Prostate cancer is an important disease. It is the second leading cause of cancer death in men who don’t smoke, and in many cases it is detectable early and curable. The rates of both diagnosis and death from prostate cancer in men are similar to the rates of breast cancer in women.1

The current practical screening test for prostate cancer is the prostate specific antigen (PSA). Making routine use of it, as we know, however, is controversial.

The false positive rate for PSA testing is high, for example, in men with chronic prostatitis and benign prostatic hypertrophy.2 In addition, many prostate cancers are diagnosed that will never harm the patient. Treatment for prostate cancer may result in complications, such as incontinence and impotence. Because of these facts, the US Preventive Services Task Force (USPSTF) has recommended against routine screening.2

The PSA test itself never hurt anyone
It is just a lab value, a piece of information. What doctors do with the information is the issue. Physicians may cause more harm than good by being overly aggressive with elevated PSA levels and indolent or low-grade prostate cancer—and 75% of prostate cancer is considered indolent (Gleason score of 6 on biopsy).3 Patients with such a finding can be watched, using active surveillance. The majority will never need treatment.3

Common sense tells us we must screen for prostate cancer. Not doing so on the basis of evidence-based medicine is not a defense when advanced cancer is diagnosed and screening was not offered to the patient.4 Rather than using the data from past physician behavior and recommending against screening with PSA, the USPSTF should have criticized the response to PSA test results and recommended a better way. I see this change rapidly becoming current practice.

PSA testing saves lives
Since the early 1990s, when PSA testing became widespread, there has been a 40% decline in prostate cancer mortality.5 A randomized trial in 7 countries in Europe clearly showed a survival benefit from screening for prostate cancer.6 Clinical trials in the United States have been ambiguous.

Not screening for prostate cancer with PSA is unacceptable to many physicians and patients. Most physicians have seen preventable prostate cancer deaths. Two patients in my practice illustrate this point. The PSA of one of them—a 62-year-old man—went from 2.4 to 24 in 2 years. The PSA of another, age 56, went from 2.6 to 34 in one year. Both men had no symptoms, and their prostate cancer was found on routine screening. Both had a high Gleason score and locally invasive prostate cancer. Now, years after

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In his book, *How We Do Harm: A Doctor Breaks Ranks About Being Sick in America*, Otis Brawley1 writes, “I believe that a man should know what we know, what we don’t know, and what we believe about prostate cancer. I have been concerned that many patients and physicians have confused what is believed with what is known.” I agree.

Common sense is what we believe. Does common sense trump science? Did the US Preventive Services Task Force (USPSTF) get it wrong? I don’t think so.

The USPSTF bases its recommendations on an explicit assessment of the science that informs us of the benefits and harms of a preventive service, and a judgment about the magnitude of net benefit.

**What do we know about the benefits of prostate cancer screening?** When attempting to answer the question of whether an intervention is beneficial, there is a hierarchy of evidence, from most likely to be wrong to most likely to be right. Relying on our personal stories is the former; relying on well-conducted randomized trials is the latter.

In the multicenter Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial2 conducted in the United States, there was a nonsignificant increase in prostate-cancer mortality in the screening group, while the European Randomized Study of Screening for Prostate Cancer (ERSPC)3 trial showed a statistically significant absolute reduction of 0.10 prostate-cancer deaths per 1000 persons-years after a median follow-up of 11 years. In the ERSPC trial, all-cause mortality was 19.1% in the screened group and 19.3% in the control group, a difference that was not significant. What we know is that after 10 years, even with aggressive treatment of 80% to 90% of screen-detected cancers, very few, if any, men will have lived longer because they were screened.

**What don’t we know about the benefits?** We don’t know whether following screened and nonscreened men for 15 or 20 years or longer will demonstrate a larger difference in mortality. Competing causes of mortality make it progressively less likely that men who are screened will actually live longer. The average age of death from prostate cancer is 80 years, and 70% of all deaths occur after age 75.4 Contrast those statistics to breast cancer, for which the average age of death is 68 years and 63% of all deaths occur before age 75.5

**What do we believe about the benefits?** Some certainly believe the trials must be wrong; common sense tells us that early detection and treatment must provide more benefit than what the evidence has shown. Common sense tells us that the decline in prostate cancer mortality over the past 2 decades must be due to screening, although the ERSPC results clearly show that neither the magnitude nor the timing of the decline can be attributed to screening.

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![The USPSTF got it right](image)
undergoing cancer treatment, both have undetectable PSA levels and full function. They think the USPSTF’s recommendation not to screen is evidence of the government’s attempt to save money, reinforcing the notion that the government cannot be trusted.

Patients are increasingly savvy

With all the controversy around prostate cancer screening and the adverse effects of treatment, patients are getting savvier. Shared decision making between doctor and patient is becoming the standard of care, and physicians can meet their professional obligations by offering screening and answering any questions the patient may have. I find that most men with low-grade disease are happy to avoid surgery and radiation if active surveillance is offered and explained.

