1. In reference to the optimal frequency of screening mammography, it seems that finding the “most efficient” screening strategy by focusing on the group most likely to show a reduction in mortality per test performed will yield a public policy that deprives younger women of the opportunity to detect breast cancer at an early stage. In contrast, defining efficiency by number of life years gained through screening would favor screening younger women. In these times of limited health care resources, how should these complexities and apparent contradictions be resolved to develop a coherent and fair public policy for breast cancer screening?

Response from Drs. Griffin and Pearlman:
This question is at the crux of the debate. Putting a dollar value on lives saved is, at its core, a very difficult ethical dilemma. Yet, we make those clinical decisions every day (e.g., ordering a pelvic ultrasound in a menopausal woman with vague abdominal pain). There are approximately 40,000 women under age 50 diagnosed with breast cancer each year in the United States, which accounts for more diagnoses of cancer in U.S. women than any other single gynecologic cancer at any age. Clearly, breast cancer in women under age 50 is an important public health issue.

However, when a screening test exists that demonstrates an improvement in mortality, it does make good public health sense to assure that the decision to routinely utilize that test is a balanced one in terms of possible harms and cost. In this case, harms from routine mammogram screening for average risk women in their 40s includes increased callbacks and biopsies performed on women without breast cancer, as well as overdiagnosis (i.e., ductal...
carcinoma in situ [DCIS] that would eventually not become invasive cancer). Resource consumption, while not specifically measured by the United States Preventive Services Task Force (USPSTF), is the cost of testing (including mammograms, callbacks, and biopsies) consumed for each invasive cancer diagnosis or, alternatively, for each life saved due to earlier breast cancer diagnosis. It would also be important to analyze whether these “up front” costs would be diminished by the potential savings of diagnosing breast cancer at an earlier stage.

So, what public policy decision should be made when there are both benefits and harms weighted differently by different groups? One of the factors that I think deserves heightened recognition is the measure of number of life years saved. Without trying to place an absolute value of a loss of life at age 45 compared to age 65, it is important to acknowledge that these younger women do play a different societal role. Frequently, women in their 40s are raising young children, are at the peak of their business careers, and are much more likely to have others dependant on their vitality. It seems to make good public policy sense to consider not only the frequency of the disease, but the impact of these young lives lost balanced against the resource consumption. Since a detailed analysis like this does not exist, one has to make a judgment about the relative benefit versus harm/cost of routine screening in these women. While public policy and public opinion appears to be lining up in favor of routine screening in young women, a difference of opinion still exists.

2. Considering the evidence you cited showing suboptimal sensitivity for mammograms in women with dense breasts (even with full-field digital mammography), should these women have annual—rather than biennial—mammograms?

Response from Drs. Griffin and Pearlman:
The sensitivity of mammography in women with dense breasts has not been used as a reason to alter screening recommendations. Specific recommendations for these women should be guided by their age and other risk factors. That said, sensitivity and mortality reduction are maximized by annual screening. In addition, women with mammographically dense breasts have been shown to have a higher risk of breast cancer than age-matched controls. This may be a factor to consider when discussing screening mammography frequency with women in this category, although there are no direct data studying annual versus biennial screening in women with dense breasts. Of course, these women should be informed of the limitations of mammography particularly in women with dense breasts, and should be encouraged to report changes in their breasts to their physician regardless of recent mammogram results.
3. Has full-field digital mammography been shown to be a cost-effective improvement over traditional film images?

Response from Drs. Griffin and Pearlman:

Digital mammography has been demonstrated to detect more cancers in certain populations (younger women, women with dense breasts) when compared to film-screen mammography.(4) Because digital mammography is more costly than film-screen mammography, cost-effectiveness has been questioned. The selective use of digital mammography has been evaluated in populations where it is more sensitive (i.e., women under 50 and women with dense breasts). In a cost-efficacy study published in 2008, digital mammography was shown to be favorable in women under age 50 ($26,000 per quality adjusted life year [QALY]). This favorable cost effectiveness was diminished when it was employed in women with just dense breasts ($97,000 per QALY), and least cost effective when utilized in all women ($236,000 per QALY).(5)

4. Is there a role for ultrasound alone for future screening of women with extremely dense breasts found on an initial mammogram? If not, should ultrasound be ordered concurrently with mammogram for these women to decrease the frequency of callbacks?

Response from Drs. Griffin and Pearlman:

Ultrasound alone is not recommended for screening of any population of women. Despite the potential limitations of mammographic screening, no other screening modality alone has been demonstrated to reduce morbidity and mortality from breast cancer.

