Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement

The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Summary of Recommendations and Evidence

The decision about whether to be screened for prostate cancer should be an individual one. The USPSTF recommends that clinicians inform men ages 55 to 69 years about the potential benefits and harms of prostate-specific antigen (PSA)–based screening for prostate cancer. Screening offers a small potential benefit of reducing the chance of dying of prostate cancer. However, many men will experience potential harms of screening, including false-positive results that require additional testing and possible prostate biopsy; overdiagnosis and overtreatment; and treatment complications, such as incontinence and impotence. The USPSTF recommends individualized decisionmaking about screening for prostate cancer after discussion with a clinician, so that each man has an opportunity to understand the potential benefits and harms of screening and to incorporate his values and preferences into his decision. (C recommendation)

The USPSTF recommends against PSA-based screening for prostate cancer in men age 70 years and older. (D recommendation)

Please see the Clinical Considerations sections on screening in African American men and men with a family history of prostate cancer for more information on these higher-risk populations.

Rationale

Importance
Prostate cancer is one of the most common cancers that affects men. The Centers for Disease Control and Prevention estimates that more than 2.5 million American men were diagnosed and living with prostate cancer in 2013 (1). Many men with prostate cancer never experience symptoms, and without screening, would never know that they have it. In autopsy studies of men who died of other causes, more than 20% of men ages 50 to 59 years and more than one third of men ages 70 to 79 years were found to have prostate cancer (2). In some men, the cancer is more aggressive and leads to death. In the United States, more than 25,000 men died of prostate cancer in 2016. The median age of death from prostate cancer is 80 years, and more than two thirds of all men who die of prostate cancer are older than age 75 years (1).

Detection
Screening for prostate cancer begins with a test that measures the amount of PSA protein in the blood. An elevated PSA level may be caused by prostate cancer but can also be caused by other conditions, including an enlarged prostate (benign prostatic hyperplasia) and inflammation of the prostate (prostatitis). Some men without prostate cancer may therefore have positive screening results (or “false-positive” results). Men with a positive PSA test may have a transrectal ultrasound-guided core-needle biopsy of the prostate to diagnose prostate cancer.

Current methods cannot definitively distinguish between cancer that is likely to be aggressive and metastasize and cancer that will not progress or will progress so slowly that the patient will not experience symptoms.

**Benefits of Early Detection and Treatment**
The goal of screening for prostate cancer is to identify high-risk, localized prostate cancer that can be successfully treated, thereby preventing the morbidity and mortality associated with advanced or metastatic prostate cancer.

Adequate evidence from randomized clinical trials shows that PSA-based screening programs in men ages 55 to 69 years may prevent up to 1 to 2 deaths from prostate cancer over approximately 13 years per 1,000 men screened (3). Screening programs may also prevent up to 3 cases of metastatic prostate cancer per 1,000 men screened over 13 years (3).

Adequate evidence from randomized clinical trials is consistent with no mortality benefit of PSA-based screening for prostate cancer in men age 70 years and older.

**Harms of Early Detection and Treatment**

*Harms of Screening and Diagnostic Procedures*
Potential harms of screening include frequent false-positive results. One major trial in men screened every 2 to 4 years concluded that, over 10 years, more than 15% of men experienced at least one false-positive test result (4). Harms of diagnostic procedures include complications of prostate biopsy, such as pain, hematospermia (blood in semen or ejaculate), and infection. Approximately 1% of prostate biopsies result in complications requiring hospitalization. The false-positive and complication rates from biopsy are higher in older men (3). Adequate evidence suggests that the harms of screening and diagnostic procedures are at least small.

*Harms of Treatment*
PSA-based screening for prostate cancer leads to the diagnosis of prostate cancer in some men whose cancer would never have become symptomatic during their lifetime. Treatment of these men provides them with no benefit. This is known as “overdiagnosis,” and followup of large randomized trials suggests that 20% to 50% of men diagnosed with prostate cancer through screening may be overdiagnosed (3). Due to, in part, reduced life expectancy and delays in treatment benefits, overdiagnosis rates increase with age and are highest in men age 70 years and older.

Harms of prostate cancer treatment include sexual impotence, urinary incontinence, and bothersome bowel symptoms. About 1 in 5 men who have a radical prostatectomy develop long-term urinary incontinence requiring diaper use and more than 2 in 3 men experience long-term sexual impotence. More than half of men who have radiation therapy experience long-term sexual impotence and up to 1 in 6 men experience long-term bothersome bowel symptoms, including bowel urgency and fecal
incontinence (3). Adequate evidence suggests that the harms of overdiagnosis and treatment are at least moderate.

