

SKEPDOG

A Skeptical Look at Screening Tests

By Harriet Hall, M.D.

I'm an equal opportunity skeptic. I'm skeptical about alternative medicine, pseudoscience, and quackery; but I apply the same standards of skepticism to conventional medicine. I don't write about conventional medicine so much, because I don't need to. Science itself is inherently skeptical and scientific medicine is self-criticizing and self-correcting. When better evidence comes along, medical practices change. Sometimes the change is slower than we would wish, and sometimes the new information is even slower to reach the general public, or reaches them in a distorted form. I thought it would be worthwhile to look at an area of conventional medicine that is fraught with misunderstandings and where evidence-based recommendations are in flux: screening tests for the general population.

Breast Cancer Screening

Women should do breast self-exams every month and get a mammogram every year, right? We take it for granted that this will detect cancers early and save lives. I used to conscientiously teach breast self-exam (BSE) to my patients and hand out a breast self-exam pamphlet. (Once, when we sent in for more pamphlets, I caught my secretary's omission of an "r" just in time: she had requested "beast" exam pamphlets. I've always wondered what they would have sent...)

Despite my well-intentioned diligence, all my efforts may have been wasted. The evidence doesn't show that teaching or performing routine BSE saves lives. The U.S. Preventive Services Task Force (USPSTF) has concluded that the evidence is insufficient to recommend for or against BSE. Current recommendations in the U.S. are for mammograms every 1-2 years starting at age 40 (or 50) and ending at age 70 or 75. In the UK, mammograms are done every 3 years. Studies have not shown any clear benefit from the more frequent schedule.

Various studies suggest that between 10% and 33% of the women identified as having breast cancer didn't actually need to be treated. Some cancers will never metastasize; some are so slow-growing that the patient dies of something else before they ever cause symptoms; sometimes pathology reports are wrong; some small early cancers spontaneously regress.

There's a phenomenon called lead time bias. Mammography may detect a cancer earlier but not affect the final outcome of the disease: it will appear that survival has been prolonged, but really the only difference is that the woman was diagnosed earlier and lived with knowledge of the disease (and anxiety) for a longer period.

A survey asked women "If you have a positive mammogram, how likely is it that you actually have breast cancer?" Most guessed between 90 and 100%. Even many doctors guessed around 90%. But the right answer is only about 10%. Mammography is 90% accurate in spotting those who have cancer (the sensitivity of the test) and 93% accurate in spotting those who don't (the specificity of the test). The prevalence of cancer among women getting mammograms is 0.8%. This means that of every 1000 women screened, 8 of them actually have cancer. Of those 8 with cancer, 7 will have true positive results and one will have a false negative result. The other 992 women do not have cancer: 922 of them will have true negative results, while 70 of them will have false positive results. So of 77 women with positive tests, only 7 of them have cancer. And of the 923 negative results, one woman will have cancer but will be falsely reassured that she doesn't.

Women don't just get one mammogram. After 3 mammograms, 18% of women will have had a false positive result. After ten exams, the rate rises to 49.1%. In a study of 2400 women who had an average of 4 mammograms over a 10-year period, the false positive tests led to

- 870 outpatient appointments
- 539 diagnostic mammograms
- 186 ultrasound examinations
- 188 biopsies
- 1 hospitalization.

And that doesn't count the psychological distress.

How many lives are saved? If 1000 women are screened for 10 years starting at age 50:

- 1 life will be saved
- 2-10 women will be overdiagnosed and treated needlessly
- 10-15 women will be told they have breast cancer earlier than they would otherwise have been told, but this will not affect their prognosis
- 100-500 women will have at least 1 "false alarm" (about half these women will undergo biopsy)

Another way to look at this is that of every 1000 women screened, 999 would have lived just as long if they had never had a mammogram. Keep in mind that these statistics are only for screening the general population. The results are much better among women who are at high risk for breast cancer. And the results of diagnostic mammography are even better (for instance in someone who has a breast lump). Also, an unscreened woman might spend the last years of her life suffering with cancer, while a screened woman might have had her cancer diagnosed and cured and might enjoy good health in her latter years.