However, screening whole-breast ultrasound is being evaluated as an adjunct to mammography for screening of women at higher risk of breast cancer, which may include those with heterogeneously dense breast tissue. In this population, whole-breast ultrasound appears to increase cancer detection, but at the cost of increased numbers of biopsies and decreased positive predictive value of imaging.(6-8) Whole-breast ultrasound is recommended as a second screening modality for women who are candidates for breast MRI based on high risk factors such as BRCA gene mutation status, but who have a contraindication to MRI. In this population, whole-breast ultrasound plus mammography appears to be more sensitive than mammography alone, but not as sensitive as mammography plus MRI for cancer detection.(3)

There is ongoing research into appropriate uses of screening whole-breast ultrasound, but at present, whole-breast ultrasound is not recommended as an adjunct for screening of women.
with dense breasts by the American Cancer Society, the National Comprehensive Cancer Network, or the U.S. Preventative Services Task Force.

5. You note that length of time spent with clinical breast examination is the most important factor in detecting suspicious changes. What are reasonable guidelines for duration of a structured, standardized breast examination? At what frequency should clinical breast examinations be scheduled for a woman with average risk for breast cancer? Should this ideal frequency be adjusted for frequency of screening mammograms?

Response from Drs. Griffin and Pearlman:
Evidence regarding specific time of palpation and cancer detection are limited, but 3 minutes per breast has been promulgated as an appropriate goal.(9) Clinical judgment should be used in determining when a clinical breast examination is complete; for example, more time is typically necessary to examine a woman with large, glandular breasts than to examine a woman with smaller, smoother breast tissue.

We advocate annual clinical breast examination at the time of the health maintenance exam for women at average breast cancer risk. As mammographic screening guidelines become more personalized, and assuming some women choose the biennial screening mammography approach, annual clinical breast examination may arguably become even more important, as it is the only clinically-based screen in that 2-year interval. While the USPSTF found insufficient evidence to recommend for or against clinical breast examination, it is clear that clinical breast examination detects some potentially curable breast cancers that are missed by mammography.(9)

6. What are the essential learning objectives in teaching “breast self-awareness” and how do they differ from those traditionally taught for breast self-examination?

Response from Drs. Griffin and Pearlman:
Breast self-awareness is a concept that has arisen from two key pieces of information. First, approximately half of all breast cancers in women 50 years and older and 70+% of cancers in women under age 50 are detected by women themselves, primarily incidentally.(10, 11) Breast self-examination was introduced as a way to self-detect cancer earlier. The second key piece of information is that the effectiveness of self-examination was at odds with what was anticipated based on the above statistics. As discussed in the article, studies of the effectiveness of breast
self-examination, performed on foreign populations who were not routinely screened with mammography, showed no improvement in mortality with an increase in biopsies (morbidity). In an attempt to combine these pieces of evidence, cancer advocacy groups such as the American Cancer Society began to advocate “breast self-awareness” rather than self-examination as a means for women to play a role in earlier detection.

Breast self-examination is a standardized breast examination, like the clinical breast examination, performed by the woman herself on a periodic (typically monthly) basis. Importantly, self-examination requires that a health care provider teach the patient specific techniques for performing the examination. Though some women find this exercise to be difficult and stressful, it may still be appropriate for certain high risk populations and other women who choose to take on this routine.

Breast self-awareness is much more conceptual. It is simply educating a woman on the limitations of screening mammogram and clinical breast examination, and encouraging her to be familiar with the way her breasts look and feel and to report new changes in her breasts to her health care practitioner promptly. The key to the potential success of this strategy is making women aware that cancers can be missed by traditional screening methods and new cancers can arise during screening intervals, with the hope that women will not delay in reporting breast changes irrespective of normal screening results. Women may incorporate a self examination as a way to familiarize themselves with their normal breast anatomy, but the emphasis here is not on examination techniques. Breast self-awareness aims to capture the importance of self-detection and prompt evaluation of symptoms. However, the effect of breast self-awareness education has not yet been studied.

7. Will most women in their 40s with a first-degree relative with breast or ovarian cancer qualify for genetic counseling? The premenopausal patient at high risk in the clinical scenario had no other family or personal historical factors aside from her mother, which does not qualify her for genetic counseling according to Box 2, but had enough risk factors with the Gail risk-assessment tool to have a lifetime risk greater than 20%.

