In this issue of the Journal, Welch and Albertsen (1) presented information that every man considering prostate cancer screening and treatment should know and understand. Prostate cancer screening has resulted in substantial overdiagnosis and in unnecessary treatment. It may have saved relatively few lives. Results from this article and recent results from prostate cancer screening and prevention trials demand reflection about what we as a society have done and are doing. Lessons to be learned have ethical and economic implications and involve our lack of respect for the scientific process and scientific evidence.

As I sat down to write this editorial, I heard a radio commercial that brings perspective to the issue. A local celebrity was promoting prostate cancer awareness. He said, “Prostate cancer is 100% curable when caught early.” He encouraged all men to get screened and announced that a van was touring the area offering screening in supermarket parking lots. This was a community service project sponsored by the radio station, the supermarket chain, and a radiation oncology practice.

A commercial like this plays to our fears and prejudices. All of us have been taught from an early age that the best way to deal with cancer is to find it early. With the development of the prostate-specific antigen test, prostate cancer screening and early detection efforts surged in the United States in the late 1980s and continue to this day (2,3). By 1991, there were large prostate cancer awareness campaigns, health systems, and others who stood to profit from prostate cancer screening and treatment and encouraged it, implying benefit to those screened (4). Many were eager to push screening because of a financial incentive; some simply did not think too deeply due to the financial gain. Others truly thought they were doing a public service and felt urgency because prostate cancer is a leading cause of cancer death.

Although there was clear evidence of early detection, there was little evidence to show that screening decreased prostate cancer mortality or saved lives. There was strong vocal “expert opinion” that surrogate endpoints of earlier stage at diagnosis and increased survival indicated that screening saved lives. Some experts expressed legitimate concern that screening was unproven and premature (5). Collins and Barry (6) noted that screening advocates were using the same mistaken arguments that caused the advocacy of lung cancer screening with chest X-ray in the 1960s. This intervention was abandoned in the 1970s after trials showed it ineffective.

Many screening advocates (both physician and lay) have had difficulty accepting that some cancers are not going to progress and cause symptoms or death within the lifetime of the patient (7). The distinguished urologist Willet Whitmore recognized overdiagnosis as a problem in his famous quote, “The quandary in prostate cancer: Is cure necessary in those for whom it is possible, and is cure possible in those for whom it is necessary?”(8)

Truth be known, most of our pathological definitions of cancer were developed in the mid-1800s using light microscopy (9). Prostate cancer has not moved fully into the molecular and genetic age (10). We desperately need the ability to predict which patient has a localized cancer that is going to metastasize and cause suffering and death and which patient has a cancer that is destined to stay in the patient’s prostate for the remainder of his life.

Because of overdiagnosis, the true effect of prostate cancer screening cannot be assessed by the increased proportion of low-stage tumors at diagnosis. Overdiagnosis also artificially prolongs survival statistics meaning survival statistics cannot be used to determine a positive screening effect. Indeed, the only trusted measure of screening success can be decreased cause-specific mortality as seen in a randomized clinical trial (7).

Lesson 1: Have respect for science and the scientific process. Understand and address the truly important questions.

“Does prostate cancer screening save lives?” is still a legitimate question. A recently published analysis of an American prospective randomized trial (11) showed no benefit to screening with up to 10 years of follow-up. A European study (12) showed a 20% decline in mortality after 9 years of follow-up with substantial overdiagnosis. More than 1400 men have to be screened and 48 additional men diagnosed and treated to avert one prostate cancer death after 9 years.

There has been a 40% decline in US prostate cancer mortality since 1993. The reasons are not known. It could be because of screening, more effective treatment of metastatic disease, changes in attribution of cause of death, or other factors (13). The American screening trial (hindered by our prejudice for screening) would suggest that screening attributed nothing to the statistic. The European study would estimate screening caused about half of the decline. It is of note that countries that do not have widespread screening as a policy have seen some declines in prostate mortality without the harm of frequent overdiagnosis (14).

