Prostate Cancer Screening

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KEYWORDS

- Prostate • Prostate cancer • Prostate cancer screening
- Prostate cancer screening guidelines • Prostate-specific antigen • PSA
- History of prostate cancer screening • United States Preventive services Task Force

KEY POINTS

- Prostate cancer (PCa) screening is controversial. PSA-based screening has effected a dramatic stage shift from mostly incurable to mostly curable disease along with a greater than 53% reduction in the US PCa mortality rate; however, concerns have arisen about overdiagnosis and treatment of screen-detected indolent tumors.
- Randomized clinical trials of varying quality and much of their misinterpreted data have created confusion about the benefits versus harms of screening, leading to flawed recommendations in 2008 and 2012 against PSA screening by the US Preventive Services Task Force (USPSTF).
- In the aftermath of the USPSTF recommendations, the widespread rejection of screening by many primary care physicians has had far-reaching consequences, notably, a reversion to more PCa cases being high-grade and advanced at diagnosis.
- A 2017 statistical modeling reanalysis of the large European Randomized Study of Screening for Prostate Cancer (ERSPC) and the US Prostate, Lung, Colorectal, and Ovarian (PLCO) screening trials by the Cancer Intervention and Surveillance Modeling Network of the National Cancer Institute revealed that screening in ERSPC produced a 25% to 31% reduction in PCa mortality versus a 27% to 32% reduction in PLCO.
- The USPSTF has now issued a revised draft recommendation, suggesting shared decision making for screening healthy men 55 years to 69 years of age.
- Consequently, the USPSTF has dropped its total opposition to PCa screening, with a draft recommendation for shared decision making for patients ages 55 years to 69 years old. Further consideration is needed for more intensive screening in men with high-risk factors, such as African ancestry and/or a strong family history of PCa, as well as for healthy men aged greater than or equal to 70 years.
- Further consideration is needed for more intensive screening in men with high-risk factors, such as African ancestry and/or a strong family history of PCa, as well as for healthy men age greater than or equal to 70 years. When correctly interpreted, the data are clear: PSA screening significantly reduces suffering and death from PCa.

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INTRODUCTION

The US Preventive Services Task Force (USPSTF) has dropped its opposition to routine prostate cancer (PCa) screening in favor of a shared decision-making process between men aged 55 years to 69 years and their physicians. Screening for prostate cancer is controversial, but it should not be. In the United States, PCa is the third leading cause of cancer death in men, with an estimated 161,360 new cases diagnosed in 2017 and 26,730 projected cancer deaths.[1] PCa seldom produces symptoms until it is incurable, and currently available methods cannot accurately distinguish between tumors that progress so slowly that they do not produce symptoms and those that are likely to cause suffering or death. Therefore, with no known means of preventing PCa or for curing metastatic disease, the sole hope for reducing suffering and death from PCa is through early detection and appropriate and effective patient management.

THE PRE–PROSTATE-SPECIFIC ANTIGEN SCREENING ERA

In the 6 decades before the PSA screening era, PCa death rates progressively increased, because more men lived long enough to succumb to PCa,[1] and most PCa patients were diagnosed with incurable disease. For those who did not die of other causes within 15 years, many died from PCa.

Prostate-Specific Antigen as a First-Line Screening Test

Because of overlap in PSA levels in men with benign prostatic hyperplasia, prostatitis, and PCa, it was believed that PSA could not be not used for early detection of PCa. In 1991, Catalona and colleagues[2] showed that PSA could be used as a first-line screening test for PCa in men without suspicious digital rectal examination (DRE) findings. Subsequently, PSA testing was widely adopted, causing a spike in PCa incidence rates, because the inventory of previously undetectable PCa was unmasked. This led to the creation of a new clinical-stage classification (T1c), that is, PCa with a normal DRE that has become the most common stage in practice.[3]

Randomized Clinical Trials of Prostate-Specific Antigen Screening

Randomized clinical trials (RCTs) were launched to evaluate PSA screening. Of these, the Swedish Göteborg trial is the highest-quality study. It is population based, included younger men, used lower PSA cutoffs for biopsy, had the longest follow-up, and had the lowest rate of contamination. Göteborg initially reported a 41% lower rate of advanced-stage PCa at diagnosis in the screening arm (66% lower in men actually screened) and a 44% lower PCa mortality rate (56% lower in men actually screened), despite 33% of patients being managed with active surveillance. The trial subsequently contributed 59% of its data from men in the core age group of the multinational European Randomized Study of Screening for Prostate Cancer (ERSPC)[4] that reported a 21% lower PCa mortality rate in the screening arm (29% after adjustment for noncompliance with screening, and 38% for those with 10 to 11 years of follow-up).[4–6]

Among the other RCTs of PSA screening,[7,8] the US Prostate, Lung, Colorectal, and Ovarian (PLCO) trial that reported no overall PCa mortality benefit from screening was noninformative on the benefits of screening versus no screening, because nearly 90% of PLCO controls had PSA testing before or during the trial.[9–12] A recent statistical modeling reanalysis of ERSPC and PLCO by the Cancer Intervention and Surveillance Modeling Network (CISNET) of the National Cancer Institute estimated that screening in ERSPC produced a 25% to 31% reduction in PCa mortality versus a 27% to 32% reduction in PLCO.[13]