JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Prostate Cancer
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE In the United States, the lifetime risk of being diagnosed with prostate cancer is approximately 11%, and the lifetime risk of dying of prostate cancer is 2.5%. The median age of death from prostate cancer is 80 years. Many men with prostate cancer never experience symptoms and, without screening, would never know they have the disease. African American men and men with a family history of prostate cancer have an increased risk of prostate cancer compared with other men.

OBJECTIVE To update the 2012 US Preventive Services Task Force (USPSTF) recommendation on prostate-specific antigen (PSA)–based screening for prostate cancer.

EVIDENCE REVIEW The USPSTF reviewed the evidence on the benefits and harms of PSA-based screening for prostate cancer and subsequent treatment of screen-detected prostate cancer. The USPSTF also commissioned a review of existing decision analysis models and the overdiagnosis rate of PSA-based screening. The reviews also examined the benefits 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.

FINDINGS Adequate evidence from randomized clinical trials shows that PSA-based screening programs in men aged 55 to 69 years may prevent approximately 1.3 deaths from prostate cancer over approximately 13 years per 1000 men screened. Screening programs may also prevent approximately 3 cases of metastatic prostate cancer per 1000 men screened. Potential harms of screening include frequent false-positive results and psychological harms. Harms of prostate cancer treatment include erectile dysfunction, urinary incontinence, and bowel symptoms. About 1 in 5 men who undergo radical prostatectomy develop long-term urinary incontinence, and 2 in 3 men will experience long-term erectile dysfunction. Adequate evidence shows that the harms of screening in men older than 70 years are at least moderate and greater than in younger men because of increased risk of false-positive results, diagnostic harms from biopsies, and harms from treatment. The USPSTF concludes with moderate certainty that the net benefit of PSA-based screening for prostate cancer in men aged 55 to 69 years is small for some men. How each man weighs specific benefits and harms will determine whether the overall net benefit is small. The USPSTF concludes with moderate certainty that the potential benefits of PSA-based screening for prostate cancer in men 70 years and older do not outweigh the expected harms.

CONCLUSIONS AND RECOMMENDATION For men aged 55 to 69 years, the decision to undergo periodic PSA-based screening for prostate cancer should be an individual one and should include discussion of the potential benefits and harms of screening with their clinician. Screening offers a small potential benefit of reducing the chance of death from prostate cancer in some men. 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 erectile dysfunction. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race/ethnicity, comorbid medical conditions, patient values about the benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening. (C recommendation) The USPSTF recommends against PSA-based screening for prostate cancer in men 70 years and older. (D recommendation)

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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

For men aged 55 to 69 years, the decision to undergo periodic prostate-specific antigen (PSA)–based screening for prostate cancer should be an individual one. Before deciding whether to be screened, men should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and preferences in the decision. Screening offers a small potential benefit of reducing the chance of death from prostate cancer in some men. 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 erectile dysfunction. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race/ethnicity, comorbid medical conditions, patient values about the benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening (C recommendation) (**Figure 1**).

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Animated Summary Video
Screening for Prostate Cancer: USPSTF Recommendation Statement

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

See the Clinical Considerations section for more information on screening higher-risk populations, including African American men and men with a family history of prostate cancer.

Rationale

Importance

Prostate cancer is one of the most common types of cancer that affects men. In the United States, the lifetime risk of being diagnosed with prostate cancer is approximately 11%, and the lifetime risk of dying of prostate cancer is 2.5%.[1] Many men with prostate cancer never experience symptoms and, without screening, would never know they have the disease. In autopsy studies of men who died of other causes, more than 20% of men aged 50 to 59 years and more than 33% of men aged 70 to 79 years were found to have prostate cancer.[2] In some men, the cancer is more aggressive and leads to death. 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 75 years.[1] African American men have an increased lifetime risk of prostate cancer death compared with those of other races/ethnicities (4.2% for African American men, 2.9% for Hispanic men, 2.3% for white men, and 2.1% for Asian and Pacific Islander men).[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 (ie, "false-positive" results). Men with a positive PSA test result may undergo a transrectal ultrasound-guided core-needle biopsy of the prostate to diagnose prostate cancer.