**USPSTF Assessment**

PSA-based screening for prostate cancer has both potential benefits and harms. The USPSTF does not recommend automatically screening all men for prostate cancer. The decision about whether to be screened for prostate cancer requires that each man incorporate his own values and preferences with an understanding of the potential benefits and harms of screening. The potential harms of screening, diagnostic procedures, and treatment occur soon after screening takes place. While the potential benefits may occur any time after screening, they generally occur years after treatment, because progression from asymptomatic, screen-detected cancer to symptomatic, metastasized cancer or death (if it occurs at all) may take years or decades.

The USPSTF considered whether there are screening and followup approaches that increase the potential for benefit while reducing the potential for harms. Variation across sites in randomized trials of screening suggests there may be greater mortality benefit from screening every other year compared with longer intervals and from using lower PSA thresholds for diagnostic biopsy. Although these approaches may have increased the potential benefit reported in studies, they also resulted in substantially more harms—more false-positive results, more prostate biopsies, and more cases of overdiagnosis. This tradeoff was also observed in a review of decision analysis models; screening protocols using lower PSA thresholds (<4.0 ng/mL) for biopsy and more frequent screening intervals offered greater potential reductions in prostate-specific mortality but higher rates of overdiagnosis and other harms (5).

Although new screening methods are being developed (such as single- and adjusted-threshold testing, PSA velocity and doubling time), evidence is insufficient to support one method of PSA-based screening over another. Evidence is also insufficient that using a prebiopsy risk calculator, with or without measurement of free PSA levels, meaningfully changes the potential benefits and harms of screening or that using genetic or adjunctive imaging tests meaningfully changes the potential benefits and harms of screening. This is an important area of current research that has the potential to decrease the harms of PSA-based screening for prostate cancer.

The USPSTF concludes with moderate certainty that, overall, the potential benefits and harms of PSA-based screening for prostate cancer in men ages 55 to 69 years are closely balanced. Each man’s individual values and preferences will determine whether he feels that the overall balance of potential benefits and harms is positive or negative.

The USPSTF concludes with moderate certainty that the potential benefits of PSA-based screening for prostate cancer in men age 70 years and older do not outweigh the expected harms.

**Clinical Considerations**

**Patient Population Under Consideration**

This recommendation applies to adult men in the general U.S. population without symptoms or a previous diagnosis of prostate cancer. It also applies to men at increased risk of death from prostate cancer due to race or family history of prostate cancer. Please see the sections below for more information on how this recommendation applies to African American men and men with a family history of prostate cancer.
This recommendation does not apply to the use of the PSA test for surveillance after diagnosis or treatment of prostate cancer.

**Screening**

PSA-based screening for prostate cancer has been studied in two very large randomized clinical trials with more than a decade of followup: the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the U.S.-based Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. These two trials used varying screening intervals (every 1 to 4 years) and PSA thresholds (2.5 to 10.0 ng/mL) for diagnostic biopsy (3).

The PLCO trial may be viewed as a trial of organized versus opportunistic screening for prostate cancer because of the substantial screening rate in the control group and the high rate of screening in men in both the control and intervention groups prior to the study. Men in the intervention group were screened more often than men in the control group, and more men in the intervention group were diagnosed with prostate cancer than in the control group. The trial found no difference between groups in death from prostate cancer after almost 15 years of followup (relative risk [RR], 1.04 [95% confidence interval (CI), 0.87 to 1.24]) (6).

Overall, in the ERSPC trial, the results suggest that screening 781 men ages 55 to 69 years at enrollment (95% CI, 490 to 1,929) would prevent 1 man from dying of prostate cancer after 13 years. The results varied substantially across the individual ERSPC sites, from no significant benefit observed in Finland (the largest site) to an absolute risk reduction of 0.72% (95% CI, 0.50 to 0.94) in Sweden (a 42% relative reduction) (7). No ERSPC trial site offered screening more often than every 2 years, and many sites screened every 4 years.

Four ERSPC trial sites reported data on the effect of PSA-based screening for prostate cancer on the development of metastatic cancer after 12 years of followup. Among men randomized to screening, the risk of developing metastatic prostate cancer was 30% lower than among men in the control group. This translates to an absolute reduction in the long-term risk of metastatic prostate cancer of 3.1 cases per 1,000 men screened (8).

Based on clinical stage, tumor grade, and PSA level, prostate cancer is classified as low, medium, or high risk for clinical progression and prostate cancer death. While treatment is thought to be most immediately beneficial for men with high- and medium-risk prostate cancer, the vast majority of cases of screen-detected cancer are low risk.

As with all screening tests, some men without prostate cancer will receive positive PSA test results. This is called a false positive. The false-positive rate for the PSA test depends on the PSA threshold used. Among five ERSPC sites that reported the false-positive rate, approximately 1 in 6 men who were screened at least once had one or more false-positive results, and of the positive results in the first round of screening, two thirds were false positives. In Sweden, where a low PSA threshold was used to determine a positive test and men were screened every 2 years, more than 45% of men who participated in all screening rounds had a false-positive result over 10 years of screening (4). In the PLCO trial, more than two thirds of men who had a prostate biopsy because of a positive PSA test were found not to have prostate cancer (9).