Response from Drs. Griffin and Pearlman:

The Gail model is most useful because of its simplicity. However, the only family history question in the Gail model asks about breast cancer in either a mother or sister. So, women with a family history of breast cancer on the paternal side, in second or third degree relatives, or any family member with ovarian cancer are not considered at increased risk based on this model. In
women who have these types of family history, models other than the Gail model should be used for assessing likelihood of genetic predisposition to breast/ovarian cancer. For assessing BRCA risk, the two models most commonly utilized are BRCAPRO and BOADICEA, both of which are available at no cost, but do require more time to input data than the Gail model. So, while we advocate a referral to a genetic counselor for any woman who meets the criteria in Box 2, women with concerns about their family history of cancer would also be well served to meet with a genetic counselor. Genetic counseling is a valuable resource and adjunct to discuss the advantages, disadvantages, costs, and implications of testing as well as the likelihood of a family harboring a genetic defect based on these other models. For the busy practitioner, utilizing a skilled cancer genetic counselor can provide added value by helping to determine the best candidates for testing, choosing the appropriate genetic test, determining the appropriate individual to be tested, interpretation of testing (e.g., a variant of uncertain significance), and can often assist with questions about criteria for insurance coverage. Of course, some Ob/Gyn providers may choose to incorporate sophisticated genetic counseling within their practice.

8. In your case presentation of a woman with average risk, you did not mention the use of risk-assessment tools. Should these tools be incorporated into the annual well-woman visit or for new patients? Which model is the most useful for a busy obstetrics and gynecology practice?

Response from Drs. Griffin and Pearlman:
The most important risk assessment tool that should be used at every annual and new patient visit is detailed history taking. A medical history for the well-woman should include reproductive factors such as age of menarche, first birth, and menopause; gravidity and parity; detailed cancer family history (type of cancer and age of onset); and previous breast biopsies and abnormal breast imaging results.

If this history identifies a significant concern regarding the family history such as multiple relatives with breast or ovarian cancer (see article for details), then the patient should either be referred for genetic counseling or, if the Ob/Gyn provider has the time, experience, and interest, the provider may use tools such as BRCAPRO or BODACEA to evaluate the family history and determine the appropriateness of genetic testing or other risk mitigation strategies. In our practice, we work closely with a genetic counselor that has the expertise and time to evaluate the family history thoroughly, and we base our decisions regarding screening and/or risk reduction, in part, on information gleaned from that visit. In addition, our genetic counselor provides us with an estimate of risk based on family history that can be used to determine eligibility for MRI screening and other interventions.
If the history reveals more subtle findings that may increase breast cancer risk, such as late menopause, nulliparity, or a single first degree female relative with cancer, the Gail Model is quick and can easily be done during an office visit. It gives the provider and patient a good idea of how this woman compares to other women her age in terms of breast cancer risk. We do recommend annual mammography and offer twice yearly clinical breast examination for women whose risk is greater than 1.7% in 5 years (the risk equivalent of being 61 years old), and tamoxifen or raloxifene may also be offered to these women.

In short, risk assessment tools beyond a detailed history are not necessary for proper care of most women, but may be used in selected circumstances.

9. Is chemoprophylaxis with tamoxifen something a general obstetrician–gynecologist should administer or should a patient with high risk for breast cancer be treated by a breast specialist?

Response from Drs. Griffin and Pearlman:
Ob/Gyn physicians, more than any other specialty, are accustomed to prescribing hormone therapy, typically as either oral contraceptives or menopausal hormone therapy. The benefits of tamoxifen in women at high risk for breast cancer risk are impressive, with a 50% decrease in invasive and non-invasive breast cancer in high risk women.(12) Like hormone therapy, the side effect profile of tamoxifen includes an increase in venous thromboembolism (twofold increase), and, unlike menopausal hormone therapy, there is a small increase in endometrial cancer in menopausal women taking tamoxifen, as well as an more substantial increase in benign polyp formation in both pre- and post-menopausal women.(13)

So, given the recognized benefits of the drug, and the familiarity that Ob/Gyn physicians have with these types of drugs and their side effects, one might expect a widespread adoption of use. Somewhat surprisingly though, in a 2006 study, primary care physicians (about 20% of whom were Ob/Gyn physicians) were surveyed as to whether they had previously prescribed tamoxifen for breast cancer prevention. In this study, 74% indicated that they had not prescribed tamoxifen in the previous 12 months.(14)

Why the disparity between expected and actual use of tamoxifen for breast cancer prevention? Concerns about side effect profile, lack of knowledge in estimating risk to identify appropriate candidates for tamoxifen, lack of patient interest, or lack of physician time may interfere with the prescribing of tamoxifen. However, as indicated above, Ob/Gyn physicians are in a very
favorable position to both prescribe and follow patients on tamoxifen and should prescribe tamoxifen in appropriate candidates, or refer to an appropriate specialist if they are not comfortable prescribing this drug.(13)

References


