## **Examining the EVIDENCE**

## Do screening mammograms in women aged 70 and older improve stage at diagnosis or breast cancer-specific mortality?

No. In an observational study that used Medicare claims data matched with the SEER (Surveillance, Epidemiology, and End Results) database, the **incidence** of overdiagnosis, defined as finding a cancer that would not have caused clinical problems during a person's lifetime, increased with age (from 31% for women aged 70-74 to 54% for women aged 85 and older). There was no difference in the stage of diagnosed cancers and no statistically significant reduction in breast cancer-specific mortality between people who continued mammogram screening and those who did not.

## TRACK

Overdiagnosis refers to the finding of a cancer that would not have caused clinical problems during a person's lifetime

Richman IB, Long JB, Soulos PR, et al. Estimating breast cancer overdiagnosis after screening mammography among older women in the United States. Ann Intern Med. 2023;176:1172-1180. doi:10.7326/M23-0133

#### **EXPERT COMMENTARY**

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screening test is performed to detect potential health disorders or diseases in people who do not have any symptoms of disease. The goal of screening is to detect the condition early enough to treat it most effectively, and ultimately to decrease morbidity and mortality related to the disease. Overdiagnosis refers to the finding of a cancer that would not have caused clinical problems during a person's lifetime.

Current guidelines for the early detection of breast cancer vary considerably, including recommendations for

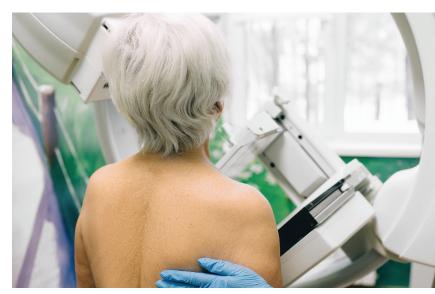
age to initiate screening, the cadence of screening (annual or biannual), the use of ancillary screening for people with dense breasts, and importantly the upper age limit for which screening is advised. The US Preventive Services Task Force recommends continuing screening to age 74. The American Cancer Society suggests ongoing screening if life expectancy is estimated at more than 10 years, and the American College of Physicians recommends stopping screening at age 75, or younger if life expectancy is less than 10 years. The American College of Obstetricians and Gynecologists states that women at average risk of breast cancer should continue screening mammography until at least age 75.

Overdiagnosis is a difficult concept for clinicians to understand let alone explain to our patients. Recently, Richman and colleagues published the results of their study aimed at estimating overdiagnosis associated with breast cancer screening among older women.1 As Dr. Otis Brawley, former Chief Medical and Scientific Officer of the American Cancer Society and current Distinguished Professor of Oncology and Epidemiology at Johns Hopkins University, states in the editorial that accompanies the study by Richman and colleagues, "Some tumors are not destined to grow, spread, and kill due to their genomics or their microenvironment. A second type of overdiagnosis involves small tumors that do have the potential to grow but will not grow fast enough to bother the patient within their natural lifetime."2

Although screening mammography in older women results in frequent false positives that require additional imaging as well as biopsies, we have become more aware of the potential of overdiagnosis as an important downside of screening mammography in an elderly population.

#### **Details of the study**

Using the SEER registry to identify breast cancers linked to a 5% sample of Medicare beneficiaries, Richman and colleagues (funded by the National Cancer Institute and based at Yale University) conducted a retrospective



cohort study to estimate the likelihood of overdiagnosis associated with screening mammography among older women over 15 years of follow-up. Specifically, they assessed the difference in cumulative incidence of in situ and invasive breast cancer among women aged 70 years and older without a history of breast cancer when screened in 2002. During the subsequent 3 years, participants either continued screening (screened group) or did not (unscreened group). Women were followed through 2017.

Among almost 55,000 women followed, 88% were White, 6% were Black, and 3% were Hispanic. Mean follow-up was 13.7 years among women aged 70 to 74 years at baseline. For those aged 75 to 84 at baseline, mean follow-up was 10 years, and for those aged 85 years and older, mean followup was 5.7 years.

