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FPIN's Clinical Inquiries

Screening Mammography in Women 40 to 49 Years of Age

Clinical Inquiries provide answers to questions submitted by practicing family physicians to the Family Practice Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/levels_of_evidence.asp).

This series of Clinical Inquiries is coordinated for American Family Physician by John Epling, M.D., State University of New York Upstate Medical University, Syracuse, N.Y. The complete database of evidence-based questions and answers is copyrighted by FPIN. If you are interested in submitting questions to be answered or writing answers for this series, go to http://www.fpin.org or contact CI2Editor@fpin.org.

Searchable Question

Does screening with mammography reduce breast cancer mortality in women 40 to 49 years of age?

Evidence-Based Answer

While there is strong agreement among experts and evidence in the literature to recommend that women 50 to 69 years of age undergo screening with mammography for breast cancer, the question of screening women 40 to 49 years of age is controversial.

The results of most studies suggest that screening with mammography in women 40 to 49 years of age may reduce mortality from breast cancer, but these reductions are small (i.e., fewer than 1 in 10,000 per year).1-8 [Strength of recommendation: B, based on meta-analysis and systematic review of randomized controlled trials (RCTs) with inconsistent findings]

The balance of benefits and potential harms (i.e., cost, unnecessary biopsies, anxiety) is less favorable for women in their forties than for women older than 50. The precise age at which the potential benefits justify the possible harm is a subjective choice.

There is not enough evidence to recommend optimal intervals for screening with mammography in women in their forties.[Strength of recommendation: C, based on extrapolations from studies with inconsistent findings]

Evidence Summary

Of the eight published RCTs on breast cancer screening using mammography, seven included women in their forties.1-5 Only one study4 was specifically designed to evaluate screening in this age group. Data from these trials have been analyzed in at least eight meta-analyses. The conclusions vary among the meta-analyses because of the varying length of follow-up in the analyses, or exclusions related to methodologic concerns.6

A Cochrane review of the seven studies concluded that current evidence does not show an overall survival benefit from mass screening for breast cancer and is inconclusive for breast cancer mortality.7 Among women in their forties, the review reported a relative risk for death from breast cancer of 1.03 (confidence interval [CI], 0.77 to 1.38), although this risk was based on data from only two of the trials because of bias concerns and inappropriate methods used in the remaining trials.

The U.S. Preventive Services Task Force (USPSTF) conducted a meta-analysis of six of the studies (excluding one1 of the seven trials for methodologic reasons) to evaluate the effectiveness of screening women in their forties with mammography.6 The results of the meta-analysis found a relative risk of 0.85 (credible interval [CrI], 0.79 to 0.99), and a 15 percent relative risk reduction. (CrI is a Bayesian statistical distribution, similar to the confidence interval.) The number of 40-year-old women who would have to be screened for 14 years to prevent one death from breast cancer was 1,792 (CrI, 764 to 10,540).

With a longer period of observation, there appears to be an increasing benefit from screening among women in their forties. While some earlier meta-analyses showed no benefit,8 subsequent meta-analyses have incorporated more recent study results and have demonstrated reductions in breast cancer mortality after longer follow-up periods.

The RCTs do not directly address whether the magnitude of benefit from screening is sufficient to outweigh the harm (e.g., unnecessary biopsies). The risk for false-positive mammography results and their consequences is highest in younger women. On the basis of the USPSTF meta-analysis of more than 10 years of biennial screening among women in their forties, for each death from breast cancer prevented, approximately 400 women would have false-positive results on mammography and 100 women would undergo biopsy or fine-needle aspiration.6 It is important to note that in one cross-sectional survey, 63 percent of women indicated that they would accept 500 instances of false-positive results to save one life.9

One study10 compared the cost-effectiveness of mammography screening in women of various age groups. The results of this study concluded that screening women 40 to 49 years of age with mammography improved life expectancy by 2.5 days at a cost of \$676 per woman, resulting in a cost-effectiveness ratio of \$105,000 per year of life saved.

