Screening Mammography Benefit Controversies
Sorting the Evidence

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KEYWORDS

• Screening • Mammography • Benefit • Controversies

KEY POINTS

- Numerous clinical studies have confirmed that screening women age 40 years and older reduces breast cancer mortality by 30% to 50%.
- Several factors including faster breast cancer growth rates and lower breast cancer incidence among younger women, as well as shorter life expectancy and more comorbid conditions among older women, should also be considered in screening guidelines.
- Annual screening beginning at age 40 years and continuing with no upper age limit, as long as a woman has a life expectancy of at least 5 years and no significant comorbid conditions, is currently recommended by the American Cancer Society, the American College of Radiology, and the Society of Breast Imaging.

Screening mammography by virtue of its ability to substantially reduce death rates from the most common type of malignancy among women and the second leading cause of their death from cancer represents one of the major medical achievements of our time. Yet, unlike other medical advancements, the value of screening women age 40 years and older did not become apparent until after many years of clinical trials which began in the 1960s. Lengthy observational follow-up was required, because breast cancer is a chronic disease. During subsequent decades, there have been numerous improvements in technology, beginning with the replacement of direct exposure film mammography by film/screen mammography, the more recent conversion to digital mammography, and the current clinical evaluation of digital tomosynthesis. There have also been improvements in performance of mammography, such as better breast compression paddles and automatic exposure devices, mammographic grids, use of the mediolateral oblique (MLO) view instead of the straight mediolateral view. Some advances, such as use of 2-view screening (craniocaudal and MLO), instead of a single MLO view alone, screening at an annual rate rather than semiannual intervals, and double reading by 2 radiologists, have still not been universally accepted because of concerns regarding cost-effectiveness.

Screening controversies began in 1975 and continue. Some issues are legitimate, but most have been artificially contrived. No other medical test has been more thoroughly scrutinized and debated over the past 40 years. Keeping informed on these complex issues has been challenging for all physicians, including breast imagers. The public especially deserves empathy, because their information is channeled through the nonmedical media. Thus, the purpose of this article is to assess our current knowledge of screening benefits. Comprehensive reviews of adverse consequences and costs of screening may be found in the author's previous articles in the *Radiologic Clinics of North America*.[1,2]

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RANDOMIZED TRIALS HAVE PROVEN THAT EARLY DETECTION REDUCES BREAST CANCER DEATH RATES

The ability of widespread screening to detect breast cancers at smaller size and earlier stage than encountered in the general population was first established at the Breast Cancer Detection Demonstration Project (BCDDP), a program that screened 280,000 women throughout the United States with both mammography and physical examination from 1973 to 1981, sponsored by the American Cancer Society (ACS) and National Cancer Institute. In this program, 39% (1375) of the 3548 cancers were found by mammography alone, 7% (257) by clinical examination alone, and 51% (1805) by both mammography and clinical examination.[3] The 20-year relative survival rates at the BCDDP were 80.5% (overall), 85% for cancers detected by mammography alone, 82% for cancers detected by physical examination alone, and 74% for cancers detected by both mammography and physical examination.[4] These rates can be compared with the contemporaneous 20-year survival rate of 53% among US women who were largely not being screened.[5] Although these results were promising, there are several reasons why improved survival rates among such women who volunteer to be screened do not necessarily establish benefit from screening. They include selection bias, lead time bias, length bias, and interval cancers.[6] Thus, differences in survival rates may be influenced by factors other than the screening process itself.

Selection bias refers to the possibility that women who volunteer for screening differ from those who do not volunteer in ways that may alter the outcome of their disease, such as health status and behavioral factors. Therefore, survival rates in screened and nonscreened women may be influenced by factors other than the screening process itself.

Lead time bias implies that screening may affect the date of detection but not necessarily the date of death from breast cancer. Let us suppose that a woman who has never been screened finds her breast cancer serendipitously in 2009. She dies from her disease 5 years later, in 2014. If this same woman had been screened, her cancer might have been detected by mammography in the year 2005. Although small, the cancer detected in this woman by mammography might have dissemination beyond the breast. Despite screening, the woman dies from her disease in the year 2014. Because of screening, she is said to have survived for 9 years instead of 5 years. Therefore, the seemingly 4-year improvement in survival may not be real.

Length-biased sampling postulates that cancers detected at screening contain a disproportionate number of less aggressive cancers. Their growth rates are so slow that in the absence of screening, they might never reach sufficient size to surface clinically. Even if undetected, such indolent cancers might never result in death.

Possibly, the favorable survival rates for screen-detected cancers might be negated by lower survival rates for faster-growing interval cancers, which are undetected by mammography and surface clinically between screenings.

Considering these potential biases, benefit from screening cannot be proved by observation of improved survival rates. Rather, such proof requires prospective comparison of breast cancer death rates among a study group of women offered screening and a control group of women not offered screening in a randomized clinical trial (RCT).[6] Apart from the offer to be screened, these groups should not differ in any other substantial way. Therefore, a statistically significant difference in breast cancer deaths between the groups on follow-up represents incontrovertible proof of benefit from the screening. Observation of lower mortality for the screened group in a well-designed and well-conducted RCT is not affected by selection bias, lead time bias, length bias, or interval cancers.

RESULTS OF RCTS

Seven population-based trials of breast cancer screening by mammography alone or in combination with physical examination have been conducted. They are as follows: (1) the Health Insurance Plan of Greater New York (HIP) trial,[7] (2) the Swedish Two-County trial consisting of Kopparberg and Ostergotland counties,[8–10] (3) the Malmö (Sweden) Mammographic Screening trial,[11–15] (4) the Stockholm (Sweden) trial,[14–17] (5) the Gothenburg (Sweden) Breast Screening trial,[14,15,18–20] (6) the Edinburgh (Scotland) trial,[21,22] and (7) the UK Age trial.[23] In a population-based RCT, study and control groups are randomly selected from a predefined population. There has also been 1 non–population-based RCT, the National Breast Screening Study of Canada (NBSSC).[24–26] In a non–population-based RCT, study and control groups are randomly selected from women who volunteer to participate.

Protocols and results for women of all ages at entry into these 8 RCTs are shown in **Table 1**. Mortality reduction is equal to 1 minus the relative risk (RR) of dying from breast cancer in the study group women versus the control group. The HIP trial, the

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