Estimated rates of overdiagnosis. Overall, among women aged 70 to 74 at baseline who were eventually diagnosed with breast cancer, the investigators estimated that 31% of these cancers were overdiagnosed. The corresponding percentage of breast cancers estimated to represent overdiagnosis climbed to 47% for those aged 75 to 84 years at baseline and to 54% for those aged 85 years and older at baseline.

The investigators assessed the impact of greater screening among women with a firstdegree relative with a diagnosis of breast

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#### WHAT THIS EVIDENCE MEANS FOR PRACTICE

The high prevalence of overdiagnosis and lack of a breast cancer–specific mortality benefit among older women who undergo screening mammography is sobering. Clinician recommendations and shared decision making with our patients regarding screening mammography should take into consideration overdiagnosis and the considerable harms associated with overtreatment. Although we may recognize that overdiagnosed cancers are often indolent tumors with a long presymptomatic phase, in older women, even finding a biologically aggressive cancer may represent overdiagnosis if life expectancy is limited.

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### FAST TRACK

In this large, long-term study using reliable data sources, the findings that the incidence of advanced-stage disease as well as breast cancerspecific mortality were similar in the screened and unscreened cohorts provides powerful evidence that screening mammography is not effective in older women

cancer and determined that this did not explain their results. With respect to cancer stage, the investigators noted that overdiagnosis was more prevalent among in situ and localized invasive cancers compared with those with regional or distant spread. Of note, the incidence of cancer with regional or distant spread was neither higher nor lower among those who were screened. Finally, the investigators did not observe significant differences in breast cancerspecific mortality by screening status.

The proportion of cancers that were overdiagnosed was particularly high among women with in situ as well as those with localized invasive disease. The investigators pointed out that as many as 90% of women aged 80 and older diagnosed with localized cancer undergo surgery, and almost two-thirds of those older than 70 years have radiation therapy for early-stage disease. In addition to the burdens associated with these treatments for overdiagnosed cancers in older women, simply being diagnosed with breast cancer profoundly affects the health and well-being of women, resulting in anxiety and substantial reductions in quality of life.

The authors also noted that some studies suggest that, among breast cancers diagnosed with screening, chemotherapy is less likely to be employed among older women, a screening benefit that must be weighed against the high likelihood of overdiagnosis. However, this benefit is unlikely to be

meaningful for the majority of patients in this study who presented with in situ or early invasive lesions since chemotherapy often is not recommended for such women.

#### Study strengths and limitations

If screening mammography is effective, the incidence of advanced-stage tumors and breast cancer-specific mortality should be reduced in screened populations. Accordingly, in this large, long-term study using reliable sources of data, the findings that the incidence of advanced-stage disease as well as breast cancer-specific mortality were similar in the screened and unscreened cohorts provides powerful evidence that screening mammography is not effective in older women.<sup>3</sup>

As the authors pointed out, their findings regarding a high prevalence of overdiagnosis associated with screening mammography in older women are consistent with findings of other studies, some of which used different methodology.

The authors acknowledged that some women in their Medicare cohort who initially continued screening likely stopped screening subsequently, while some who initially did not continue screening might have been screened subsequently. They went on to indicate that if patients were completely adherent with subsequent screening (or not getting screened) the likelihood that cancers among screened women were overdiagnosed would be even higher.

Lead-time bias occurs when screening finds a cancer earlier than that cancer would have been diagnosed because of symptoms. This study followed the cohorts over a long timeframe to reduce the possibility that lead time was inappropriately identified as overdiagnosis. They also observed that, among women aged 85 and older, most cohort members had died by the end of study follow-up; accordingly, lead time is not likely to have explained their findings.

**Limitations.** The authors acknowledged that miscoding the mammogram type (screening vs diagnostic) could result in higher estimates of overdiagnosis. In their most conservative

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sensitivity analysis, the overdiagnosis rates could be as low as 15% for women aged 70 to 74, 36% for those aged 75 to 84, and 44% for people aged 85 and older.

Because this was an observational cohort study, unmeasured differences in breast cancer risk and underlying health factors may have been confounders. Specifically, people with severe life-threatening conditions that limited their expected life span may have chosen not to undergo regular screening. Although the authors did attempt to adjust for these factors, there may have been unrecognized confounders. This study was designed to estimate overdiagnosis, and therefore the specific benefits and harms of screening could not be addressed based on the data collected.

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