

## Screening Mammography for Reducing Breast Cancer Mortality

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### Clinical Question

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

### Evidence-Based Answer

Screening mammography reduces breast cancer mortality in women 40 to 49 years of age who have an average risk of breast cancer. (Strength of Recommendation: A, based on eight randomized controlled trials [RCTs].) The relative risk reduction in this age group is 15 percent, similar to that of women 50 years and older (14 percent). To prevent one breast cancer death, 1,904 women 40 to 49 years of age must be screened annually for 10 years, compared with 1,339 women 50 to 59 years of age. Although both age groups appear to have a similar relative risk reduction from routine screening, women 40 to 49 years of age have a smaller absolute risk reduction and may experience greater harms from screening compared with older women. These potential harms include false-positive results, diagnosis and treatment for cancer that would not have become clinically evident during the woman's lifetime, false-negative results (i.e., false reassurance), radiation exposure, biopsies, and anxiety.

### Evidence Summary

A meta-analysis of seven RCTs (n = 187,091) found that screening mammography every one to two years in women 40 to 49 years of age results in a 15 percent relative risk reduction in breast cancer mortality after 14 years of follow-up (relative risk [RR] = 0.85; 95% credible interval [CrI], 0.73 to 0.99). A Bayesian statistical analysis was used with

CrI in place of confidence interval (CI).<sup>1</sup> In this meta-analysis, the relative risk reduction is smaller than the 22 percent relative risk reduction in women 50 years and older (RR = 0.78; CrI 0.70 to 0.87).<sup>1</sup>

In a Cochrane review of seven RCTs (n = 600,000), three trials with adequate randomization showed a 10 percent relative risk reduction in breast cancer mortality (RR = 0.90; 95% CI, 0.79 to 1.02), although this was not statistically significant.<sup>2</sup> The other four trials had inadequate randomization. The overall conclusion was an estimated relative risk reduction of 15 percent corresponding to an absolute risk reduction of 0.05 percent (number needed to treat = 2,000).<sup>2</sup> The Cochrane authors note that the benefit of screening may have been favorably accentuated because of the inherent bias in reporting the cause of death in these trials.<sup>2</sup>

A meta-analysis of eight RCTs (n = 348,219) incorporated data from a European trial with a specific focus on patients 40 to 49 years of age.<sup>3</sup> This meta-analysis estimated a 15 percent relative risk reduction in breast cancer death (RR = 0.85; CrI, 0.75 to 0.96) and an absolute risk reduction of 0.025 percent (number needed to treat = 4,000).<sup>3</sup> Women 50 to 59 years of age in this meta-analysis had a 14 percent relative risk reduction (RR = 0.86; 95% CrI, 0.75 to 0.99).<sup>3</sup> Although the estimates of relative risk reduction for these two age groups are nearly identical, the absolute risk reduction is less for women 40 to 49 years of age because of a decreased incidence of baseline disease compared with older women.<sup>3</sup>

The European RCT (n = 160,921) is the only study that specifically addresses the ►

effectiveness of screening women in their 40s and reflects current screening practices.<sup>4</sup> Previous trials of screening mammography for women in their 40s had included women up to 49 years of age at the time of trial entry, and it was unclear how beneficial screening was after they reached 50 years of age. This study was specifically designed to overcome these limitations by enrolling women 39 to 41 years of age and offering screening up to only 48 years of age.<sup>4</sup> The reduction in breast cancer mortality noted in the women undergoing screening beginning at 40 years of age was similar to that of previous trials, but the reduction was not statistically significant (RR = 0.83; 95% CI, 0.66 to 1.04).<sup>4</sup>

Statistical models evaluating mammography screening starting at 40 years of age estimate a small gain (an additional 3 percent reduction in breast cancer deaths) that requires a larger number of additional screenings.<sup>5</sup> Furthermore, approximately 60 percent more false-positive results occur per 1,000 women screened at 40 to 49 years of age, leading to a marked increase in potentially unnecessary testing and procedures.<sup>5</sup>

### Recommendations from Others

The U.S. Preventive Services Task Force recommends biennial screening mammography for women 50 to 74 years of age.<sup>6</sup> The decision to start regular biennial screening before 50 years of age should be individualized and take into account patient context, including the patient's values regarding specific benefits and harms.<sup>6</sup> The American Academy of Family Physicians endorses these recommendations.<sup>7</sup> The American Cancer Society recommends yearly mammography starting at 40 years of age.<sup>8</sup> The American College of Obstetricians and Gynecologists recommends mammography every one to two years in women 40 to 49 years of age.<sup>9</sup> The American College of Physicians recommends that screening mammography decisions be based on patient preference and individualized risk assessment in women 40 to 49 years of age.<sup>10</sup>

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Author disclosure: No relevant financial affiliations to disclose.

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