Breast Cancer Screening:
How Important Is It?

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Over the last few years, breast cancer screening in the form of mammography and palpatory breast examination have come under intense scrutiny. The scrutiny is due to new reports which suggest no benefit to these decade long tenets.

In 2001, the Cochrane Collaborative Group published the results of a meta-analysis of the effectiveness of screening mammography in decreasing mortality from breast cancer. Authors concluded that mammography failed to decrease breast cancer mortality and, hence, screening mammography is unjustified. In contrast, the U.S. Preventive Services Task Force (USPSTF) updated their screening recommendations in 2002. A meta-analysis of the same randomized, controlled trials (RCTs) recommended screening mammography for all women starting at age 40 (evidence B recommendation). Depending upon what academic society one reads for guidelines, there is support for the use of mammography and multiple variations about who should be screened, when, and how.

Breast cancer risk factors

- Age
- Female
- Family history
- Fibrocystic breast disease
- Age at menarche and menopause
- Age at first pregnancy
- Genetic BRCA1 and BRCA2
- Environmental

When do I start screening?

Disturbingly, there have been only two Canadian RCTs for screening by mammography. Both trials have been negative. Furthermore, a recent trial regarding breast self-examination (BSE) has suggested the practice is deleterious to the female population, and should be discouraged and discontinued, such that the Canadian Task Force on Preventive Health Care no longer recommends BSE (D Recommendation).

Why the opposing conclusions?

Except for the Canadian studies, other randomized, controlled (RC) screening studies have shown that mammography decreases breast cancer death. Controversies exist about the validity of some of the RC screening mammography trials and, hence, their inclusion in the various meta-analyses differ. As a result, the conclusion about the efficacy of screening mammography is polarized.

In 1995, Kerlikowske and colleagues combined the results of the randomized trials and case-controlled studies to date, and used statistical models to evaluate the data. They found a protective benefit of screening mammography for women aged 50 to 74 (a 26% decrease in breast cancer mortal-

ity). There was no benefit for women aged 40 to 49 (Table 1).

In the Cochrane meta-analysis, eight RC screening studies were reviewed. All but two (the Canadian and Malmo studies) were excluded. With the Canadian and Malmo studies, there was no reduction in mortality in women less than or greater than 50 at seven and 13 years duration. When the three poor validity studies were included, there was a decrease in breast cancer mortality of 15% and 20% at seven and 13 years, respectively. The protective effect of screening was slightly higher for women older than 50, with a 25% and 24% risk reduction at seven and 13 years of followup, respectively (Table 2).

In contrast to the Cochrane Group, the USPSTF performed their own meta-analysis of the same trials and came to the conclusion that mammography does decrease breast cancer mortality. The pooled effect of the valid studies that included women aged 40 and older was a 16% reduction in breast cancer death in women who were screened. For women aged 50 and older, the protective effect was 22% after 14 years of observation.

One must acknowledge the limitations to RCTs and meta-analyses. RCTs are not true efficacy studies for testing a technology, and are analyzed on the intent-to-treat basis, whether the patients actually complete the arm or not. Compliance and crossover from one study group to another is an issue. All the mammography trials reviewed reported crossover contamination, which was as high as 25% in the Malmo and Canadian studies.

With respect to the limitations of the mammography meta-analyses, the intervention combinations differed with only some, including CBE. The imaging techniques and views also differed, as did the equipment. The degree of compliance and crossover, and the varying duration of followup, all are important factors impacting on the final outcome.

Frequently Asked Questions

What has resulted from the confusion in the media about breast cancer screening?

Death due to breast cancer is decreasing. Early detection through mammograms and good clinical examination play a part. Better treatments with new drugs, radiation, and surgery are also are important. At this time, we believe that mammography does help to prevent breast cancer in some women. In others, treatment may be important. With more information, we will be able to figure out how to improve the prevention and cure for breast cancer.

When should your patients have a mammogram?

If your patients are otherwise healthy, without a history of a close relative with breast cancer, they may benefit from clinical breast examination and mammography every year or two starting from the age of 50. It is unclear whether it is beneficial to have screening mammograms before 50 in this patient group. Their breasts tend to be denser and more difficult to evaluate. A number of non-cancerous lumps and bumps are common and may be detected. It is therefore important that you discuss breast health with your physician and make a plan for breast examination within your overall health plan.

When should patients examine their breasts?