**Treatment**
Because most cases of prostate cancer advance very slowly, if at all, the 10-year survival rate for screen-detected, localized prostate cancer is very high. In a recent major trial that enrolled more than 1,500 men who were randomized to receive either active treatment or active surveillance, the 10-year survival rate in all groups was 99% (10). The good prognosis for early-stage prostate cancer makes it difficult to study the effectiveness of treatment.

Multiple treatment options exist for prostate cancer and new ones are being developed. In current practice, the three most common treatment options for men with screen-detected, localized prostate cancer are surgical removal of the prostate gland (radical prostatectomy), radiation therapy (external-beam radiation therapy, proton beam therapy, or brachytherapy), and active surveillance. The USPSTF considered available evidence on treatment when evaluating the effectiveness of screening and found that current evidence suggests that treatment of early-stage, screen-detected prostate cancer with radical prostatectomy or radiation therapy likely reduces risk of clinical progression and metastatic disease and may reduce prostate cancer mortality. More details about the effectiveness and side effects of active treatment can be found in the Discussion section.

Active surveillance is a treatment approach that seeks to limit the harms of treatment by allowing men with apparent low-risk prostate cancer to forego surgery or radiation in favor of ongoing monitoring of their cancer. This surveillance includes regular, repeated PSA testing and often repeated digital rectal examination and prostate biopsy. Men whose cancer is found to be changing are offered definitive treatment with surgery or radiation. Active surveillance reduces the chance of overtreatment and offers men the opportunity to delay or avoid complications associated with radical prostatectomy and radiation therapy. Active surveillance has become a more common treatment choice in the United States over the past several years. In a study assessing community-based urology practice in the United States between 2010 and 2013, about half of men with low-risk prostate cancer were treated with radical prostatectomy. The active surveillance rate, however, increased from 14.3% in 2009 to 40.4% in 2013 among men with low-risk prostate cancer (11). In the multicenter Prostate Testing for Cancer and Treatment (ProtecT) trial—a recent randomized trial that compared radical prostatectomy, radiation therapy, and active surveillance in men with screen-detected prostate cancer—there was no statistically significant difference in prostate cancer–specific mortality or all-cause mortality among the three treatment groups after 10 years of followup. The overall 10-year survival rate across all three groups was more than 98%, which may limit detection of mortality differences in this trial. Approximately 50% of men randomized to active surveillance underwent active treatment (radical prostatectomy or radiation therapy) over the 10-year followup period. Men randomized to active surveillance had higher rates of metastatic disease. To prevent 1 additional case of metastatic prostate cancer during the 10-year followup, 27 men would need to have radical prostatectomy or 33 men would need to have radiation therapy instead of active surveillance (3).

The potential benefit of screening for prostate cancer is made possible through treatment. Thus, it is important for men to consider the potential harms of treatment as they consider whether to be screened. Men who are not able or willing to tolerate treatment should not be screened for prostate cancer.

Active treatment of prostate cancer can result in life-altering side effects. About 3 in 1,000 men die during or soon after radical prostatectomy and about 50 in 1,000 men have serious surgical complications requiring intervention. About 1 in 5 men who have radical prostatectomy develop long-term urinary incontinence requiring regular use of pads and more than 2 in 3 men experience long-term sexual impotence. More than half of men who have radiation therapy experience long-term sexual
Impotence and up to 1 in 6 men experience long-term bothersome bowel symptoms, including bowel urgency and fecal incontinence (3).

**Screening for Prostate Cancer in African American Men**

**Burden**

In the United States, African American men are more likely to develop prostate cancer than white men (203.5 vs. 121.9 cases per 100,000 men). African American men are also more than twice as likely as white men to die of prostate cancer (44.1 vs. 19.1 deaths per 100,000 men) (1). The higher death rate is due in part to an earlier age at cancer onset, more advanced cancer stage at diagnosis, and higher rates of more aggressive cancer (i.e., higher tumor grade). The disparity in death from prostate cancer may also reflect that African American men have lower rates of receiving high-quality care.

**Available Evidence**

The USPSTF searched for evidence about the potential benefits and harms of PSA-based screening for prostate cancer in African American men.

**Potential benefits.** The PLCO trial enrolled 4% African American men, which is not enough to determine whether the overall trial results differed for African American men (12). The ERSPC trial did not record or report any race-specific subgroup information. The low proportion of persons of African descent in European countries during the study period makes it likely that these groups were not well represented.

**Potential harms.** An analysis from the PLCO trial found that African American men were significantly more likely to have major infections after prostate biopsy than white men (odds ratio, 7.1 [95% CI, 2.7 to 18.0]) (9). Evidence is insufficient to compare the risk of false positives, potential for overdiagnosis, and magnitude of harms from prostate cancer treatment in African American versus other men.