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 (RCTs) shows that PSA-based screening programs in men aged 55 to 69 years may prevent approximately 1.3 deaths from prostate cancer over approximately 13 years per 1000 men screened.[3,4] Screening programs may also prevent approximately 3 cases of metastatic prostate cancer per 1000 men screened.[3] Current results from screening trials show no reductions in all-cause mortality from screening. There is inadequate evidence to assess whether the benefits for African American men and men with a family history of prostate cancer aged 55 to 69 years are different than the benefits for the average-risk population. There is also inadequate evidence to assess whether there are benefits to starting screening in these high-risk groups before age 55 years.

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

Harms of Early Detection and Treatment

The harms of screening for prostate cancer include harms from the PSA screening test and subsequent harms from diagnosis and treatment. Potential harms of screening include frequent false-positive results and psychological harms. One major trial in men screened every 2 to 4 years concluded that, over 10 years, more than 15% of men experienced at least 1 false-positive test result.[5] Harms of diagnostic procedures include complications of prostate biopsy, such as pain, hematospermia (blood in semen or ejaculate), and infection. Approximately 1% of

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Figure 1. US Preventive Services Task Force (USPSTF) Grades and Levels of Certainty

What the USPSTF Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as the number, size, or quality of individual studies. inconsistency of findings across individual studies. limited generalizability of findings to routine primary care practice. lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of the limited number or size of studies. important flaws in study design or methods. inconsistency of findings across individual studies. gaps in the chain of evidence. findings not generalizable to routine primary care practice. lack of information on important health outcomes. More information may allow estimation of effects on health outcomes.
The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.	

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.

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 results in harms and provides them with no benefit. This is known as overdiagnosis, and follow-up of large randomized trials suggests that 20% to 50% of men diagnosed with prostate cancer through screening may be overdiagnosed.[3] Overdiagnosis rates would be expected to increase with age and to be highest in men 70 years and older because older men have high risk of death from competing causes.

Harms of prostate cancer treatment include erectile dysfunction, urinary incontinence, and bothersome bowel symptoms. About 1 in 5 men who undergo radical prostatectomy develop long-term urinary incontinence requiring use of pads, and 2 in 3 men will experience long-term erectile dysfunction. More than half of men who receive radiation therapy experience long-term sexual erectile dysfunction 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.

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Figure 2. Clinical Summary: Screening for Prostate Cancer

Population	Men aged 55 to 69 y	Men 70 y and older
Recommendation	The decision to be screened for prostate cancer should be an individual one. Grade: C	Do not screen for prostate cancer. Grade: D

Informed Decision Making	Before deciding whether to be screened, men aged 55 to 69 years should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and preferences in the decision. Screening offers a small potential benefit of reducing the chance of death from prostate cancer in some men. 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 erectile dysfunction. Harms are greater for men 70 years and older. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race/ethnicity, comorbid medical conditions, patient values about the benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening and should not routinely screen men 70 years and older.
Risk Assessment	Older age, African American race, and family history of prostate cancer are the most important risk factors for prostate cancer.
Screening Tests	Screening for prostate cancer begins with a test that measures the amount of prostate-specific antigen (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 false-positive results. Men with a positive PSA test result may undergo a transrectal ultrasound-guided core-needle biopsy of the prostate to diagnose prostate cancer.
Treatments	The 3 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.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to https://www.uspreventiveservicestaskforce.org.

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Adequate evidence shows that the harms of screening in men older than 70 years are at least moderate and greater than in younger men because of increased risk of false-positive results, harms from diagnostic biopsy, and harms from treatment.

USPSTF Assessment

PSA-based screening for prostate cancer has both potential benefits and harms. The USPSTF does not recommend screening for prostate cancer unless men express a preference for screening after being informed of and understanding the benefits and risks. The decision about whether to be screened for prostate cancer requires that each man incorporate his own values about the potential benefits and harms. The potential harms of screening, diagnostic procedures, and treatment occur soon after screening takes place. Although 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 to occur.