The American Academy of Family Physicians adopted the recommendation of the USPSTF to advise against screening for prostate cancer. The American College of Physicians recommends that men ages 50 to 69 be given the opportunity for informed decision making before screening. The American Urological Association recently recommended that men ages 55 to 69 be offered screening, with a discussion about the risks and benefits; and the American Cancer Society recommends screening starting at age 50, and earlier for high-risk men.

Not satisfied that any of these organizations really knows what is best and aware that the data are confusing and evolving, I continue to follow my overall practice approach: Start routine cancer screening at age 50 in the general population and at age 40 for high-risk groups. This works for colon, breast, and prostate cancer, the big 3 that are common, sometimes fatal, and often curable with early detection.

Men in my practice are offered a PSA test starting at age 50, and every one to 2 years thereafter based on both patient preference and the results. Black men and those with a family history of prostate cancer before age 60 are offered screening starting at age 40. I suggest that screening be stopped at age 80, or earlier if the patient has a serious chronic illness with a life expectancy of less than 10 years.

Active surveillance for low-grade disease

What is done with elevated or rising PSA levels is most controversial, with lots of room for doing harm. Dramatic rises in PSA, like those of the patients I described earlier, are easy: Go right to biopsy and usually, treatment. Gleason 6 prostate cancer is likely to remain localized and indolent, and not threaten life. I work with urologists who are not aggressive and are willing to follow patients with PSA levels up to 10. Noninvasive options are available, such as fractionating the PSA (free and total) and imaging such as MRI. Genetic testing is available and can add to the evaluation of the patient’s risk.

Active surveillance has become a standard of care in monitoring patients with low-grade disease. The outcomes for survival with active surveillance are as good as radical prostatectomy. The goal is to be aggressive in treatment only with patients who have life-threatening disease. A collaboration among the patient, the primary care physician, and the urologist is crucial to optimizing patient outcomes.

Recommending against screening for prostate cancer is not tenable. The responsible approach is to continuously improve cancer detection and therapy to maximize good and minimize harm. This approach is available today.

References
What do we know—and not know—about the harms?

We know that much of the suffering from prostate cancer is a consequence of the diagnosis and management of the disease, rather than the disease itself. Complications of both diagnosis and treatment of prostate cancer are frequent and serious. We also know that many screen-detected cancers would never become apparent in a man’s lifetime without screening.

We don’t know the precise magnitude of overdiagnosis, although all estimates suggest it is substantial. In the ERSPC trial, 9.6% of the screened group received a prostate cancer diagnosis, vs 6.0% of the control group—a 60% increase in the rate of diagnosis. The recently published long-term results from the Prostate Cancer Prevention Trial are enlightening. Finasteride reduced the incidence of screen-detected cancers by 30%, with no impact on all-cause mortality at 18 years. If those screen-detected cancers had been a significant threat to health, then after 18 years we would have expected some mortality benefit from finasteride.

What do we believe about the harms of screening?

We believe that by being more conservative about who gets treated, we shift the balance of benefits and harms of screening. There is no question that reducing the burden of overdiagnosis and overtreatment would provide a welcome reduction in the harms. But can we do it?

In the United States 90% of men found to have prostate cancer are treated (including about 75% of men with low-risk cancers). And although we hope to be able to reduce harms without changing benefits, we do not know what impact more conservative management of screen-detected cancers would have on the already small effect of screening on prostate cancer mortality.

So what is the balance of benefit and harms? Should we make that judgment on what we know, or on what we believe?

Science trumps common sense. For every 1000 men screened, at most, one will avoid a prostate cancer death at 10 years. But 30 to 40 will have erectile dysfunction, urinary incontinence, or both due to treatment. Two men will experience a serious cardiovascular event, one will have a venous thromboembolic event, and one in 3000 screened will die from complications of surgical treatment.

The USPSTF concluded that the benefits of PSA screening do not outweigh the harms, but acknowledged that shared decision making is still appropriate when a physician feels obliged to offer the test or a patient requests it.

What does shared decision making look like? Just offering screening and answering any questions is not good enough. We do an enormous disservice to our patients if we pretend that this is just a blood test and that we can decide later what to do with the information. Men will get biopsies and there will be complications. Cancer will be detected, and men will be treated, many unnecessarily.

We need to tell our patients that the likelihood of avoiding a prostate cancer death over 10 years as a result of regular PSA screening is at most very small, and that many more men will suffer the harms of unnecessary treatment than will benefit. A few will die prematurely as a result of the complications of treating a screen-detected cancer.

If, with this knowledge, a patient places a higher value on the possibility of avoiding a prostate cancer death than he does on the known harms of diagnosis and treatment, he can still decide to be screened. He has made an informed decision. However, routine screening for prostate cancer in the absence of a truly informed decision is unacceptable.

References


