Commentary

Daniel B. Kopans, MD



Annual screening mammography beginning at age 40 saves the most lives

Solution If women wait until age 45 to begin annual screening, then shift to biennial screening at age 55, more than 38,000 women now in their 40s will die unnecessarily

ith the recent publication of new American Cancer Society (ACS) guidelines on breast cancer screening,¹ we finally have achieved a consensus. All major organizations, including the US Preventive Services Task Force (USPSTF), agree that the most lives are saved by annual screening beginning at age 40. This is the only science-backed finding of their reviews.

Here is a statement from the USPSTF: "[We] found adequate evidence that mammography screening reduces breast cancer mortality in women ages 40 to 74 years."² And from the ACS: "Women should have the opportunity to begin annual screening between the ages of 40 and 44 years."¹

Regrettably, the USPSTF, whose guidelines determine insurance coverage, endangers women by going on to suggest that they can wait until the age of 50 to begin screening and then wait a full 2 years between screens. The new ACS guidelines have been misreported as recommending the initiation of annual screening at age 45, moving to biennial screening at the age of 55. This misunderstanding arose because the ACS describes annual screening starting at age 40 as a "qualified recommendation." However, it defines this qualified recommendation as meaning that "The majority of individuals in this situation would want the suggested course of action, but many would not."¹

Why would screening guidelines be based on "what many [women] would not" choose? No one forces women at any age to participate in screening. Each woman, regardless of age, should choose for herself whether or not to participate in screening. In fact, the ACS panel provides no data on what screening option women would prefer. Members of the ACS and USPSTF panels, none of whom provides care for women with breast cancer, injected their own personal biases to qualify what the scientific evidence shows by claiming to have "weighed" benefits against "harms." Yet they provide no description of the scale that was used. They state only that there are 2 major harms: "false positives" and "overdiagnosis."

"False positive" is a misnomer

Recalls from screening have been called, pejoratively, "false positives," leading some to believe that women are being told that they have breast cancer when they do not. In reality, most recalled women ultimately are told that there is no reason for concern.

Approximately 10% of US women who undergo screening mammography are recalled—the same percentage as for Pap testing.³ (The ACS and USPSTF panels ignore the benefit for the 90% of women who are reassured by a negative screen.)

Among the women recalled, more than half are told that everything is fine, based on a few extra pictures or an ultrasound. Approximately 25% (2.5% of those screened) are asked to return in 6 months just to be careful, and approximately 20% (2% of women screened) will be advised to undergo imaging-guided needle biopsy using local anesthesia. Among these women, 20% to 40% will be found to have cancer.⁴

This figure is much higher than in the past, when women had "lumps" surgically removed, only 15% of which were cancer. Most of these lesions were larger and less likely to be cured than screen-detected cancers.⁵

CONTINUED ON PAGE 16

Dr. Kopans is Professor of Radiology at Harvard Medical School and Senior Radiologist in the Breast Imaging Division at Massachusetts General Hospital in Boston, Massachusetts.

Dr. Kopans reports that he receives grant or research support from General Electric and is a consultant to General Electric and Hologic. Massachusetts General Hospital holds his patent on digital breast tomosynthesis.

Commentary

CONTINUED FROM PAGE 15

Panels fail to justify breast cancer deaths that would occur with proposed screening intervals

The main reason the ACS and USPSTF panels decided to compromise on their recommendations was to try to reduce the number of recalls, yet they never explain how many fewer recalls are equivalent to allowing a death that could have been avoided by annual screening starting at age 40.

The National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (CISNET)used by both panels-shows that, if women in their 40s wait until age 50 and then are screened every 2 years (as the USPSTF recommends), as many as 100,000 lives will be lost that could have been saved by annual screening starting at age 40.6 If women wait until age 45 to begin annual screening and then shift to biennial screening at age 55 (as the ACS recommends), more than 38,000 women now in their 40s will die, unnecessarily, as a result.7

Neither panel states how many recalls avoided are equivalent to allowing so many avoidable, premature deaths.

No invasive cancers resolve spontaneously

The other alleged harm of screening is "overdiagnosis"—the exaggerated suggestion that mammography screening finds tens of thousands of breast cancers each year that, if left undetected, would disappear on their own.^{8,9} Such analyses have been shown to be scientifically unsupportable.¹⁰⁻¹³ In fact, no one has ever seen an invasive breast cancer disappear on its own without therapy. The claim is tens of thousands each year, yet no one has seen a single case. There certainly are legitimate questions about the need to treat all cases of ductal carcinoma in situ (DCIS). However, if an invasive breast cancer is found during screening and then left alone, it will grow to become a palpable cancer, with lethal capability.

