-County Swedish triallists noted that the incidence of grade 3 tumours in the screened group aged 50-74 years was significantly lower than that in the unscreened group, but this was not the case for women aged 40-49 years.[16] The authors ascribed the lower efficacy of screening in the latter to the 2-year screening interval and recommended that these women should be screened annually.

Jansen and Zoetelief[47] have calculated that the benefits of screening are more marked in younger than in older women, with a high screening frequency resulting in more lifetime gained. However, the cost of saving years of life in this age group would be at least twice as much for each cancer detected as for women in the 50-69 years age group. After some internal debate, a compromise was adopted for this prognosis. Women aged 50-64 years would be actively invited to participate, while women aged 40-49 years and >65 years were not actively invited, but would be permitted to participate. All participants would be reminded to have repeat screening annually from the ages of 40-49, and at 2-year intervals if they were >50 years old.

*Funding*

The Ministry of Health had determined that this was to be a co-funded programme. Participants would pay part of the cost for screening, assessment and diagnostic biopsies under existing subsidy rules. This meant that, with the exception of subsidised mammography, the existing funding mechanisms and the underlying co-payment philosophy of the Singapore health system could remain unchanged.

In other national breast screening programmes, screening is free to the clients up to the point of diagnosis. However, one major criticism of such programmes is that, without a long-term self-sustaining funding strategy, the cost to the society becomes progressively greater. The ability to expand as needed, also becomes progressively more difficult. Finally, they may divert money away from other valuable programmes that may benefit more people.

A central tenet of the healthcare system in Singapore is the emphasis on personal responsibility. Hence, co-payment is the norm for all health services. This aspect of BreastScreen Singapore may prove to be crucial for the long-term financial health of the programme. Financial modelling shows that the screening mammography should become self-sustaining after 3 full years of operation, provided the projected screening targets are met. However, at this point, there is a significant discrepancy in subsidised reimbursement among the existing assessment centres.

*Film-Screen versus Digital Mammography*

Consideration was given to using digital mammography from the beginning of the programme. In concert with a fully computerised registration, reading and results database, digital mammograms would permit higher speed screening

and more efficient storage than would be possible with film. Digital mammography also enables image distribution for reading to a variety of centres, allowing balancing of the screen reading load amongst radiologists at different locations. Digital mammograms can also be easily and automatically "read" by computer-aided diagnosis (CAD) systems, which hold the promise of replacing one of the readers with no significant loss in accuracy, while greatly improving the throughput of the screening system.

It should be noted that the cost of storing and retrieving digital mammograms is dependent mainly on the cost of disk space, which falls markedly each year. The cost of storage of digital mammography falls as the number of examinations increases, while the cost of film storage increases geometrically over time. Because of the need to review cases in detail and to compare screening films, film-screen mammograms must be stored at the reading centres; in most programmes they are never culled. With this model, and using the HPB projections for the target population and screening participation, it is estimated that more than 3 million films will be stored by the end of 2008 if the programme continues to be based solely on films (Fig. 3).

Unfortunately, the start-up cost of digital mammography systems remains very high. It would have been necessary to develop expensive high-speed network connections between polyclinic sites and reading centres, as well as a large-scale Picture Archiving and Communication System. This would have taken at least 2 years to plan and implement, which would have greatly delayed the launch of the programme. There is only limited evidence that digital mammography should replace film-screen mammography in mass breast screening, or that CAD could actually replace a second human screen reader. In the short term, the benefits of digital mammography would derive from increased daily throughput, more consistent image quality and lower long-term costs of image storage and retrieval.

*Standards and Accreditation*

Throughout the debate over the effectiveness of population-based screening mammography, there was no discussion about the ineffectiveness of sporadic or opportunistic breast screening. On 27 June 2002, a new controversy erupted over an article published in the New York Times.[48] It pointed out that, despite various regulations and excellent published guidelines, even experienced radiologists could miss up to 30% of detectable cancers on screening mammography. It should be noted that there is no national breast screening programme in the US, and that the vast majority of mammograms are read by a single reader.