There can be many changes and conditions that are not indicative of cancer. It is important to know about changes and what is normal for your patients. Patients should conduct a breast self-exam every time they partake of daily hygiene. Before their period, breasts become tender and the glands inside them may become firm and fuller. This gets better after their period.

Table 1
Summary of randomized control trials of mammography screening

Study (year began)	Age	Screening interval (months)	Followup (years)	ARR in BC mortality (per 1,000)	BC mortality* RR	Number needed to screen†
HIP(1963)	40-64	12	13	1.4193	0.83	916
Malmo (1976)	45-70	18-24	11-13	1.0127	0.81	1,185
2 Country (1977)	40-74	24-33	10	1.8095	0.68	553
Stockholm (1981)	40-64	24-28	7.4	0.5369	0.71	1.378
Gothenberg (1982)	39-59	18	8	0.3286	0.86	2,435
Edinburgh (1979)	45-64	24	14	0.945	0.71	1,482
Canada 1 (1980)	40-49	12	13	No reduction	0.98	N/A
Canada2 (1980)	50-59	12	10.5	No reduction	1.14	N/A

ARR: Absolute risk reduction BC: Breast cancer RR: Relative risk N/A: not applicable
*Length of followup reported for various times up to 20 years. Data estimates were closest to 10-year point
†Number needed to screen corrected for 10 years of screening

Why did the Canadian studies fail to show a benefit?

In the Canadian trials, all women received a thorough clinical breast examination (CBE) (at least 10 to 20 minutes of thorough palpation at the time of mammography and in the control setting). A possible interpretation is that the thorough CBE was equal to mammogram in these women over 50. Concerns and criticisms included using a volunteer self-selected population as opposed to an invited group after randomization at the initiation of the intervention, and having many more cases than controls with poorer prognosis breast cancer (four or more lymph nodes). Fewer deaths than expected occurred in both groups, hence there was insufficient power to detect a 40% difference in outcome (beta error).

In contrast, all the other studies that included women under 50 found some benefit with the USPTF finding (a 15% reduction in breast cancer deaths). It took eight years to see these effects, so the younger women were older than 50 before they benefited from screening. If the Canadian study was excluded (in a separate analysis because its participants were prescreened volunteers), the risk reduction of breast cancer death increased to 20%. Similarly, there is also controversy about whether the Malmo trial was a negative trial, as positive results emerged after the eighth year for women 55 to 69.

What are the adverse events?

Participants of screening mammography are more likely to undergo an intervention than non-participants. According to the Cochrane review, 23% of

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Table 2
Summary of meta-analyses

Title (year)	Trials included	Outcomes
Kerlowskie 1995	All RCT and case controlled studies to date	RR: 0.74 in women 50 to 74 (95% CI, 0.45-0.77).
Cochrane 2001	Canadian, Malmo (medium validity)	Zero benefit in any woman at 7-13 years.
	Adding 3 poor validity trials: Two-country Stockholm, Gothenberg	RR: 0.85 (95% CI, 0.73-0.99) at 7 years.
		RR: 0.80 (95% CI 0.71-0.89) at 13 years. Benefit slightly higher in women > 50, 25% RR at 7 years, 24% RR at 13 years.
U.S. Preventive Services Task Force 2002	All 7 studies except Edinburgh	For women > 40, RR, 0.84 (96% CI, 0.77-0.91). NNS=1008 (95% CI, 531-2128).
		For women > 50, RR, 0.78 (95% CI, 0.70-0.87) after 14 years. NNS=838 (CI, 494-1676).
	All studies except Edinburgh and Canadian	RR, 0.80. NNS = 1385, no CI specified.

RCT: Randomized control trial
RR: Relative risk
CI: Confidence interval
NNS: Number to screen to prevent 1 death

screened women were more likely to have a radical mastectomy, 35% more likely to have a simple mastectomy or lumpectomy, and 25% more likely to have radiotherapy. It has also been suggested that some women would be excessively treated for indolent quiescent tumours that would otherwise not require intervention if they were not artificially detected. These conclusions are troubling and have been challenged by a number of independent reviews which believe the Cochrane analysis is flawed and, hence, the conclusions suspect. The claim that radiotherapy resulted in excess CVS deaths was attributed to older studies and believed to be inconsistent with current practices for radiation planning to the chest area. A recent Italian study showed that mastectomy rates had fallen 40% since the establishment of a policy of offering breast cancer screening with mammography.

