# Overdiagnosis of Breast Cancer at Screening is Clinically Insignificant

Stephen A. Feig, MD

Long-term follow-up of randomized trials provide the most accurate estimates of overdiagnosis. Estimates from follow-up of service screening studies are almost as accurate if there is sufficient adjustment for lead time and risk status. When properly analyzed data from both of these types of trials indicate that the rate of overdiagnosis at screening mammography is clinically negligible: 0–5%. Population trend studies are a potentially highly inaccurate means to estimate overdiagnosis. Most cases of DCIS detected at screening are medium and high grade with substantial potential to become an invasive disease. To avoid overtreatment, clinicians need to tailor their treatment of DCIS to the histologic and molecular characteristics of each case.

**Key Words:** Screening mammography; breast cancer screening; overdiagnosis.



As the evidence that screening can substantially reduce breast cancer mortality was being confirmed in numerous studies during the past 30 years, the focus of screening controversies shifted from the existence and measurement of benefit to potential "harms" and costs of screening, as well as to proposals to reduce the frequency of screening and to limit the age of women offered screening to those aged 50–70 years or to deny screening to those with no known risk factors. It is sadly ironic that these issues have gained the forefront of media attention, whereas the lifesaving results of screening have been marginalized. Indeed, women should now be aware that breast cancer mortality among screened women aged 40–69 years in the Swedish Two-County Randomized Trial was reduced by 31% among those invited to screening (1). Randomized trials underestimate the actual benefit from screening due to noncompliance of some study group women and contamination of some control group women. Service screening studies provide higher, more accurate estimates.

Among seven European service screening studies analyzed with incidence-based mortality methods, breast cancer mortality was 25% lower for invited versus not invited women, and 38% lower for screened versus not screened women (2). Among seven other European service screening studies analyzed using case-control methods, corresponding breast cancer mortality reductions were 31% for invited versus not invited women and 52% for screened versus not screened women (2).

The purpose of this review article on overdiagnosis, which has recently gained the spotlight as a purported major harm from screening, was to demonstrate that among screen-detected cancers the possibility of overdiagnosis is extremely low, less than 5%. Furthermore, this review article demonstrates that overdiagnosis has less clinical significance than the vastly larger clinical benefits of early detection established in screening studies. It should also be appreciated that more recent improvements in imaging technology such as 2D digital mammography and 3D digital tomosynthesis should allow even greater benefits than shown in the randomized trials and service screening studies (3).

The concept of overdiagnosis postulates that some breast cancers detected at screening would never be known to the patient or her physician in the absence of screening. It has been alleged that such overdiagnosed breast cancers never produce any clinical signs or symptoms and never represent a cause of death. There is no way to determine by pathologic examination whether an individual cancer has been overdiagnosed. Thus, the existence and frequency of overdiagnosis has only been inferred by mathematical calculation based on trends of breast cancer incidence or on data from screening trials. Yet, such calculations may be grossly misleading if based on basic misassumptions or improper flawed techniques such as insufficient follow-up or failure to correct for risk factors in the populations (4,5). If overdiagnosis does actually occur in the real world, women with overdiagnosed cancers would receive "unnecessary" treatments such as lumpectomy, mastectomy, chemotherapy, and radiation therapy. Additionally, these women would experience the unnecessary anxiety of knowing that they have breast cancer. These women and their families, employers, and medical insurance providers would incur "needless" costs for the consequent diagnostic and therapeutic procedures. Thus, if existent, overdiagnosis would represent harm from screening. The frequency of overdiagnosis would determine whether this harm is trivial or substantial when weighed

**Acad Radiol 2015;** 22:961–966

From the Department of Radiological Sciences, University of California Irvine Medical Center, 101 City Drive South, Orange CA 92869-3298 (S.A.F.). Received January 12, 2015; accepted January 22, 2015. **Address correspondence to:** S.A.F. e-mail: sfeig@uci.edu


http://dx.doi.org/10.1016/j.acra.2015.01.020

against the benefits from early detection of breast cancer. Overdiagnosis is completely different from a "false-positive biopsy," which is an abnormality that is biopsied on the basis of suspicious imaging findings and subsequently found to be benign on examination of the biopsy specimen.