Here are the proven facts about breast cancer screening

- The most lives are saved when annual screening begins at age
 40. This fact has been proven by randomized, controlled trials.^{14,15} All of the data models in CISNET agree that the most lives are saved by annual screening beginning at age 40.¹⁶
- There is no scientific or biological reason to use the age of 50 as a threshold for screening. None of the parameters of screening changes abruptly at age 50—or any other age.¹⁷
- More than 30,000 new cases of breast cancer occur each year among women in their 40s.¹⁸
- More than 40% of years of life lost to breast cancer are among women diagnosed in their 40s.¹⁹ The ACS found that the years of life lost to breast cancer for women aged 40 to 44 are the same as for women aged 55 to 59.²
- Despite access to modern therapies, numerous observational studies show that when screening is introduced into the population, the breast cancer death rate goes down, in relation to participation in screening, for women aged 40 and older.²⁰⁻³⁵
- In the 2 largest Harvard teaching hospitals, more than 70% of women who died from breast cancer were among the 20% who were not participating in screening, including women in

their 40s, despite the fact that all had access to modern therapies.³⁶ It is likely that many of the 40,000 women who still die in the United States each year, despite improvements in therapy, were also not participating in screening.

 The death rate from breast cancer remained unchanged from 1940 until screening began in the mid-1980s. Soon after, in 1990, the rate began to fall for the first time in 50 years. Today, 36% fewer women die each year from breast cancer.37 Men with breast cancer have access to the same therapies but, in 1990, the death rate for men began to increase as it began to fall for women. The death rate for men remained elevated until 2005 and then returned to 1990 levels, where it has remained, as the death rate for women has continued to decline.³⁸ Women are being screened, whereas men present with larger and later-stage cancers. Therapy has improved, but the most lives are saved when breast cancer is treated early.

Why not screen only high-risk women?

It has been suggested that only highrisk women should participate in screening. However, women who inherit a genetic predisposition account for only about 10% of breast cancers each year.³⁹ If we add to that number other women with family histories or other known risk factors, these cases account for another 15% of cancers.⁴⁰

Regrettably, high-risk women account for only a quarter of breast cancers diagnosed each year. If only high-risk women are screened, the vast majority of women who develop breast cancer (75%) will not benefit from early detection.

CONTINUED ON PAGE 18

Commentary

CONTINUED FROM PAGE 16

The bottom line

Mammography is not perfect. It does not find all cancers and does not find all cancers early enough for a cure.

References

- Oeffinger KC, Fontham ET, Etzioni R, et al. Breast cancer screening for women at average risk. 2015 guideline update from the American Cancer Society. JAMA. 2015;314(15):1599–1614.
- U.S. Preventive Services Task Force. Draft Recommendation Statement. Breast Cancer: Screening [Web page]. Rockville, MD: USPSTF Program Office; 2015. http://www.uspreventiveservices taskforce.org/Page/Document/Recommenda tionStatementDraft/breast-cancer-screening1. Accessed November 11, 2015.
- Saraiya M, Irwin KL, Carlin L, et al. Cervical cancer screening and management practices among providers in the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). Cancer. 2007;110(5):1024–1032.
- Rosenberg RD, Yankaskas BC, Abraham LA, et al. Performance benchmarks for screening mammography. Radiology. 2006;241(1):55–66.
- Spivey GH, Perry BW, Clark VA, et al. Predicting the risk of cancer at the time of breast biopsy. Am Surg.1982;48(7):326–332.
- Hendrick RE, Helvie MA. USPSTF Guidelines on screening mammography recommendations: science ignored. Am J Roentgenol. 2011; 196(2): W112-116.
- 7. Based on CISNET models. Personal communication: R. Edward Hendrick, PhD.
- Jorgensen KJ, Gotzsche PC. Overdiagnosis in publicly organised mammography screening programmes: systematic review of incidence trends. BMJ. 2009;339:b2587.
- Bleyer A, Welch HG. Effect of three decades of screening mammography on breast-cancer incidence. N Engl J Med. 2012;367(21):1998–2005.
- Puliti D, Duffy SW, Miccinesi G, et al; EURO-SCREEN Working Group. Overdiagnosis in mammographic screening for breast cancer in Europe: a literature review. J Med Screen. 2012;19(suppl 1):42–56.
- Kopans DB. Arguments against mammography screening continue to be based on faulty science. Oncologist. 2014;19(2):107–112.
- Helvie MA, Chang JT, Hendrick RE, Banerjee M. Reduction in late-stage breast cancer incidence in the mammography era: implications for overdiagnosis of invasive cancer. Cancer. 2014;120(17):2649–2656.
- Etzioni R, Xia J, Hubbard R, Weiss NS, Gulati R. A reality check for overdiagnosis estimates associated with breast cancer screening. J Natl Cancer Inst. 2014;106(12). doi: 10.1093/jnci/dju315.
- Duffy SW, Tabar L, Smith RA. The mammographic screening trials: commentary on the recent work by Olsen and Gotzsche. CA Cancer J Clin. 2002;52(2):68–71.
- Hendrick RE, Smith RA, Rutledge JH, Smart CR. Benefit of screening mammography in women ages 40-49: a new meta-analysis of random-

However, there is no universal cure on the horizon, while screening is available today and is saving thousands of lives each year. All women should have access to, and be encouraged to participate in, annual screening starting at age 40. ⁽²⁾

ized controlled trials. J Natl Cancer Inst Monogr. 1997;22:87-92.

