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Can Cancer Ever Be Ignored?

By SHANNON BROWNLEE and JEANNE LENZER

As chief medical and scientific officer of the American Cancer Society, Otis Webb Brawley — who is also a professor of oncology and epidemiology at Emory University — is the public face of the cancer establishment. He operates in a world of similarly high-achieving, multiple-credentialed, respectable professionals, where insults tend to be delivered, stiletto-style, in scientific language that lay people aren't meant to understand. So it can be more than a little jarring to hear, for example, James Mohler, chairman of the urology department and associate director of the Roswell Park Cancer Institute in Buffalo, say of his friend: "I have known Otis for over 20 years. He doesn't come off as being ignorant or stupid, but when it comes to prostate-cancer screening, he must not be as intelligent as he seems." Or Skip Lockwood, the head of Zero, a prostate-cancer patient advocacy group, charge that Brawley is more concerned about saving men's sex lives than about saving the men themselves.

Brawley has become the target of these attacks because of his blunt and very public skepticism about the routine use of the prostate-specific antigen, or P.S.A., test to screen men for early prostate cancer. "I'm not against prostate-cancer screening," Brawley says. "I'm against lying to men. I'm against exaggerating the evidence to get men to get screened. We should tell people what we know, what we don't know and what we simply believe."

The P.S.A. test, which was approved by the U.S. Food and Drug Administration in 1986, has become an annual ritual for millions of middle-aged men who assume that finding prostate cancer early will prevent death. By 2008, nearly half of men over 50 reported that they were screened in the previous 12 months. Despite the seeming logic of the P.S.A. test, the evidence that it saves lives is far from conclusive, and Brawley is not the only one questioning it. A growing cadre of doctors, epidemiologists, patients and cancer biologists are rethinking its value. And the most recent studies, while not ending the debate, indicate that routine P.S.A. testing appears not to reduce the number of deaths, and if it does, the benefit is exceedingly modest.

Patients and their doctors are now faced with radically polarized views about the logic of routine testing. On one side are physicians like Mohler, who argue that the test can reduce a

man's chances of dying of prostate cancer, plain and simple. This side of the debate is passionate, backed by the persuasive conviction of men who have survived prostate cancer and well financed by the multibillion-dollar industry that has grown up around the testing and treatment of the disease.

The other camp makes a less emotionally satisfying argument: on balance, scientific studies do not support the claim that screening healthy men saves lives. Screening, Brawley and others argue, can lead healthy men into a cascade of further testing and treatments that end up injuring or even killing them. As Richard Ablin, who discovered a prostate-specific antigen, put it in an Op-Ed in The New York Times, using the P.S.A. test to screen for cancer has been "a public health disaster."

So what should a man do when his doctor suggests a routine P.S.A. test? The U.S. Preventive Services Task Force, a panel of independent experts that evaluates the latest scientific evidence on preventive tests and treatments, is charged with making recommendations in just such situations. It already recommends against routine screening for men over 75. According to an internal document, in 2009 the task force conducted an in-depth analysis of data and seemed poised to give routine P.S.A. testing a "D" rating — "D" as in don't do it — for any man of any age. But this was around the time that the task force stated that routine mammography for women ages 40 to 50 was not necessary for every woman. That recommendation caused a public uproar, and Ned Calonge, the task-force chairman at the time, sent the P.S.A. recommendation back for review. One year later, in November 2010, just before midterm elections, the task force was again set to review its recommendation when Calonge canceled the meeting. He says that word leaked out that if the November meeting was held, it could jeopardize the task force's financing. Kenneth Lin, the researcher who led the review, quit his job in protest, and now, nearly two years after its initial finding, it remains uncertain when the task force will release its rating for P.S.A. screening.

Cancer screening is a growing field; existing tests are becoming more sensitive, and new tests are constantly developed. We now have CT scanning for lung cancer, and there is also a blood test marketed by Johnson & Johnson known as a "liquid biopsy," which searches for stray cancer cells in the bloodstream. More testing inevitably brings more treatment, because the urge to correct every cellular anomaly, no matter how small or potentially harmless, is practically irresistible. But if there is one lesson from the P.S.A. test, it is that more information and intervention do not always lead to less suffering.

The popularity of the P.S.A. test as the main weapon against prostate cancer is due in large measure to the earnest and passionate advocacy of William Catalona, a urologist from Northwestern University Feinberg School of Medicine. During his residency training at

Johns Hopkins Hospital in the mid-1970s, Catalona set up a clinic for late-stage prostate-cancer patients. Back then, the only tool for finding prostate cancer was a digital rectal exam — actually feeling the prostate through the rectal wall. By the time many tumors could be detected, the cancer was already advanced, and removing the prostate surgically did not offer a reliable cure.