Reading screening mammography is a difficult perceptual skill with a significant learning curve. It is also prone to human error. A single reader can miss up to 31% of cancers,[49] and that a second reader may increase the cancer

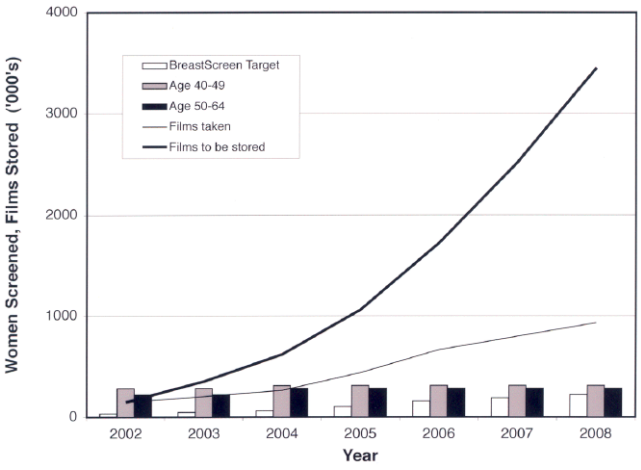


*Fig. 3. Projections of women to be screened in Singapore 2002-2008, compared to the number of films to be taken and stored over this period. These figures assume the Singapore population estimates for 40-49 years and 50-59 years are correct and that the BreastScreen Singapore targets for screening participation are met (the screening target of 35,000 for the first year was met). A uniform 6% recall rate has been assumed.*

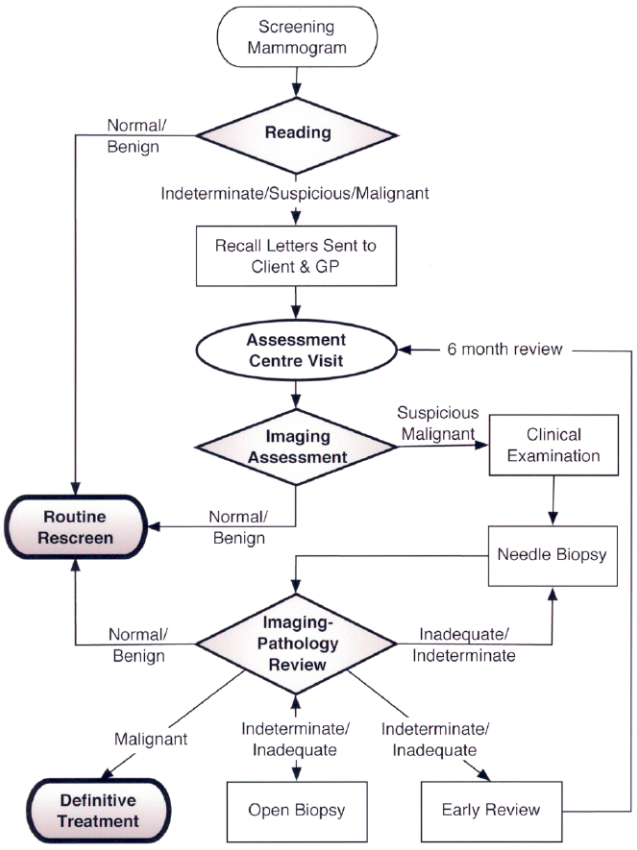


*Fig. 4. Screening and recall assessment flowchart. This simplified diagram shows the main steps in breast screening workflow. Findings after biopsy must be concordant with the imaging findings at Imaging-Pathology Review. Discordant findings may require repeat biopsy or surgical excision. In general, the use of Early Review is discouraged as it is of limited value.*

detection rate over a single reader significantly.[50,51] Nevertheless, despite the almost universal use of dual readings in population-based programmes, it is recognised that the interval cancer rate (cancers that appear between routine screening episodes) will be about 10% of all cancers detected, typically at a level of about 10 per 10,000 screens at 2 years.[52-55] Only about one-third of these will be deemed detectable as suspicious lesions on retrospective review.[56] Thus, it is likely that there is a minimum level of interval cancers when mammography is used in screening,[16] which depends on the screening interval and size of the tumours at detection.[57] More effective screening would require the use of additional tests, none of which has been trialled using survival as an endpoint, and all of which currently increase the cost of screening with a high false positive rate.