The frequency of overdiagnosis has been estimated on the basis of data from randomized screening trials, service screening studies, changes and trends in incidence, and stages of cancer in populations. Analytic methods applied to these databases differ substantially in their accuracy and their conclusions. Accurate estimates indicate that the frequency of overdiagnosis is extremely low. Between 0% and 5% of screen-detected cancers are overdiagnosed (6). Inaccurate estimates have led to the erroneous conclusion that as many as 30% of breast cancers are being overdiagnosed. It is understandable that many women may feel confused and frightened and consequently deterred from being screened, and some physicians may be dissuaded from advising screening for their patients. To clarify the controversy, this review article demonstrates why the risk of overdiagnosis has been greatly exaggerated and that the risk is negligible or nonexistent compared to the substantial benefits from screening.

## WHY ESTIMATION OF OVERDIAGNOSIS BY MEANS OF TREND STUDIES IS UNRELIABLE AND INACCURATE

In a widely publicized article in the New England Journal of Medicine in late 2012, Bleyer and Welch (7) made the audacious claim that as a result of screening 31% of all breast cancers in the US are being overdiagnosed. To reach this implausible conclusion, the author compared the breast cancer incidence from 1976 to 1978, when very few women were being screened, with the breast cancer incidence from 2006 to 2008, when 60% of women in the US aged 40 and older were being screened at least once every 2 years. The key misassumption in their analysis was that in the absence of screening, breast cancer incidence during that 30-year period would have increased by only 0.25% per year. They ignored the fact that for a longer 40-year period (1940–1980) the increase in breast cancer incidence had been 1% per year, four times greater than used in Bleyer's model (8–10). In fact, breast cancer incidence during 2006–2008 (128 invasive cancers per 100,000 women per year) was actually lower than expected (132 cancers per 100,000 women per year) from a 1% per year increase (10). Thus, temporal comparison of breast cancer incidence rates in the US population is an unreliable method to gauge the frequency of overdiagnosis.

From 1950 to 2014, the breast cancer incidence rate has varied each year and each decade, but the overall trend of increase has been continuous. Changes in diet, lifestyle, and environmental factors are the likely reasons. Screening mammography appears to be a relatively minor reason. In the US, the increased incidence began many years before the screening mammography era. As evident from 30 years of follow-up in the Swedish Two-County Trial, screening did not lead to any cumulative increased incidence in the study group compared to the control group that was not offered screening (11). Rather, screening leads to a temporary increase in incidence because of earlier detection of already existent disease. The claim by Bleyer and Welch that 31% of breast cancers in the US are overdiagnosed is implausible and should have received a more critical journal manuscript review before publication. Equally disturbing is the widespread publicity for the claim provided by television broadcasts, newspaper headlines, and magazine articles. Such irresponsible coverage by the media may discourage women from being screened and persuade medical insurance providers to curtail their support for screening.

Relative changes in incidence rates for early-stage and late-stage breast cancers in the US were the basis for the opinion of Esserman et al. (12) that screening detects an "excessive" number of slow-growing or biologically inert cancers. The authors observed that after the introduction of screening in our country, breast cancer incidence never returned to prescreening levels and that although the incidence of regional cancer has decreased during the screening era, this decrease was less than the increased detection of early-stage disease. The authors acknowledged that breast cancer mortality decreased during the screening era, but were uncertain about the relative contributions of screening versus treatment. The authors fail to appreciate that increased detection of early disease may precede the decrease in late-stage disease by as long as 5–30 years because breast cancer is a chronic disease comprising a whole spectrum from slower growing to rapidly growing tumors. They do not appreciate that the incidence of all regional disease is influenced by many factors, including the overall increasing breast cancer incidence, inadequate screening compliance, and excessively long screening intervals. The breast cancer mortality reduction of 30%–50% seen among women screened in randomized trials and service screening studies cannot be negated by distracting observations requiring the persistence of regional disease. Fully 34% of American women aged 40 years and older have not been screened in the past 2 years and 50% have not been screened annually as recommended by the American Cancer Society (13). In my opinion, the disproportionate number of regional cancers cited by Esserman et al. can be attributed to late-stage cancers among women not being screened often enough or not being screened at all.

## ACCURATE ESTIMATION OF OVERDIAGNOSIS USING SERVICE SCREENING REQUIRES SUFFICIENT ADJUSTMENT FOR DETECTION LEAD TIME AND RISK STATUS

Service screening studies compare breast cancer death rates among screened versus nonscreened women but unlike randomized trials, do not randomize individual women (14). Comparison may be made between women offered screening and those in the same geographic area or an adjacent