Catalona grew close to many of the men he treated, as well as to their families. “Prostate cancer is a terrible death,” he said. “They developed bone fractures, they had a lot of pain, they lost weight. They required heavy doses of narcotics.”

Catalona wanted to catch these cancers early, when they might be curable. He noticed that men with more advanced cancers at the time of surgery tended to have the highest P.S.A. levels. Could there be a bright line, a “safe” level of P.S.A. that could distinguish healthy men from those with prostate cancer? After reviewing his own patient records, he decided the cutoff level should be 4 nanograms of P.S.A. per milliliter of blood. He followed up with a study of 1,653 patients. The results, published in 1991 in The New England Journal of Medicine, showed that P.S.A. testing could detect prostate cancer several years earlier than a digital rectal exam.

The test quickly gained powerful support: Gerald Murphy, who held the position at the American Cancer Society now held by Brawley, pushed the society to endorse the test. In 1996, Gen. H. Norman Schwarzkopf, a prostate-cancer survivor, appeared on the cover of Time magazine over the statement “There’s a simple blood test everyone should know about.”

By then, doctors were using the test for routine screening. “P.S.A. testing was so easy,” says H. Gilbert Welch, a professor of medicine at the Dartmouth Institute (full disclosure: one author of this article is an instructor at Dartmouth). Doctors were predisposed to use the test for several reasons. First and foremost, there was the perception that early detection could save lives. It was also easy to administer. “It was a blood test,” Welch says. “You didn’t need equipment. . . . You didn’t need to put any scopes up any part of the body. Heck, you didn’t even need to ask the patient if he wanted it; you could just check off the box on a list of tests, like cholesterol, when you did a blood draw.” Today it’s common for doctors to order the P.S.A. test and patients to take it without talking about what it might really mean.

At one time, Otis Brawley, too, assumed that routine screening was the best medical practice. Sitting in his living room in an Atlanta suburb, Brawley recounted his transformation from believer to skeptic. In 1988, after medical school at the University of Chicago, Brawley landed a prestigious fellowship at the National Cancer Institute in

Bethesda, Md. There he came under the tutelage of Barnett Kramer, an oncologist and epidemiologist who went on to become the associate director of the institute's early detection and community oncology program. Kramer walked Brawley through a short history of screening, beginning with the Pap smear, which has been an unqualified success, significantly cutting cervical-cancer deaths.

But other cancer screening tests had not worked out so well. For example, researchers at the Mayo Lung Project conducted a study between 1971 and 1983 to determine whether frequent chest X-rays could help reduce deaths from lung cancer. Chest X-rays detected lots of suspicious spots and shadows on the lungs and probably led to some cures of early lung cancers, but the study ultimately found no difference in death rates between the patients who were screened and those who were not. Kramer suggested one probable explanation: diagnosing the spots picked up by X-ray often requires surgery, which carries a small but definite risk. Brawley knew that many spots seen on X-rays are simply old scars or minor abnormalities commonly seen in healthy people. With so many innocent blips detected, complications from lung biopsies and other invasive tests, along with treatment complications, could kill enough patients to negate any benefit from early detection.

Prostate cancer is the second-leading cause of cancer death among men, after lung cancer. In 2009, it was diagnosed in approximately 192,000 men. A small number of tumors are very aggressive, but the majority of prostate tumors are not likely to cause death. They grow very slowly, and only a fraction break out of the prostate, seed new tumors in other parts of the body and kill the patient. The current thinking is that about 30 percent of men in their 40s have prostate cancer, 40 percent of men in their 50s and so on, right up to 70 percent of men in their 80s. Yet only 3 percent of all men die from the disease. In other words, far more men die *with* prostate cancer than *from* it, and only a tiny fraction of prostate cancers ever cause symptoms, much less death.

But here is the tricky part: Unless there are symptoms or a finding on a physical exam, doctors generally cannot accurately predict which cancers are destined to be indolent, to sit around for years growing slowly, if at all, and those that will ultimately prove lethal.

In his discussions with Kramer, Brawley saw that these two pieces of information — the fact that a certain number of prostate cancers will never cause harm, and that doctors can't reliably predict which cancers will be dangerous — had powerful and potentially devastating consequences for men. The first implication was that using the P.S.A. test to screen men who had no symptoms would uncover a huge reservoir of indolent cancers. Most of those cancers that men previously died with — and not from — would now theoretically be detectable. And once detected, the majority of those cancers would be treated.