The quality assurance subcommittee decided to model the standards and processes of BreastScreen Singapore on the Australian and UK national breast cancer programmes, as well as to learn from the Scandinavian programmes and the extensive documentation produced by the American College of Radiology and the US Mammography Quality Standards Act (1994). In doing so, the Singapore national programme explicitly embraced the best international standards of practice. Members of the HPB visited breast screening programmes in Australia and the UK. The former Director of the most established breast screening centre in Australia, Dr. Mary Rickard, was engaged to advise the HPB and the quality assurance subcommittee on the development of the programme and its processes.

The quality assurance subcommittee established documented standards for all the polyclinic and private screening centres. Accreditation teams were also created to perform site accreditation visits for each centre. Dual readings were adopted as the screening paradigm to maximise cancer detection and to minimise unnecessary assessment recalls. A scoring system with 5 categories adapted from the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) was used. The scores signify the level of suspicion for cancer and indicate a specific course of action (Table II). This system is similar to that used by BreastScreen Australia.

Discrepancies are "super-read" by a third breast radiologist. The resulting forms are sent to the HPB for data collation and to generate recall letters, explicitly requesting clients to return to a designated assessment centre for assessment. Each reader must satisfy the experience criteria in order to read for the programme, attend regular continuing medical education (CME) on breast imaging each year, attend regular feedback sessions on biopsy results and imaging, and read a minimum number of examinations in a year for the programme, with recall, miss and diagnosis rates for cancers lying within the target ranges for the programme.

Recently, one reading centre in Singapore has adopted the same criteria and methodology to read *all* screening mammograms, regardless of whether the women are enrolled in BreastScreen Singapore. It was illogical and impractical to perform breast screening with 2 differing sets of standards and principles. This is an example of a major benefit of structured screening mammography that is largely not discussed in the literature: it raises the general standard of practice for breast cancer detection and management.

### *Target Standards*

As discussed above, breast screening without any explicit performance targets for individuals and centres, as well as without any audited detection and miss rates, cannot ensure a consistently high standard of mammographic screening. Open and transparent targets allow the detection of poor performance and to take the necessary corrective actions.

In a 1992 review of the Swedish Two-County trial, Tabar et al[58] noted that in order to achieve significant mortality reduction, certain targets should be met by screening mammography:

- Fifty per cent of screen-detected invasive cancers should be <15 mm in size.
- Thirty per cent of screen-detected grade 3 tumours should be <15 mm.
- Seventy per cent of screen-detected tumours should not have lymph node metastases.
- Breast cancer prevalence at the first screen should be 3 times the expected incidence rate in the absence of screening.
- The recall rate for further examination should be 9%.

The Australian experience has shown that these standards can generally be exceeded under appropriate conditions. The HPB has adopted similar targets for the Singapore programme. Radiologists and centres under BreastScreen

TABLE II: BREASTSCREEN SINGAPORE MODIFIED BI-RADS SCORING SYSTEM

| Score | Interpretation | Risk of CA | Action |
|---|---|---|---|
| 1 | Normal | <0.1% | Routine re-screen |
| 2 | Benign lesion | <0.1% | Routine re-screen |
| 3 | Indeterminate | 2% | Recall for assessment |
| 4 | Suspicious | 30% | Recall for assessment |
| 5 | Malignant | 97% | Recall for assessment |

BI-RADS: Breast Imaging Reporting and Data System; CA: carcinoma
Statistics adapted from Orel et al.[65]

Singapore receive regular reports on individual and centre recall and cancer diagnosis rates.

*Standardisation of Pathologic Reporting*

A key component of accurate diagnosis and optimal management, particularly for borderline and early breast malignancy, was standardisation of criteria and terminology for pathology reporting for the various centres. The pathologists are key members of the quality assurance sub-committee and have been very active in developing the reporting standards, pathologic reporting fields for collation and analysis, and educational programmes for pathologists involved in the programme. It is to be expected that these measures to publicise the requirements and improved pathology reporting standards for patients with breast cancer will result in better data collection and the ability to monitor the efficacy of the programme before mortality data become available.

## Practical Issues

*Participation*

It is generally accepted that high participation and compliance rates are necessary for a breast screening programme to achieve significant mortality reduction, though there is no agreement on the precise level needed. A rate of over 70% has been reported by the Stockholm programme.[59] While the Singapore Breast Cancer Screening Project had a response rate of only 42%,[11] this was obtained through electoral roll-generated letters of invitation only, with no general practitioner involvement, mass education campaign or community recruitment programme. BreastScreen Singapore has adopted a target of 70% participation rate for women aged 50-64 years by the end of 2008.