The early detection prejudice delegitimized the questions concerning screening and what are now clearly important scientific questions concerning disease prognostic factors and predictors of biological behavior. Indeed, over the past 20 years, many research dollars were spent addressing the question “how can men be...
encouraged to get screened?” when projects to better understand prostate cancer biology were not funded.

After we determine who needs treatment and who does not, we need to know how good the treatments are. Today there are nearly a dozen treatments for localized prostate cancer. Some of these treatments are very expensive and some have serious and long-lasting side effects (15,16). Little has been done to figure out which therapies are most effective. Every treatment looks good, when more than 90% of men getting it do not need it.

Lesson 2: In the past we have truly not appreciated the need for scientific evidence. In the future, will we accept scientific evidence?

Prostate cancer screening is not the only intervention we have adopted prematurely. Medicine and especially American medicine has often relied on the opinion of experts (often biased experts) rather than on the objective interpretation of scientific data. Too often, we have allowed opinion to undermine support for scientific study. Indeed, the list of medical interventions adopted and later withdrawn or substantially modified after initial assessment was determined incomplete is long. Among them are 1) the Halsted mastectomy for breast cancer (17), 2) bone barrow transplant for high-risk breast cancer (18), 3) neuroblastoma screening with a urine test (18,19), 4) lung cancer screening with chest X-ray (20), 5) erythropoetin therapy during chemotherapy (21), and 6) post-menopausal hormone replacement therapy (22).

The current political rhetoric supports “comparative effectiveness research.” In principle, this is good. The strongest scientific supports for an intervention are findings from a prospective randomized controlled trial. In the case of prostate cancer screening, many screening advocates actually discouraged such trials even while the trials were under way.

Unfortunately, prospective randomized trials are not always practical because of expense or the needed duration. Some clinical decisions do need to be made through interpretation of results of lesser studies. These results need to be interpreted carefully and with an open mind. At times, the opinions of respected authorities based on clinical experience will need to be used. These authorities must remain objective.

Lesson 3: The rational use of medicine, not the rationing of medicine.

An important element of health-care reform is a reform of how we consume health care. The irrational tendency to adopt treatments and technologies without adequate assessment is a form of “medical gluttony” and a major reason that US per capita health-care costs are the highest in the world. We do not get what we pay for; our life expectancy is 29th among developed countries. Medical costs are approaching one-fifth of our gross domestic product (23). The economy cannot afford the continued growth of health-care costs seen over the past 30 years. Economic realities have already led to some restrictions or rationing. More will occur unless we begin the rational practice of medicine.

Lesson 4: Know what is known, know what is not known, and know what is believed. Label them accordingly.

The most important lesson of the prostate cancer screening saga is that we should appreciate the truth and clearly explain it as best as possible. Many men who thought their lives were saved by being screened, diagnosed, and treated for localized prostate cancer are perplexed to learn that so few benefi t. They may be even more amazed that this is not a new finding. What is new is the fact that many health professionals are fi nally accepting it as true. They are accepting that there is overdiagnosis, unnecessary treatment and overtreatment, and questions regarding screening for this disease. They do this after several studies using varying methodologies have clearly shown that prostate cancer screening and treatment are very complicated (24–29).

I come from and have been supported by an African American community, where many are suspicious of physician motives and are convinced that doctors and those in medicine will take advantage of them and not tell them the truth. Distrust is actually a major reason for many disparities in health faced by black Americans (30). A closed-minded medical culture is a part of the problem. The well-meaning uninformed layman with a sound bite is also a part of the problem. Both can cause serious harm.

Given the estimates of Welch and Albertsen and the results of screening (11,12) and prevention (31) trials, we now know that prostate cancer is a highly complicated disease and prostate cancer screening is a complicated intervention. The benefits of prostate cancer screening are still open to question. This means that informed or shared decision making should be done using the data now available before screening is performed. Some of the confusion of prostate cancer screening can be avoided if we all clearly label what we know, as what we know; what we do not know, as what we do not know; and what we believe, as what we believe. Of course, one must not confuse what is believed with what is known to do this.

References


**Note**

No conflicts of interest.