**Advising African American Men**

Based on the available evidence, the USPSTF is not able to make a separate, specific recommendation on PSA-based screening for prostate cancer in African American men. Although it is possible that screening may offer greater benefits for African American men compared with the general population, currently no direct evidence demonstrates whether this is true. Screening, and subsequent diagnosis and treatment, has the potential to increase exposure to potential harms. Decision analysis models suggest that given the higher rates of aggressive cancer in African American men, PSA-based screening may provide greater benefit to African American men than the general population. These models also suggest a potential mortality benefit for African American men when beginning screening before age 55 years. The USPSTF believes that a reasonable approach for clinicians is to inform African American men about their increased risk of developing and dying of prostate cancer as well as the potential benefits and harms of screening so they can make an informed, personal decision about whether to be screened. The USPSTF does not recommend screening for prostate cancer in men, including African American men, who are older than age 70 years.

The USPSTF strongly encourages research on screening for and treatment of prostate cancer in African American men. It is important to consider both the potential additional benefits and harms to fully understand the value of screening. Studies are needed to confirm that African American men who undergo screening receive similar or greater reductions in prostate cancer mortality compared with men in the general population, as well as to explore the optimal screening frequency and whether beginning screening before age 55 years provides additional benefits in African American men. Studies are also
needed to better understand strategies to mitigate harms and maximize benefits of screening, diagnostic followup, and treatment (including active surveillance) in African American men. It is also important that research and quality improvement activities continue to work to eliminate disparities in access to high-quality care for men with prostate cancer.

Screening for Prostate Cancer in Men With a Family History

**Burden**
The introduction of PSA-based screening for prostate cancer has substantially altered the epidemiologic statistics for prostate cancer, greatly increasing the number of men with a diagnosis of prostate cancer and thus also the number of men with a father, brother, or son with a history of prostate cancer.

**Available Evidence**
It is generally accepted that men with a family history of prostate cancer are more likely to develop prostate cancer. A study of twins in Scandinavia estimated that genetic factors may account for up to 42% of prostate cancer risk (13). An analysis from the Finnish site of the ERSPC trial concluded that men with at least one first-degree relative with prostate cancer were 30% more likely to be diagnosed with prostate cancer than men without a family history (14). Men with three first-degree relatives with prostate cancer or two close relatives on the same side of the family with prostate cancer diagnosed before age 55 years may have an inheritable form of prostate cancer associated with genetic changes that are passed down from one generation to the next. This type of prostate cancer is thought to account for less than 10% of all prostate cancer cases (15).

The USPSTF searched for evidence about the potential benefits and harms of PSA-based screening for prostate cancer in men with a family history of prostate cancer.

**Potential benefits.** Of the 7% of men in the PLCO trial who reported a family history of prostate cancer on a baseline questionnaire, prostate cancer–specific mortality among white men was lower in the intervention group than in the control group (hazard ratio, 0.49 [95% CI, 0.22 to 1.10]; p=0.08) (16), but the difference was not statistically significant, possibly due to an insufficient sample size.

**Potential harms.** No studies have assessed the risk of harms related to screening for, diagnosis of, or treatment of prostate cancer based on family history of prostate cancer.

**Advising Men With a Family History of Prostate Cancer**
Based on the available evidence, the USPSTF is not able to make a separate, specific recommendation on PSA-based screening for prostate cancer in men with a family history of prostate cancer. Although it is possible that screening may offer additional potential benefits for these men compared with the general population, screening also has the potential to increase exposure to potential harms, especially among men with relatives whose cancer was overdiagnosed. Men who have a first-degree relative who had advanced prostate cancer at diagnosis, who developed metastatic prostate cancer, or who died of prostate cancer are probably the most likely to benefit from screening. The USPSTF believes that a reasonable approach for clinicians is to inform men with a family history of prostate cancer, particularly those with multiple first-degree relatives with prostate cancer, about their increased risk of developing cancer as well as the potential earlier age at disease onset. This discussion should include the potential benefits and harms of screening for prostate cancer so these men have the opportunity to make an informed, personal decision about whether to be screened. The USPSTF does not recommend screening
for prostate cancer in men, including men with a family history of prostate cancer, who are older than age 70 years.

Epidemiologic studies examining outcomes in men with relatives who died of prostate cancer versus men with relatives diagnosed with prostate cancer who died of other causes may help provide better guidance. Studies are needed that explore the optimal screening frequency and whether beginning screening before age 55 years provides additional benefits for men with a family history of prostate cancer. Additional research is also needed to help identify men with an inheritable form of prostate cancer and to understand how the potential benefits and harms of screening, including screening intervals and starting ages, may differ in these men compared with the general population.