The most frequent treatment then, as it is now, was the surgical removal of the entire prostate gland. The prostate sits at the base of the penis, wrapped around the urethra, which is the tube that carries urine and semen out of the penis. Trying to separate gland from urethra is a difficult job, and even the best of surgeons can damage the urethra or the bundle of nerves that initiate erections. About half of men who undergo radiation or surgery will have permanent side effects like impotence and incontinence. Up to 1 in 200 men die within 30 days from complications related to the surgery.

“You didn’t have to be brilliant to see that history was repeating itself,” Brawley says. “Doctors were just substituting a blood test for chest X-rays.”

Tim Glynn, a self-described country lawyer from Setauket, N.Y., was 47 in 1997 when he went to his primary-care doctor, troubled by a vague feeling of being down. After his physical exam, Glynn was sent to have his blood drawn. Along with thyroid and cholesterol levels, the doctor ordered a P.S.A. test. A week later, Glynn returned to hear the results. His P.S.A. was elevated. He was told to get a biopsy as soon as possible.

After the biopsy, he walked into a bar in the middle of the afternoon and ordered a martini. A few weeks later, Glynn’s urologist told him the biopsy showed prostate cancer and recommended that he have his prostate removed immediately. Glynn chose to do some homework first.

One of Glynn’s clients happened to be Richard Ablin, the scientist. Ablin told him that not all prostate cancers are alike, and that he could wait; if he developed symptoms, or if his P.S.A. shot up, he could always opt to be treated at that time. (Some doctors recommend “active surveillance,” in which the patient is periodically given P.S.A. testing and biopsies, rather than immediate treatment.) Glynn chose to hold off on surgery.

Kerri Glynn, Tim’s wife of now 39 years, was terrified by her husband’s decision. “I felt as if an ax had fallen,” she says. In her mind it was better to be safe than sorry, and safe meant being treated immediately. “She was a wreck,” Glynn says. “She was scared witless.”

His colleagues were also worried about his decision to forgo treatment. “My business partner was clearly very anxious, and my assistant asked if she should look for a new job,” Glynn recalls. “And there was the fear that if this became public knowledge, there would be clients who wouldn’t want to deal with us because they wouldn’t want to engage a lawyer who was going to be dead the next day. When you see the people around you falling apart, you sort of have to get treated for them, so you can go back to a normal life.”

For many people, not being treated after a diagnosis of cancer is psychologically unbearable. Our view of cancer, says Barnett Kramer, is still shaped by the fact that until relatively recently, cancers were only discovered when they were causing symptoms. Before current treatments were available, such cancers were often fatal. We can now screen for cancers long before they become symptomatic, but it's still very difficult to imagine that they can safely be left untreated. Brawley says, "I have had patients say, 'Damn it, I'm an American — you can't tell me I have cancer and we're going to watch — you have to treat it.' "

Glynn had the surgery. Fourteen years later, he still takes drugs for impotence. It would be more than a year following surgery before he had the energy to play a set of tennis again. "The toll that this took on energy and physicality was like being aged five years," he says.

One way to look at Glynn's story is as a success. His cancer was removed. His impotence is being managed. But Glynn sees it differently, and so do many other men who have been treated for prostate cancer. Darryl Mitteldorf is the executive director of Malecare, a cancer-patient support group. He says it is not uncommon for men to regret their decision to be tested and treated for prostate cancer. "We have men come in very upset, week after week, telling us what they're not telling their doctors," he says. One-third of men who are given a P.S.A. test were never asked if they wanted it. Of men who are asked, more than half say their doctor failed to mention possible side effects that result from treatment.

Brawley tells the story of a patient who had surgery and then underwent radiation, which left him with severe damage to both his rectum and ureter. "He had every side effect known to man," Brawley says. "He had a bag for urine, a bag for stool, he was a terrible mess, in and out of the hospital with infections." The man died six years after his surgery, from an overwhelming infection. Yet cancer statistics would list such a man as a success story, Brawley says, "because he survived past the five-year mark." Would an untreated prostate cancer have killed him within six years, too? There is simply no way to know.

Many doctors suggest that African-American men and those with a family history should be tested as early as age 40, because they are at increased risk of dying of prostate cancer. But Brawley, who is African-American and has declined P.S.A. screening himself, says this recommendation is based on conjecture, and even for men at higher risk, the test may cause more harm than good. Until the proper studies are done, he asserts, "We just don't know."

The dueling narratives of P.S.A. testing boil down to the way each side frames the potential for harm from the disease compared with the collateral damage from the test and subsequent treatment. Mohler says, "P.S.A., when used intelligently to detect prostate cancer early in men after proper education . . . performs pretty well; it actually performs better than

a mammogram." P.S.A. advocates are concerned that statistics play down the value of each life saved. Some also argue that the statistics will validate their view as men are followed beyond 14 years. More important, they worry that if men reject screening, malignant cancers will go undiagnosed.