The USPSTF concludes with moderate certainty that the net benefit of PSA-based screening for prostate cancer in men aged 55 to 69 years is small for some men. How each man weighs specific benefits and harms will determine whether the overall net benefit is small.

The USPSTF concludes with moderate certainty that the potential benefits of PSA-based screening for prostate cancer in men 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 US population without symptoms or a previous diagnosis of prostate cancer. It also applies to men at increased risk of death from prostate cancer because of race/ethnicity or family history of prostate cancer (**Figure 2**). The sections below provide more information on how this recommendation applies to African American men and men with a family history of prostate cancer.

Risk Assessment

Older age, African American race, and family history of prostate cancer are the most important risk factors for the development of prostate cancer. Other factors with weaker associations and less

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evidence include diets high in fat and low in vegetable consumption. Cigarette smoking is associated with higher risk of prostate cancer mortality.

Screening

PSA-based screening is the usual method of screening and has been studied in several large trials. Although new screening methods are being developed (such as single- and adjusted-threshold testing and 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, or 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 use of digital rectal examination as a screening modality is not recommended because there is a lack of evidence on the benefits; digital rectal examination was either eliminated from or not included in the major screening trials.

PSA-based screening for prostate cancer has been studied in 3 very large RCTs, each with at least a decade of median follow-up: the US-based Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, the European Randomized Study of Screening for Prostate Cancer (ERSPC), and the Cluster Randomized Trial of PSA Testing for Prostate Cancer (CAP). These trials used varying screening intervals (from 1-time screening to 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 vs opportunistic screening for prostate cancer because of the substantial screening rate in the control group and the high screening rate among men in both the control and intervention groups prior to study enrollment.[6] 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 follow-up (absolute risk, 4.8 per 1000 person-years in the intervention group vs 4.6 per 1000 person-years in the control group; relative risk [RR], 1.04 [95% CI, 0.87-1.24]).[7]

In the ERSPC trial, the results suggest that, overall, the number needed to screen is 781 men aged 55 to 69 years at enrollment (95% CI, 490-1929) to prevent 1 man from dying of prostate cancer after 13 years. The results varied across the individual ERSPC sites, and prostate cancer mortality was significantly reduced only at the sites in the Netherlands and Sweden. However, point estimates were in favor of screening at all sites except Switzerland. At the largest site (Finland), there was no significant benefit observed for prostate cancer mortality (rate ratio, 0.91 [95% CI, 0.75-1.10]), and in Sweden there was an absolute risk reduction of 0.72% (95% CI, 0.50%-0.94%), a 42% relative reduction.[8-10]

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 follow-up. The risk of developing metastatic prostate cancer was 30% lower among men randomized to screening than among men in the control group (absolute risk, 7.05 per 1000 men in the screening group vs 10.14 per 1000 men in the control group [calculated from numbers in the study]). This translates to an absolute reduction in the long-term risk of metastatic prostate cancer of 3.1 cases per 1000 men screened.[11]

The CAP trial was a cluster-randomized trial of a single invitation to PSA-based screening in the United Kingdom among 415 357 men. Overall, 34% of invited men received a valid PSA screening test. After a median follow-up of 10 years, there was no significant difference in prostate cancer mortality between the invited group and the control group (absolute risk, 0.30 per 1000 person-years vs 0.31 per 1000 person-years, respectively).[12]

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. Although 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 (ie, "false-positive" results). The false-positive rate for the PSA test depends on the PSA threshold used. Among 5 ERSPC sites that reported the false-positive rate, approximately 1 in 6 men screened at least once had 1 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 (3.0 ng/mL) was used to determine a positive test result 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.[5] In the PLCO trial, more than two-thirds of men who underwent a prostate biopsy because of a positive PSA test result were found not to have prostate cancer.[13] In addition to false-positive results, there are other harms associated with screening and subsequent diagnostic evaluation; biopsies may result in pain, fever, hematospermia, and hospitalization.