**Research Needs and Gaps**

There are many areas in need of research to improve screening for and treatment of prostate cancer, including:

- Comparing different screening strategies, including different screening intervals, to fully understand the effects on benefits and harms
- Developing, validating, and providing longer-term followup of screening and diagnostic techniques, including risk stratification tools, use of baseline PSA level as a risk factor, and use of non-PSA–based adjunctive tests that can distinguish nonprogressive and slowly progressive cancer from cancer that is likely to become symptomatic and affect quality or length of life, to reduce overdiagnosis and overtreatment
- Screening for and treatment of prostate cancer in African American men, including understanding the potential benefits and harms of different starting ages and screening intervals and the use of active surveillance; given the large disparities in prostate cancer mortality in African American men, this should be a national priority
- How to better inform men with a family history of prostate cancer about the benefits and harms of PSA-based screening for prostate cancer, including the potential differences in outcomes between men with relatives who died of prostate cancer and men with relatives diagnosed with prostate cancer who died of other causes
- How to refine active prostate cancer treatments to minimize harms
- How to better understand patient values about the known benefits and harms of screening for and treatment of prostate cancer; how these values influence men’s assessment of the overall benefit versus harm; how to best implement informed decisionmaking programs that incorporate the values and preferences of men and their families about screening; how to adapt the informed decisionmaking process to a range of diverse patient populations as screening, diagnosis, and treatment strategies evolve; and the effects of informed decisionmaking on health outcomes and patient experience

**Discussion**

**Burden of Disease**

In 2013, the most recent year for which data are available, approximately 176,000 men in the United States were diagnosed with prostate cancer and almost 28,000 died from prostate cancer (17). From 2003 to 2012, the prostate cancer–specific mortality rate among U.S. men decreased significantly by 3.4% per year (3.3% and 3.9% per year in white and black men, respectively) (18). Most cases of prostate cancer found in autopsy studies are microscopic, well-differentiated lesions that did not affect men’s
health during their lifetime. Cases of prostate cancer found after screening in asymptomatic men are similar; most are low-risk lesions that are unlikely to cause symptoms or affect men’s health during their lifetime.

Scope of Review
To update its 2012 recommendation, the USPSTF commissioned a systematic review of the evidence regarding the benefits and harms of PSA-based screening for prostate cancer and subsequent treatments of screen-detected prostate cancer (3). The USPSTF also commissioned a review of multiple contextual questions, including a review of existing decision analysis models and what they suggest about the potential for mitigating the harms of screening and treatment and the overdiagnosis rate of PSA-based screening (5, 19). The commissioned reviews also examined the effectiveness and harms of PSA-based screening in patient subpopulations at higher risk of prostate cancer, including older men, African American men, and men with a family history of prostate cancer.

Effectiveness of Early Detection

Potential Benefits of Screening
To understand the potential benefits of PSA-based screening for prostate cancer, the USPSTF examined the results of the ERSPC and PLCO trials and site-specific reports from four ERSPC trial sites. To understand the effectiveness of treatment of screen-detected, early-stage prostate cancer, the USPSTF also examined the results of three randomized trials, including the ProtecT trial, and nine cohort studies (3).

The ERSPC trial randomly assigned a core group of more than 160,000 men ages 55 to 69 years from seven European countries to PSA-based screening versus usual care (7). The specific screening and diagnostic protocols varied among countries (details can be found in the systematic evidence review [3]). After an average followup of 13 years, many more men in the screening group were diagnosed with prostate cancer than in the usual care group (95.5 vs. 62.3 cases per 10,000 person-years) (7). Four ERSPC sites reported on the cumulative incidence of metastatic prostate cancer. After a median followup of 12 years, the risk of developing metastatic prostate cancer was 30% lower among men randomized to screening compared with usual care (RR, 0.70 [95% CI, 0.60 to 0.82]; p=0.001). The absolute reduction in long-term risk of metastatic prostate cancer associated with screening was 3.1 cases per 1,000 men (8). After a median followup of 13 years, the prostate cancer–specific mortality rate among men ages 55 to 69 years was 4.3 deaths per 10,000 person-years in the screened group and 5.4 deaths per 10,000 person-years in the usual care group (RR, 0.79 [95% CI, 0.69 to 0.91]; p=0.001) (7). This means that 781 men would need to be invited to screening to prevent 1 man from dying of prostate cancer (3). The ERSPC trial did not find a reduction in all-cause mortality (7). The effect of screening on prostate cancer–specific mortality differed across the ERSPC sites. Finland, which had the largest enrollment, did not find a statistically significant reduction in prostate cancer–specific mortality (RR, 0.85 [95% CI, 0.69 to 1.04]; p=0.10) (20). An expanded cohort in Sweden, which had the longest followup period, found the largest reduction of 42% (RR, 0.58 [95% CI, 0.46 to 0.72]), which is an absolute risk reduction of 0.72% (95% CI, 0.50 to 0.94) (21).