It has been estimated there is a 6.5% probability of false positive results with each mammogram and a 5% to 7% probability of a false negative result in light of a palpable cancer. Women have a one in three chance of having a false positive mammogram 24%, or CBE 13%, after 10 years.

What is the role of clinical and breast self-exam?

The USPTF concluded there is insufficient evidence to recommend routine CBE, since there have been no studies comparing CBE to no screening in the general population. Studies looking only at CBE suggest that the sensitivity of CBE for picking up invasive breast cancers is 69% in women who have not had regular screening, and 30% in regularly-screened women. Because breast cancer is more common with increasing age, a mass found in an older woman, on CBE is four times more likely to be cancer than a mass detected in a younger woman. Three to five women out of every 100 who undergo CBE will have a false positive finding.

The effectiveness of BSE has been criticized recently, and has received a D Recommendation by the USPTF. There has been given no evidence

of benefit, or evidence of harm in light of the excess followup, further testing, and biopsies for detected benign disease. In addition to the recent Canadian study, a Chinese study of women trained in the workplace showed there was no difference in breast cancer incidence or mortality in the BSE group, but double the biopsy rate. Women do find cancers on BSE, but whether they are on intentional BSE or accidental findings is difficult to differentiate. Other studies show that tumours found on CBE and mammography are much more likely to be localized than advanced at detection.

What's the ideal interval for screening?

Little is known about the optimal interval for screening mammography in the general population. Among the eight RC screening studies, there is wide variation in screening interval from annual to every three years. A U.K. study shows no difference between screening once per year and every three years, for the outcome of mortality or late stage disease. The study was done, however, only after a short interval of three years. Importantly, this would have to consider the natural history of breast cancer development, and identification of a growth to a detectable size on mammogram.

In contrast, cervical cancer screening with Pap smears is initiated within three years of sexual activity, or by the age of 21. Annual screening is the norm until three normal satisfactory Pap smears are obtained. Screening can then be decreased to every two or three years, at the discretion of the health-care provider and the patient.

Is there a role for organized breast cancer screening?

There is limited literature evaluating organized versus opportunistic breast cancer screening. A number of studies from British Columbia, which has the longest experience with organized breast screening, suggest there are better process measures, such as lower cost associated with organized screening. A number of provinces are now implementing organized breast cancer mammography and CBE programs.

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Where are we now?

According to the last U.S. National Health Survey, the goal established for 60% of surveyed respondents over 50 to have a breast screening mammogram and CBE in the preceding one to two years was surpassed at 64%. There was a doubling in "recent use" reported by respondents, during the late '80s and early '90s.

The controversy regarding breast cancer screening and mammography, in some ways parallels that of cervical Pap smear screening, which is now established as a standard of care to be improved upon. In contrast to the multitude of RCTs and meta-analysis pooling over 500,000 women with mammography, there has never been a RCT to evaluate the effectiveness of the Pap smear. To do so would be considered unethical.

Approximately half of cervical cancers diagnosed in the U.S. and Canada are in women who have never been screened. An additional 10% of cancers occur in women who have not been screened within the past five years. Perhaps the largest gain in reducing cervical cancer incidence

and mortality could be attained by increasing screening rates, regardless of the test used. In 10 to 20 years will we be saying the same regarding breast cancer screening mammography, or more?

Presently, the intangible arguments for public and health-care provider belief in awareness and satisfaction with performing breast cancer screening cannot be fully valued. Advances are being made in the surgical, chemotherapeutic, hormonal, radiation, biologic, and newer therapies for the treatment of breast cancer, thus further contributing to improved survival of breast cancer patients. In the future, given the power and cooperation between patient and physician, we will be able to better differentiate amongst the various biologic types and behaviours of breast cancer among women. We will also be able to know how much treatment and screening prevention contributed towards mortality reduction. CME

References available upon request. Contact *The Canadian Journal of CME* at cme@sta.ca.

Take-home message

Important facts

- Screening tests are not diagnostic tests.
- They should be simple, cost efficient, and address a significant health condition.
- Treatment should be available for the condition.
- There must be a recognized latent or early (precancerous condition identifiable).
- Natural history of disease should be understood and can be altered with intervention.

Net Readings

1. National Cancer Institute: *www.cancer.gov/cancerinfo/screening/breast*
2. U.S. Preventive Services Task Force: *www.ahcpr.gov/clinic/uspstf/uspsbrca.htm*

www.stacommunications.com

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