David Newman, a director of clinical research at Mount Sinai School of Medicine in Manhattan, looks at it differently and offers a metaphor to illustrate the conundrum posed by P.S.A. screening.

"Imagine you are one of 100 men in a room," he says. "Seventeen of you will be diagnosed with prostate cancer, and three are destined to die from it. But nobody knows which ones." Now imagine there is a man wearing a white coat on the other side of the door. In his hand are 17 pills, one of which will save the life of one of the men with prostate cancer. "You'd probably want to invite him into the room to deliver the pill, wouldn't you?" Newman says.

Statistics for the effects of P.S.A. testing are often represented this way — only in terms of possible benefit. But Newman says that to completely convey the P.S.A. screening story, you have to extend the metaphor. After handing out the pills, the man in the white coat randomly shoots one of the 17 men dead. Then he shoots 10 more in the groin, leaving them impotent or incontinent.

Newman pauses. "Now would you open that door?" He argues that the only way to measure any screening test or treatment accurately is to examine overall mortality. That means researchers must look not just at the number of deaths from the disease but also at the number of deaths caused by treatment.

Many experts agree with Newman, and two large studies of P.S.A. screening, published in The New England Journal of Medicine in 2009, came to the same conclusion: There was no difference between the screened and unscreened groups in overall deaths. One trial, conducted in the United States, showed no reduction in prostate-cancer deaths over a period of up to 10 years when men 55 and older were screened. The other, which was carried out in several European countries, showed that screening reduced mortality from prostate cancer by 20 percent, yet the overall number of deaths in each group was the same. Newman gives one possible reason for this: the benefit of early diagnosis could be offset by complications from diagnostic tests and subsequent treatment.

Each study has been criticized for design and execution issues that might have skewed the results, but the failure to reduce overall mortality reported in the European study is probably no fluke, Newman says. An analysis of six studies of screening involving nearly 400,000 men, published last year in the British medical journal BMJ, found no significant difference

in overall mortality when screened men were compared with controls. Philipp Dahm, a professor of urology at the University of Florida College of Medicine and lead investigator for the analysis, says the study shows that P.S.A. screening "does not have a clinically important impact" on overall mortality. Or as Kramer, an author of the U.S. study, crisply puts it, "Men may be trading one cause of death for another."

For Brawley, the greatest tragedy of P.S.A. screening is that it has been a distraction from making greater progress in reducing deaths with the one clear helpful thing: distinguishing between the prostate tumors that really need to come out and those that are better left alone. Instead, new types of P.S.A. screening are being promoted. "We live in a time when our failure to define questions properly has delayed our progress and harmed health," he says. "We keep pursuing son of, son of P.S.A."

As it stands, each man must decide for himself how he wants to play the odds. "Let's put this in perspective," says Welch, whose most recent book is "Overdiagnosed: Making People Sick in the Pursuit of Health." "The European trial says 50 men have to be treated for a cancer that was never going to bother them to reduce one death. Fifty men. That's huge. To me, prostate screening feels like an incredibly bad deal."

Other men, Welch acknowledges, may arrive at a different conclusion, and he is careful to avoid pushing his own patients in one direction or the other. The answer is ultimately personal, he says, and while studies of groups of people can feel unhelpful if you could be the one in the group with cancer, that is all we have to go on.

The solution, in Welch's view, and in that of a growing number of physicians, including Brawley, is to make sure men fully grasp the downstream decisions they may face as a result of screening — the risk of knowing too much. Studies have found that when men are given balanced information about both the cons and pros of P.S.A. testing, they are less likely to opt for screening than men who were merely offered the test. Given this, Brawley asks, how can it be ethical for a doctor not to inform men of the risks — or to fail to even tell a man that the test has been ordered? "If a man understands the risks and benefits and does not want to be screened, that decision should be supported," he says. "But just saying that gets you in trouble."

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As the fifth most common cancer among women, ovarian cancer is commonly nicknamed the â€œsilent killerâ€ among women over the age of 55. Though by no means linked uniquely to postmenopausal women, ovarian cancer is highly aggressive, and, according to doctors, incredibly difficult to detect. Mother Erin Barret only happened to discover she had ovarian cancer because she was pregnant. We are well-versed in the cancer symptoms that absolutely cannot be ignored (as we hope you are, too) â€” but when looking at gynecological cancers, many of these universal cancer symptoms may sound quite general and v