- 16. Mandelblatt JS, Cronin KA, Bailey S, et al; Breast Cancer Working Group of the Cancer Intervention and Surveillance Modeling Network. Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms. Ann Intern Med. 2009;151(10):738-747.
- Kopans DB, Moore RH, McCarthy KA, et al. Biasing the interpretation of mammography screening data by age grouping: nothing changes abruptly at age 50. Breast J. 1998;4(3):139-145.
- 18. US Census Bureau. 2000 Census Summary File 1 and 2010 Census Summary File 1 show 21,996,493 women ages 40-49 and SEER shows 95.5 cancers per 100,000 for these women, which means 34,578 cancers.
- Shapiro S. Evidence on screening for breast cancer from a randomized trial. Cancer. 1977;39(6 suppl):2772-2278.
- Tabar L, Vitak B, Tony HH, Yen MF, Duffy SW, Smith RA. Beyond randomized controlled trials: organized mammographic screening substantially reduces breast carcinoma mortality. Cancer. 2001;91(9):1724–1731.
- Kopans DB. Beyond randomized, controlled trials: organized mammographic screening substantially reduces breast cancer mortality. Cancer. 2002;94(2):580-581.
- Duffy SW, Tabar L, Chen H, et al. The impact of organized mammography service screening on breast carcinoma mortality in seven Swedish counties. Cancer. 2002;95(3):458–469.
- 23. Otto SJ, Fracheboud J, Looman CWN, et al; National Evaluation Team for Breast Cancer Screening. Initiation of population-based mammography screening in Dutch municipalities and effect on breast-cancer mortality: a systematic review. Lancet. 2003;361(9367):411–417.
- Swedish Organised Service Screening Evaluation Group. Reduction in breast cancer mortality from organized service screening with mammography:
 Further confirmation with extended data. Cancer Epidemiol Biomarkers Prev. 2006;15(1):45–51.
- Coldman A, Phillips N, Warren L, Kan L. Breast cancer mortality after screening mammography in British Columbia women. Int J Cancer. 2007;120(5):1076-1080.
- Jonsson H, Bordás P, Wallin H, Nyström L, Lenner P. Service screening with mammography in Northern Sweden: effects on breast cancer mortality—an update. J Med Screen. 2007;14(2):87–93.
- Paap E, Holland R, den Heeten GJ, et al. A remarkable reduction of breast cancer deaths in screened versus unscreened women: a case-referent study. Cancer Causes Control. 2010;21(10):1569–1573.
- 28. Otto SJ, Fracheboud J, Verbeek ALM, et al; National Evaluation Team for Breast Cancer

Screening. Mammography screening and risk of breast cancer death: a population-based casecontrol study. Cancer Epidemiol Biomarkers Prev. 2012;21(1):66–73.

- van Schoor G, Moss SM, Otten JD, et al. Increasingly strong reduction in breast cancer mortality due to screening. Br J Cancer. 2011;104(6):910– 914.
- 30. Mandelblatt JS, Cronin KA, Bailey S, et al; Breast Cancer Working Group of the Cancer Intervention and Surveillance Modeling Network. Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms. Ann Intern Med. 2009;151(10):738-747.
- Hellquist BN, Duffy SW, Abdsaleh S, et al. Effectiveness of population-based service screening with mammography for women ages 40 to 49 years: evaluation of the Swedish Mammography Screening in Young Women (SCRY) cohort. Cancer. 2011;117(4):714–722.
- Broeders M, Moss S, Nyström L, et al; EURO-SCREEN Working Group. The impact of mammographic screening on breast cancer mortality in Europe: a review of observational studies. J Med Screen. 2012;19(suppl 1):14–25.
- Hofvind S, Ursin G, Tretli S, Sebuødegård S, Møller B. Breast cancer mortality in participants of the Norwegian Breast Cancer Screening Program. Cancer. 2013;119(17):3106–3112.
- Sigurdsson K, Olafsdóttir EJ. Population-based service mammography screening: the Icelandic experience. Breast Cancer (Dove Med Press). 2013;5:17-25.
- Coldman A, Phillips N, Wilson C, et al. Pan-Canadian study of mammography screening and mortality from breast cancer. J Natl Cancer Inst. 2014;106(11):dju261.
- Webb ML, Cady B, Michaelson JS, et al. A failure analysis of invasive breast cancer: most deaths from disease occur in women not regularly screened. Cancer. 2014;120(18):2839–2846.
- DeSantis CE, Fedewa SA, Goding Sauer A, Kramer JL, Smith RA, Jemal A. Breast cancer statistics, 2015: Convergence of incidence rates between black and white women. CA Cancer J Clin. 2015 Oct 29. doi: 10.3322/caac.21320
- National Cancer Institute. Surveillance, Epidemiology, and End Results Program. http://seer.cancer .gov/archive/csr/1975_2010/browse_csr.php?sec tionSEL=4&pageSEL=sect_04_table.06.html. Accessed November 16, 2015.
- Claus EB, Schildkraut JM, Thompson WD, Risch NJ. The genetic attributable risk of breast and ovarian cancer. Cancer. 1996;77(11):2318–2324.
- Seidman H, Stellman SD, Mushinski MH. A different perspective on breast cancer risk factors: some implications of nonattributable risk. Cancer. 1982;32(5):301–313.