The results of the overall ERSPC trial provide some of the most important evidence about the potential benefits of PSA-based screening for prostate cancer. The trial was rated as fair quality by the USPSTF due to several important methodologic issues, including observed differences in how men in the screening and control groups were treated for prostate cancer. Among men diagnosed with nonmetastatic prostate cancer, a greater proportion of men in the screening group had radical
prostatectomy (41.3%) than in the usual care group (32.8%) (22). Although one might expect treatment differences by screening group if screening produces a shift toward more localized clinical stages, treatment differences across ERSPC study groups persisted even with stratification by clinical stage and tumor grade. The cause for these differences is not known.

In the prostate component of the PLCO trial, more than 76,000 men ages 55 to 74 years were randomized to either annual PSA-based screening for 6 years or usual care. Abnormal screening results (PSA level >4.0 ng/mL or abnormal digital rectal examination findings) were forwarded to patients and their primary care clinician, who coordinated further diagnostic evaluation (12). The majority of men were non-Hispanic white (86.2% and 83.8% of the screening and control groups, respectively). Approximately one third of men in both groups had either a PSA test or digital rectal examination within the 3 years prior to enrollment. An estimated 78% of men in the control group had a PSA test during the screening phase of the trial (22). On average, men in the intervention group received five PSA tests during the screening phase of the trial and men in the usual care group received three PSA tests (23). This high PSA testing rate in the control group limits the study’s ability to identify a potential screening benefit. Accordingly, the USPSTF characterized the trial as comparing the effectiveness of organized versus opportunistic screening. Despite the common use of PSA testing in the control group, after 13 years more cases of prostate cancer were diagnosed in the screening group than in the control group (108.4 vs. 97.1 cases per 10,000 person-years, respectively) (RR, 1.12 [95% CI, 1.07 to 1.17]). At a median followup of 14.8 years in the PLCO trial, the prostate cancer–specific mortality rate was not statistically different between the intervention and control group (4.8 vs. 4.6 deaths per 10,000 person-years, respectively) (RR, 1.04 [95% CI, 0.87 to 1.24]) (6). This result does not rule out the possibility of a reduction in prostate cancer–specific mortality from screening for prostate cancer.

Neither the ERSPC or PLCO trial, nor any of the ERSPC site-specific analyses, found an overall all-cause mortality benefit from screening for prostate cancer.

Potential Benefits of Treatment
The USPSTF examined three good-quality randomized trials of treatment of localized prostate cancer and nine observational cohort studies to understand the potential benefit of active treatment (radical prostatectomy or radiation therapy) compared with conservative treatment (active surveillance or watchful waiting) on overall mortality, prostate cancer–specific mortality, and progression to metastatic prostate cancer (3).

The U.K. ProtecT trial randomized more than 1,600 men ages 50 to 69 years with screen-detected, localized prostate cancer to radical prostatectomy, radiation therapy, or active surveillance and followed them for 10 years. Approximately 77% of men had low-grade prostate cancer (Gleason score=6) with a favorable prognosis. Thus, some men randomized to active surveillance had an intermediate-grade tumor (or other tumor characteristics) such that they may not have been considered candidates for active surveillance outside of this research study. The trial did not find a statistically significant improvement in all-cause or prostate cancer–specific mortality in any of the treatment groups. The unexpectedly high survival rate across the trial groups (99%) made any potential differences harder to detect. Longer-term followup studies may provide important additional information. The trial reported a statistically significant reduction in progression to metastatic cancer when comparing both radical prostatectomy (61% reduction [95% CI, 27% to 79%]) and radiation therapy (52% reduction [95% CI, 13% to 73%]) with active surveillance. In the active surveillance group, 6.0% of men developed metastatic cancer compared with 2.7% and 2.3% in the radiation therapy and radical prostatectomy groups,
respectively. During the 10-year followup period, 54.8% of men randomized to active surveillance crossed over to active treatment (10).

The other two randomized trials of radical prostatectomy took place prior to widespread PSA-based screening and thus recruited many men with tumors detected due to clinical symptoms. Approximately 50% of men in the U.S.-based Prostate cancer Intervention Versus Observation Trial (PIVOT) and almost 90% of men in the Scandinavian Prostate Cancer Group-4 (SPCG-4) trial had palpable tumors. The SPCG-4 trial compared radical prostatectomy with watchful waiting (a passive protocol dissimilar to active surveillance) and found a statistically significant reduction over 13 years in all-cause and prostate cancer–specific mortality (24). The PIVOT trial did not find statistically significant reductions overall in either all-cause or prostate cancer–specific mortality but did find a reduction in all-cause mortality with radical prostatectomy in men with baseline PSA levels greater than 10 ng/mL (median followup of 10 years; hazard ratio, 0.67 [95% CI, 0.48 to 0.94]) (25).

Five of six cohort studies examining radical prostatectomy and four of six studies examining radiation therapy found statistically significant reductions in prostate cancer–specific mortality when comparing active treatment with watchful waiting or other conservative approaches (3). The results of cohort studies, however, should be interpreted with caution due to the potential for bias in treatment assignment. In these real-world settings, men who are healthier may have been more likely to receive active treatment.