It has been shown that 2 factors are much more effective at ensuring participation than mass media promotion: community or grass-roots participation,[60] and family practitioner encouragement.[61] BreastScreen Singapore and the 2 health management clusters in Singapore have targetted general practitioners as key partners to involve women in breast screening. The development of a community education and participation system will take time, but it is much cheaper than mass media campaigns, and may well be the most successful recruitment and participation strategy in the long term.

## Training and Continuing Education

Several strategies have been taken to try to increase training and raise the level of skills of existing and new staff, particularly during this initial and rapid expansion phase of the programme. Accreditation guidelines for centres explicitly state the minimum requirements for various medical personnel to participate and to remain in the programme. An annual BreastScreen educational seminar for all medical personnel has been established, which invites international and local experts to teach staff both at the seminar and in their institutions. The HPB has provided partial funding for doctors in the programme to attend overseas courses in breast screening and assessment. BreastScreen Singapore has engaged experts from Australia to spend some weeks in Singapore to review our processes and to provide advice based on hard-won experience. In addition, a structured programme will be developed to train radiographers in mammography.

## Recall Assessment Process

Once a woman has had 2 readers decide that she should be recalled for further assessment, BreastScreen Singapore generates letters to the client and her nominated general practitioner to inform them that she should make an appointment to attend a designated assessment centre. The overall process for recall and assessment is outlined in Figure 4. BreastScreen Singapore's recall assessment process operates on an intention-to-diagnose basis. Once a woman is recalled, the assessment process is not complete until either the mammographic findings are shown to be benign or a diagnosis of malignancy is made. Short-term follow-up imaging at 6 months is optional, but has been shown to have an extremely low cancer diagnosis rate for lesions designated as being "probably benign";[62] therefore it is discouraged.

An assessment clinic requires several dedicated staff to evaluate up to 25 women a day who have been recalled based on their mammographic or symptomatic findings. As such, additional mammographic views, ultrasound and clinical examination may be performed. It should be emphasised that the majority of women recalled will not have breast cancer; their initial mammograms simply suggest there is a finding which requires more investigation.

## Comments and Conclusions

Despite the strong evidence that mammographic breast screening is effective in reducing breast cancer mortality, the troubling fact is that a very high number of women have to be screened in order to save a life. This is influenced by the baseline incidence and estimated RR reduction afforded by a particular programme. The number that needs to be screened has been estimated to be as high as 1300 women for 10 years in Hong Kong[41] and 666 women for 10 years in the US.[63]

It has been argued that this represents too high a cost in terms of dollars per life-year saved, and too great a cost in terms of psychological trauma associated with recall and assessment, even when the outcome is negative. However,

breast cancer is an emotive and politically charged area of healthcare. There are strong social and political pressures on a healthcare system and government to act, or be seen to act, to reduce mortality from breast cancer, particularly when it is the most common cancer in women, when the incidence is increasing progressively over time and early detection using a proven technology is a highly visible objective. Ultimately, the decision to implement a breast screening programme is not purely financial or evidence-based, but must have a strong combination of social demand and pressure, financial and technical capability to provide the requisite high standards, and administrative organisation to co-ordinate and audit the programme. Finally, a strong political will to make this decision is needed; once it is made, it is difficult to reverse.

The Singapore National Breast Screening Programme has come into being because of all these factors. It is unique as being the only mass breast screening programme in Asia, and the only co-payment, centrally co-ordinated breast screening programme in the world. Though not a trial, it nevertheless aspires to the best of international standard practice for service breast screening, with its ultimate goal to reduce the breast cancer-specific mortality rate. The financial system adopted acts to ensure that costs are minimised, service standards are optimised and there is progressive expansion of the service as screening volume grows over time. This model permits a calibrated growth of screening mammography as recruitment becomes more intensive, yet ensures a reasonable fee for screen reading that will keep radiologists interested in being involved as the workload increases.

The programme is now over 12 months old. Since its launch, international standards of accreditation, mammography, screen reading, education, training and review have been put in place, though in practice standards are still rising and more education and training are required. The initial targets set for the number of screens, recall rate and cancer detection have been met. It is hoped that the programme's results for cancer detection in Singaporean women will justify all the planning and effort to implement it.

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