The 3 large RCTs on screening predominantly included men aged 55 to 69 years. There is inadequate evidence on starting screening at a younger age in the average-risk population or to obtain a baseline PSA level. Evidence in men 70 years and older does not support routine screening because of the lack of trial evidence of benefit, the low likelihood of benefit given the time to realize benefit, and the increased risk of harms from false-positive results, biopsies, overdiagnosis, and treatment. Although the evidence does not support routine screening in all men older than 70 years, the USPSTF recognizes the common use of PSA-based screening in practice today and understands that some older men will continue to request screening and some clinicians will continue to offer it. Men older than 70 years who request screening should be aware of the reduced likelihood of benefit from screening and the increased risk of false-positive test results and complications of diagnosis and treatment.

The USPSTF considered whether there are screening and follow-up 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

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biopsies, and more cases of overdiagnosis. This trade-off 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 cancer mortality but higher rates of overdiagnosis and other harms.[14] The frequency of screening in the ERSCP sites ranged from every 2 to 7 years. No ERSPC trial site offered screening more often than every 2 years, and many sites screened every 4 years. The PSA threshold for biopsy in the ERSCP sites ranged from 2.5 to 4 ng/mL (except for 10 ng/mL in the earlier years at the Belgium site). In the Göteborg, Sweden, site, which reported the largest benefit, the frequency of screening was every 2 years, and the threshold for biopsy was 2.5 ng/mL (3.0 ng/mL in the first few years of the study).

Treatment

The potential benefit of screening for prostate cancer is because of treatment. Thus, it is important for men to consider both the potential benefits and harms of treatment (including active surveillance) as they consider whether to be screened. Men not able or willing to tolerate treatment should not be screened for prostate cancer. 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 1500 men randomized to receive either active treatment or active surveillance, the 10-year survival rate in all groups was 99%.[15] 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 3 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 adverse effects of active treatment are provided 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. Although protocols vary, active surveillance usually includes regular, repeated PSA testing and often repeated digital rectal examination and prostate biopsy, with potential for exposure to repeated harms from biopsies. Men whose cancer is found to be changing are offered definitive treatment with surgery or radiation therapy. Other treatment-monitoring strategies for men with low-risk cancer exist (for example, watchful waiting) and also vary in protocol. 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 about 10% in 2005-2009 to 40.4% in 2010-2013 among men with low-risk prostate cancer.[16]

Active treatment of prostate cancer can result in major adverse effects. About 3 in 1000 men die during or soon after radical prostatectomy, and about 50 in 1000 men have serious surgical complications requiring intervention. About 1 in 5 men who undergo radical prostatectomy develop long-term urinary incontinence requiring regular use of pads, and about 2 in 3 men experience long-term erectile dysfunction. More than half of men who receive radiation therapy experience long-term erectile dysfunction, 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 attributable in part to an earlier age at cancer onset, more advanced cancer stage at diagnosis, and higher rates of more aggressive cancer (ie, higher tumor grade). These differences 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.[17] 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 [OR], 7.1 [95% CI, 2.7-18.0]).[13] Evidence is insufficient to compare the risk of false-positive results, potential for overdiagnosis, and magnitude of harms from prostate cancer treatment in African American vs 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 prostate cancer in African American men, PSA-based screening may provide greater

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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. Although the USPSTF found inadequate evidence about how benefits may differ for African American men, it recognizes the epidemiologic data showing that African American men may develop prostate cancer at younger ages than average-risk men and understands that some African American men and their clinicians will continue to screen at younger ages. The USPSTF does not recommend screening for prostate cancer in men, including African American men, older than 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 follow-up, 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 data 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.[18] An analysis from the Finnish site of the ERSPC trial concluded that men with at least 1 first-degree relative with prostate cancer were 30% more likely to be diagnosed with prostate cancer than men without a family history.[19] Men with 3 first-degree relatives with prostate cancer or 2 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 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.[20]

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 mortality was lower among white men in the intervention group than in the control group (hazard ratio [HR], 0.49 [95% CI, 0.22-1.10]; $P = .08$),[21] but the difference was not significant and the confidence interval was wide.