**Potential Harms of Screening and Treatment**

In addition to the ERSPC and PLCO trials, the USPSTF examined the results of a good-quality cohort study embedded within the ProtecT trial (Prostate Biopsy Effects [ProbE]), a fair-quality cohort study conducted in the Department of Veterans Affairs (VA) health system, and a report on complications of prostate biopsy from the ERSPC Rotterdam site to understand the potential harms of screening and diagnosis (3).

In the large randomized controlled trials, one quarter to one third of men offered PSA-based screening had at least one positive screening test. In the PLCO trial, 13% of men had at least one biopsy. In the ERSPC trial, nearly 28 biopsies were performed for every 100 men randomized to screening (3). In the ProbE study, 7.3% of men reported moderate or greater pain, 5.5% reported moderate to severe fever, and 26.6% reported troublesome hematosperma within the 35 days after biopsy (25). Complications from transrectal prostate biopsy resulted in 1.3% of men in the U.K. cohort, 1.6% of men in the VA cohort, and 0.5% of men in the Rotterdam cohort requiring hospitalization (26,27,28). In these studies, two thirds to three quarters of biopsies demonstrated that the screening PSA test was a false positive (3).

Overdiagnosis, the identification of asymptomatic cancer that would never cause symptoms or contribute to death, is one of the most important harms of PSA-based screening programs. Although there is no way to conclusively determine the overdiagnosis rate, the USPSTF used data from trials and reviewed decision analysis models to estimate the possible overdiagnosis rate. Trial data suggest that 21% of screen-detected cancers in the PLCO trial and 50% in the ERSPC trial were overdiagnosed (3). Using a different type of methodology than estimates based directly on single trials, three decision analysis models produced by the Cancer Intervention and Surveillance Modeling Network consortium estimated that between 1988 and 2000 in the United States, the overdiagnosis rate among cases of screen-detected prostate cancer was 22% to 42% (19).
The USPSTF identified three good-quality and one fair-quality randomized trials and seven large fair-quality observational studies that examined the potential harms of active treatment of prostate cancer (3). A meta-analysis of the harms of radical prostatectomy concluded that 1 man will experience substantial urinary incontinence for every 6 men who have a radical prostatectomy rather than conservative management (95% CI, 3.4 to 11.7) and 1 man will experience long-term erectile dysfunction for every 2.7 men who have a radical prostatectomy rather than conservative management (95% CI, 2.2 to 3.6) (3). Additionally, more than 20% of men in the PIVOT trial had a perioperative complication and 5.3% of men in a large U.S. cohort study required re-intervention due to a surgical complication (3). A meta-analysis of the harms of radiation therapy found that 1 man will experience long-term sexual impotence for every 7 men treated with radiation therapy rather than conservative management (95% CI, 4.9 to 11.3) (3). While results are conflicting across cohort studies regarding the association of urinary incontinence and radiation therapy, rates of fecal incontinence and bowel urgency were as high as 31.8% after radiation therapy in one cohort study (30), and both complications were more common when compared with conservative management in two trials and three cohort studies (3).

After a median followup of 6 years in the ProtecT trial, there was no significant difference among men randomized to radical prostatectomy, radiation therapy, or active surveillance in reported anxiety, depression, health status, and cancer-related quality of life (30). The older SPCG-4 trial had similar results after a median followup of 12 years when comparing men who received radical prostatectomy versus watchful waiting (31).

**Estimate of Magnitude of Net Benefit**

Conclusions from decision analysis models, which are consistent with the findings of randomized trials and cohort studies, suggest that more aggressive screening strategies, particularly those that use a lower PSA threshold for biopsy than generally used in the United States, provide the greatest potential reduction in death from prostate cancer. Unfortunately, these strategies are also associated with more false positives, more biopsies, and higher rates of overdiagnosis (19).

Options for reducing the overdiagnosis rate include lowering the age at which to stop screening, extending the interval between screenings, and using higher PSA thresholds for biopsy. Unfortunately, no strategy completely eliminates overdiagnosis. PSA-based screening for prostate cancer every 2 or 4 years instead of annually appears to provide a good tradeoff between a reduction in overdiagnosis and a small reduction in mortality benefit (19).

Decision analysis models confirm the USPSTF’s conclusion that the overall benefit of PSA-based screening for prostate cancer is sensitive to the values and preferences of individual men. The magnitude of net benefit of PSA-based screening depends on how each individual weighs the potential harms of diagnosis and treatment. The value a man places on potential benefits and harms may also change over time. It may therefore be useful for clinicians to regularly revisit the decision to screen (or not screen) with their patients. (Table)

Although active surveillance may reduce exposure to the potential harms of active treatment, it may not be viewed favorably by some men who value definitive action, are concerned about repeat biopsies, or want to avoid a potential increase in metastatic cancer.