Prostate Cancer Screening

Does PSA screening for prostate cancer save lives? The PCLO trial showed no reduction in mortality with screening. The European Randomized Study of Screening for Prostate Cancer showed that out of every 10,000 men screened, 7 fewer died of *prostate cancer* but the *total* number of deaths was not reduced. And 17,000 out of 73,000 men got prostate biopsies. Is it worth screening 1068 men and treating 48 to

save one man from dying of prostate cancer while not reducing the total number of deaths? There are significant risks to PSA screening: biopsies, surgery, hormone treatment, chemotherapy, impotence, incontinence.

Colon Cancer Screening

Colon cancer screening is strongly recommended but the evidence is weak. There are 3 main options: fecal occult blood testing (FOBT) every year, sigmoidoscopy every 5 years, or colonoscopy every 10 years. Colonoscopy is considered the "gold standard" because it directly visualizes the entire colon and permits removal of polyps and other suspicious lesions. Colonoscopy apparently reduces the risk of colon cancer death from cancers in the left colon, but surprisingly it has no effect on the death rate from cancers in the right colon.

And colonoscopy is not benign: it can cause bleeding, perforation of the colon, infections, and reactions to sedation. It can even lead to death, especially in the ill or elderly.

By one estimate, screening 1173 patients with FOBT for 10 years will prevent one death from colon cancer. No studies have directly compared colonoscopy with FOBT, and *we have no direct evidence* (i.e. from randomized controlled trials) that any colon cancer screening test reduces total all-cause mortality.

Other Screening Tests

The PCLO trial evaluated multiple screening tests for four cancers: prostate, colon, lung, and ovarian. By the 14th screening test, 60% of men and 49% of women had had false positives. This led to invasive diagnostic procedures in 29% of men and 22% of women; 15.8% were moderately invasive (like biopsy) and 1.6% involved major surgical procedures (like hysterectomy).

The U.S. Preventive Services Task Force (<http://www.ahrq.gov/clinic/uspstfix.htm>) periodically evaluates all the published evidence and issues updated screening recommendations like this one for glaucoma: "[given] the uncertainty of the magnitude of benefit from early treatment and given the known harms of screening and early treatment, the USPSTF could not determine the balance between the benefits and harms of screening for glaucoma." Reading their various findings is an eye-opener.

Some screening tests have proven value, like Pap smears and blood pressure measurements. The major preventable cause of death in the U.S. today is smoking. "The USPSTF strongly recommends that clinicians screen all adults for tobacco use and provide tobacco cessation interventions for those who use tobacco products." If patients complied, 440,000 lives could be saved each year in the U.S. alone.

Criteria for Screening Tests

How do we know what screening tests to offer the general population? We have learned that routine annual urinalyses, blood counts and chest x-rays aren't useful. It wouldn't make sense to screen everyone

for Ebola virus. No one would recommend doing cardiac catheterizations on everyone to screen for heart disease.

The World Health Organization lists these criteria for screening tests:

- The condition sought should be an important health problem for the individual and community.
- There should be an accepted treatment or useful intervention for patients with the disease.
- The natural history of the disease should be adequately understood.
- There should be a latent or early symptomatic stage.
- There should be a suitable and acceptable screening test or examination.
- Facilities for diagnosis and treatment should be available.
- There should be an agreed policy on whom to treat as patients.
- Treatment started at an early stage should be of more benefit than treatment started later.
- The cost should be economically balanced in relation to possible expenditure on medical care as a whole.
- Case finding should be a continuing process and not a once and for all project.

Instead of screening everyone, we could selectively screen those who are at higher risk. Whatever we do, we must continually re-examine our practices, re-evaluating whether we are really doing more good than harm. Science never claims to have final answers; it's an ongoing process. Ideally, doctors could give patients the best currently available evidence and let them decide if they want to be screened. Some will want to know at all costs, others will think the non-screening odds are pretty good and will prefer to take their chances, avoiding the expense, inconvenience, worries, and discomforts that screening entails. It's a gamble any way you look at it. Oh, for a crystal ball!