Screening intervals in the clinical trials ranged from 12 to 33 months. The period in which breast cancer can be detected before it clinically presents may be shorter in women 40 to 49 years of age, suggesting that they should be screened at shorter intervals than older women. However,

there is no clear evidence from the trials of a difference in mortality reduction related to screening interval.2,6

Recommendations from Others

Nearly all North American medical organizations support mammography screening, although they vary in the recommended age to begin screening and the interval for screening. The American Medical Association, American College of Radiology, American Cancer Society, American College of Obstetricians and Gynecologists, and the USPSTF all support mammography screening beginning at age 40.11-15

The American Academy of Family Physicians (AAFP) and the Canadian Task Force on Preventive Health Care recommend beginning mammography screening in average-risk women at age 50, and that all women aged 40 to 49 be counseled about the risks and benefits of mammography before making a decision to screen.16,17 The USPSTF recommendations suggest "the precise age at which the potential benefits of mammography justify the possible harms is a subjective choice."15p1 In addition, the AAFP recommends mammography screening in highrisk women beginning at age 40.16

Clinical Commentary

Because of the controversy about when to begin routine screening, the problems of false-positive mammography results, and possible over-diagnosis, patients and their physicians should decide together when to start screening. The decision should be made by reviewing patient education materials with the patient to help her understand the risks of breast cancer and of false-positive mammography results. The AAFP provides a booklet entitled, "Breast Cancer Screening Counseling Tools" (available online at <u>http://www.aafp.org/x19498.xml</u>) that can be used during the discussion.

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REFERENCES

1. Alexander FE, Anderson TJ, Brown HK, Forrest AP, Hepburn W, Kirkpatrick AE, et al. 14 years of follow-up from the Edinburgh randomised trial of breast-cancer screening. Lancet 1999;353:1903-8.

2. Tabar L, Fagerberg G, Chen HH, Duffy SW, Smart CR, Gad A, et al. Efficacy of breast cancer screening by age. New results from the Swedish Two-County Trial. Cancer 1995;75:2507-17.

3. Shapiro S, Venet W, Strax P, Venet L. Current results of the breast cancer screening randomized trial: the Health Insurance Plan (HIP) of greater New York study. In: Day NE, Miller AB, eds. Screening for breast cancer. Toronto: Huber, 1988.

4. Miller AB, To T, Baines CJ, Wall C. The Canadian National Breast Screening Study-1: breast cancer mortality after 11 to 16 years of follow-up. A randomized screening trial of mammography in women age 40 to 49 years. Ann Intern Med 2002;137(5 pt 1):305-12.

5. Nystrom L, Andersson I, Bjurstam N, Frisell J, Nordenskjold B, Rutqvist LE. Long-term effects of mammography screening: updated overview of the Swedish randomised trials [published correction appears in Lancet 2002;360:724]. Lancet 2002;359:909-19.

6. Humphrey LL, Helfand M, Chan BK, Woolf SH. Breast cancer screening: a summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2002;137:347-60.

7. Olsen O, Gotzsche PC. Screening for breast cancer with mammography. Cochrane Database Syst Rev 2004;(3):CD001877.

8. Glasziou PP, Woodward AJ, Mahon CM. Mammographic screening trials for women aged under 50. A quality assessment and meta-analysis. Med J Aust 1995;162:625-9.

9. Schwartz LM, Woloshin S, Sox HC, Fischhoff B, Welch HG. US women's attitudes to false positive mammography results and detection of ductal carcinoma in situ: cross sectional survey. BMJ 2000;320:1635-40.

10. Salzmann P, Kerlikowske K, Phillips K. Cost-effectiveness of extending screening mammography guidelines to include women 40 to 49 years of age [published correction appears in Ann Intern Med 1998;128:878]. Ann Intern Med 1997;127:955-65.

11. Mammographic screening for asymptomatic women. Report 16 of the Council on Scientific Affairs (A-99). Chicago: American Medical Association, 1999. Accessed online August 5, 2004, at: http://www.ama-assn.org/ama/pub/article/2036-2346.html.

12. Feig SA, D'Orsi CJ, Hendrick RE, Jackson VP, Kopans DB, Monsees B, et al. American College of Radiology guidelines for breast cancer screening. AJR Am J Roentgenol 1998;171:29-33.

13. Smith RA, Saslow D, Sawyer KA, Burke W, Costanza ME, Evans WP 3d, et al. American Cancer Society guidelines for breast cancer screening: update 2003. CA Cancer J Clin 2003;53:141-69.

14. Committee on Gynecologic Practice, American College of Obstetricians and Gynecologists. ACOG Committee Opinion. Primary and preventive care: periodic assessments. Number 292, November 2003. (Replaces no. 246, December 2000). Obstet Gynecol 2003;102(5 pt 1):1117-24.

15. U.S. Preventive Services Task Force. Screening for breast cancer: recommendations and rationale. Ann Intern Med 2002;137(5 pt 1):344-6.

16. Summary of policy recommendations for periodic health examinations. Rev. 5.4, August 2003. Leawood, Kan.: American Academy of Family Physicians, 1996.

17. Ringash J, Canadian Task Force on Preventive Health Care. Preventive health care, 2001 update: screening mammography among women aged 40-49 years at average risk of breast cancer [published correction appears in CMAJ 2001;164:753]. CMAJ 2001;164:469-76.

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