**Update of Previous USPSTF Recommendation**
This recommendation replaces the 2012 USPSTF recommendation (32) on PSA-based screening for prostate cancer. In 2012, the USPSTF concluded that while there are potential benefits of screening for prostate cancer, these benefits do not outweigh the expected harms enough to recommend routine screening (D recommendation). The USPSTF continues to find that the potential benefits and harms are closely balanced. The change in recommendation grade is based in part on additional evidence that increased the USPSTF’s certainty about the reductions in risk of dying of prostate cancer and risk of metastatic disease. Longer-term followup of the ERSPC trial and from some ERSPC sites found that PSA-based screening for prostate cancer prevents 1 to 2 men from dying of prostate cancer for every 1,000 men screened. Additionally, a subset of ERSPC sites has since reported that screening 1,000 men ages 55 to 69 years may prevent approximately 3 men from developing metastatic prostate cancer. Trials continue to demonstrate the harms of PSA-based screening, including false-positive results, complications from transrectal prostate biopsies, overdiagnosis (which, based on estimates from trial data, may occur in 20% to 50% of cases of screen-detected cancer), and harms of treatment, including urinary incontinence and sexual impotence. The change in recommendation grade further reflects new evidence about and increased use of active surveillance of low-risk prostate cancer, which may reduce the risk of subsequent harms from screening. This recommendation also clearly identifies African American men and men with a family history of prostate cancer as having higher risk for prostate cancer, and provides additional information to help support these men in making informed decisions about screening. With the C recommendation for men ages 55 to 69 years, the USPSTF’s intention is to convey that each man’s values and preferences may shift the balance of whether there is a net benefit or a net harm of screening and to promote the importance of informed decisionmaking prior to screening. The USPSTF continues to find that the benefits of screening do not outweigh the harms in men age 70 years and older and recommends against screening in these men.

**Recommendations of Others**

The American Academy of Family Physicians (33) in 2012 and the Canadian Task Force on Preventive Health Care (34) in 2014 recommended against PSA-based screening for prostate cancer. The American Academy of Family Physicians is currently reviewing its recommendation. The American College of Physicians (35) in 2013 recommended that physicians discuss the benefits and harms of screening with men ages 50 to 69 years and only recommend screening for men who prioritize screening and have a life expectancy of more than 10 to 15 years. The American Urological Association (36) in 2013 recommended that men ages 55 to 69 years with a life expectancy of more than 10 to 15 years be informed of the benefits and harms of screening and engage in shared decisionmaking with their physician, taking into account each man’s values and preferences. It noted that to reduce the harms of screening, the screening interval should be 2 or more years. The American Urological Association also noted that decisions about screening, including potentially starting screening before age 55 years, should be individual ones for African American men and men with a family history of prostate cancer. The American Cancer Society (37) adopted detailed screening recommendations in 2016 that highlight the importance of shared decisionmaking and the need for informed discussion of the uncertainties, risks, and potential benefits of screening. It recommends conversations about screening beginning at age 50 years and earlier for African American men and men with a father or brother with a history of prostate cancer before age 65 years.

**References**


Table. Estimated Effects After 13 Years of Inviting Men Ages 55 to 69 Years in the United States to PSA-Based Screening for Prostate Cancer*

<table>
<thead>
<tr>
<th>Number of Men Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men invited to screening</td>
</tr>
<tr>
<td>Men who receive at least 1 positive PSA test result</td>
</tr>
<tr>
<td>Men who have 1 or more transrectal prostate biopsies</td>
</tr>
<tr>
<td>Men hospitalized for a biopsy complication</td>
</tr>
<tr>
<td>Men diagnosed with prostate cancer</td>
</tr>
<tr>
<td>Men who initially receive active treatment with radical prostatectomy or radiation therapy</td>
</tr>
<tr>
<td>Men who initially receive active surveillance</td>
</tr>
<tr>
<td>Men who initially receive active surveillance who go on to receive active treatment with radical prostatectomy or radiation therapy</td>
</tr>
<tr>
<td>Men with sexual dysfunction who received initial or deferred treatment</td>
</tr>
<tr>
<td>Men with urinary incontinence who received initial or deferred treatment</td>
</tr>
<tr>
<td>Men who avoid metastatic prostate cancer</td>
</tr>
<tr>
<td>Men who die of causes other than prostate cancer</td>
</tr>
<tr>
<td>Men who die of prostate cancer despite screening, diagnosis, and treatment</td>
</tr>
<tr>
<td>Men who avoid dying of prostate cancer</td>
</tr>
</tbody>
</table>

*Estimates based on benefits observed in the ERSPC trial for men ages 55 to 69 years.

†Result based on biopsy rate in the ERSPC trial. Current practice in the United States will likely result in fewer biopsies. The potential effect of fewer biopsies on other outcomes, including reductions in prostate cancer diagnosis and mortality, are not clear.