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, developed metastatic prostate cancer, or 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. Although the USPSTF found inadequate evidence about how benefits may differ for men with a family history of prostate cancer, it recognizes the epidemiologic data showing that these men are at a greater than average risk and understands that some men and their clinicians will continue to screen at younger ages in men with a family history. The USPSTF does not recommend screening for prostate cancer in men, including men with a family history of prostate cancer, older than 70 years.

Epidemiologic studies examining outcomes in men with relatives who died of prostate cancer vs 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

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- Developing, validating, and providing longer-term follow-up 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 vs harm; how to best implement informed decision making programs that incorporate the values and preferences of men and their families about screening; how to adapt the informed decision-making process to a range of diverse patient populations as screening, diagnosis, and treatment strategies evolve; and the effects of informed decision making on health outcomes and patient experience

Discussion

Burden of Disease

For men in the United States, the lifetime risk of being diagnosed with prostate cancer is approximately 11%, and the lifetime risk of dying of prostate cancer is 2.5%.[1] In 2013, the most recent year for which data are available, approximately 172 000 men in the United States were diagnosed with prostate cancer and almost 28 000 died of prostate cancer.[22] From 2003 to 2012, the prostate cancer mortality rate among US men decreased significantly by 3.4% per year (3.3% and 3.9% per year in white and black men, respectively).[23] Most cases of prostate cancer found in autopsy studies are microscopic, well-differentiated lesions that did not affect men's health during their lifetime. Data from screening trials suggest that many cases of low-risk cancer detected by screening would never have caused symptoms or affected men's health had they never been identified through screening.

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 treatment of screen-detected prostate cancer.[3,4] 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.[14,24] 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, PLCO, and CAP trials and site-specific reports from 4 ERSPC trial sites. To understand the effectiveness of treatment of screen-detected, early-stage prostate cancer, the USPSTF also examined the results of 3 randomized trials and 9 cohort studies.[3]

The ERSPC trial randomly assigned a core group of more than 160 000 men aged 55 to 69 years from 7 European countries to PSA-based screening vs usual care.[8] Four ERSPC sites reported on the cumulative incidence of metastatic prostate cancer. After a median follow-up 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, 0.60-0.82]; $P = .001$). The absolute reduction in long-term risk of metastatic prostate cancer associated with screening was 3.1 cases per 1000 men.[11] After a median follow-up of 13 years, the prostate cancer mortality rate among men aged 55 to 69 years was 4.3 deaths per 10 000 person-years in the screening group and 5.4 deaths per 10 000 person-years in the usual care group (RR, 0.79 [95% CI, 0.69-0.91]; $P = .001$).[8] The ERSPC trial did not find a reduction in all-cause mortality.[8]

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 review because of 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 underwent radical prostatectomy (41.3%) than in the usual care group (32.8%).[25] 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 aged 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.[17] 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.[25] On average, men in the intervention group received 5 PSA tests during the screening phase of the trial and men in the usual care group received 3 PSA tests.[26] This high PSA testing rate in the control group limits the study's ability to identify

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a potential screening benefit. 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, 1.07-1.17]). At a median follow-up of 14.8 years in the PLCO trial, the prostate cancer mortality rate was not significantly different between the intervention and control group (4.8 vs 4.6 deaths per 10 000 person-years, respectively) (RR, 1.04 [95% CI, 0.87-1.24]).[7] This result does not rule out the possibility of a reduction in prostate cancer mortality from screening for prostate cancer.

The CAP trial was a cluster randomized trial in the United Kingdom among 415 357 men aged 50 to 69 years invited for a single PSA-based screening for prostate cancer.[12] Men with a PSA level of 3.0 ng/mL or greater were referred for biopsy. Men with localized prostate cancer were offered enrollment into the Prostate Testing for Cancer and Treatment (ProtecT) trial, in which the primary outcome was prostate cancer mortality. At intervention sites, 34% of men received a valid PSA screening test; the percentage of men at control sites who received a PSA test for screening purposes was estimated to be about 10% to 15% over 10 years. After a median follow-up of 10 years, there was no significant difference in prostate cancer mortality between the group of men invited to screening and control group (RR, 0.99 [95% CI, 0.94-1.03]; $P = .49$).

