April 2, 2012 — Mammography screening is linked to overdiagnosis of breast cancer, according to findings from the Norwegian Screening Program reported in the April 3 issue of the *Annals of Internal Medicine*. The investigators suggest that overdiagnosis not only poses a significant ethical dilemma but also burdens the patient and the healthcare system.

"Mammography screening increases breast cancer incidence owing to earlier detection of cancer that would otherwise have been diagnosed later in life and to overdiagnosis of cancer that would not have been identified clinically in a lifetime," write Mette Kalager, MD, from the Harvard School of Public Health, Brigham and Women's Hospital, Boston, Massachusetts, and colleagues. "Overdiagnosis can theoretically occur because the tumor lacks potential to progress to a clinical stage or because the woman dies of other causes before the breast cancer surfaces clinically.... In both instances, however, the woman would
be diagnosed and treated with no possible survival benefit."

The goal of this study was to estimate the percentage of overdiagnosis of breast cancer attributable to mammography screening, defined as the percentage of cases of cancer that would not have become clinically evident during a woman's lifetime without screening. The investigators note that the absence of valid comparison groups previously hindered achievement of this goal, because incidence trends attributable to screening could not be distinguished from temporal trends in incidence.

Norway gradually implemented the nationwide mammography screening program, the Norwegian Screening Program, from 1996 to 2005 by inviting women aged from 50 to 69 years to participate. The investigators compared concurrent incidence of invasive breast cancer from 1996 to 2005 in counties that had already implemented the screening program with that in counties that had not yet implemented the program. They also assessed incidence rates during the preceding decade, which allowed adjustment for changes in temporal trends in breast cancer incidence.

The first approach to calculating the percentage of overdiagnosis was to account for the expected decrease in incidence after cessation of screening after 69 years of age. The second approach was to compare incidence in the current screening group with incidence among women 2 and 5 years older in the historical screening groups, accounting for average lead time.

Of 39,888 patients diagnosed with invasive breast cancer, 7793 received their diagnosis after implementation of the screening program. For approach 1, the estimated rate of overdiagnosis associated with the program was 18% to 25%, and for approach 2, it was 15% to 20% (P < .001 for both approaches). Assuming overdiagnosis of 15% to 25% of cases of cancer, 6 to 10 women would be overdiagnosed for every 2500 women invited for screening.

Limitations of this study include a reliance on registry-based participants and data, possible unmeasured confounding, a lack of data on ductal carcinoma in situ, and that the duration of follow-up may have been insufficient after introduction of screening in some areas to allow stable estimates of the degree of overdiagnosis.

"Mammography screening entails a substantial amount of overdiagnosis," the study authors write.

**Overdiagnosis More Likely in United States Than in Europe**

In an accompanying editorial, Joann G. Elmore, MD, MPH, from the University of Washington School of Medicine in Seattle, and Suzanne W. Fletcher, MD, from Harvard Medical School and Harvard Pilgrim Health Care Institute in Boston, Massachusetts, note that the Norwegian estimates of overdiagnosis may not apply to the United States. Overdiagnosis is probably even more common in the United States than in Norway, because US radiologists are more likely than European radiologists to report mammographic abnormalities, and because US women often start annual mammography screening at 40 years of age, whereas Norwegian women start biennial screening at 50 years of age.

"Ultimately, better tools are needed to reliably identify which breast cancer will be fatal without treatment and which can be safely observed over time without intervention, but we cannot wait for these tools to be developed," Dr. Elmore and Dr. Fletcher write. "Evaluating strategies for observing change in some lesions over time instead of recommending an immediate biopsy has been suggested. This may be a tough sell for women with anxiety as a result of the 'watch-and-wait' approach, as well as for radiologists who do not want to miss any sign of disease and fear malpractice lawsuits."

The editorialists also point out that overdiagnosis will probably increase as breast magnetic resonance imaging and other newer imaging modalities are introduced.

"Finally, we have an ethical responsibility to alert women to this phenomenon," the editorialists conclude. "Most patient-education aids do not even mention overdiagnosis, and most women are not aware of its possibility. Effective communication about overdiagnosis of breast cancer will require great care — and evaluation to determine how best to do it; otherwise, women may become fearful or angry."
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