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

There are limited data on the benefit of screening in younger men. The PLCO trial did not recruit men younger than 55 years. The ERSPC trial reported a slightly higher and nonsignificant risk reduction (RR, 0.84 [95% CI, 0.28-2.49]) for prostate cancer mortality in men aged 50 to 55 years compared with men in the core group aged 55 to 69 years (RR, 0.79 [95% CI, 0.69-0.91]).

There are few data that screening is effective in men older than 70 years. The PLCO and ERSPC trials enrolled men 74 years and younger; men older than 70 years were not in the core age group (55-69 years) in the ERSPC trial. The CAP trial did not enroll men older than 69 years. In the ERSPC trial, the prostate cancer mortality rate ratio in the screening vs control group among men 70 years and older at randomization was 1.17 (95% CI, 0.82-1.66); however, a statistical test found no significant heterogeneity across age groups. In the PLCO trial, the analogous rate ratio at a median follow-up of 13 years among men aged 65 to 74 years at randomization was 1.02 (95% CI, 0.77-1.37); the test for heterogeneity was not significant ($P = .81$).

Potential Benefits of Treatment

The USPSTF examined 3 good-quality randomized trials of treatment of localized prostate cancer and 9 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 mortality, and progression to metastatic prostate cancer.[3]

The UK ProtecT trial randomized more than 1600 men aged 50 to 69 years with screen-detected, localized prostate cancer to radical prostatectomy, radiation therapy, or active surveillance and followed them up for 10 years. Approximately 77% of men had low-grade prostate cancer (Gleason score of 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 a candidate for active surveillance in some settings. The trial did not find a significant improvement in all-cause or prostate cancer 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 follow-up studies may provide important additional information. The trial reported a significant reduction in progression to metastatic cancer when comparing both radical prostatectomy (61% reduction [95% CI, 27%-79%]) and radiation therapy (52% reduction [95% CI, 13%-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 follow-up period, 54.8% of men randomized to active surveillance crossed over to active treatment.[15]

The other 2 randomized trials of radical prostatectomy took place prior to widespread PSA-based screening and thus recruited many men with tumors detected from clinical symptoms. Approximately 50% of men in the US-based Prostate Cancer Intervention vs 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 significant reduction over 13 years in all-cause and prostate cancer mortality.[27] The PIVOT trial did not find significant reductions overall in all-cause or prostate cancer mortality.[28] Recent results from extended follow-up of the PIVOT trial to a median of 12.7 years reported similar results; radical prostatectomy did not significantly reduce prostate cancer mortality (HR, 0.63 [95% CI, 0.39-1.02]) or all-cause mortality (HR, 0.94 [95% CI, 0.81-1.09]) compared with conservative management.[29]

Several cohort studies examining radical prostatectomy or radiation therapy found significant reductions in prostate cancer mortality when comparing active treatment with watchful waiting or other conservative approaches.[3] The cohort study results, however, should be interpreted with caution because of the potential for bias in treatment assignment. In these clinical settings, men who are healthier may have been more likely to receive active treatment.

Two studies reported on the difference in benefit by age. The PIVOT trial reported no significant differences by age (younger or older than 65 years) in the association between radical prostatectomy and all-cause mortality. In the SPCG-4 trial, the risk of all-cause mortality after radical prostatectomy vs watchful waiting was not significantly reduced among men 65 years and older (but was significantly reduced in men younger than 65 years).

Potential Harms of Screening and Treatment

Potential Harms of Screening and Diagnosis

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 US Department of Veterans Affairs (VA) health system, as well as a report on complications of prostate biopsy from the ERSPC Rotterdam site to understand the potential harms of screening and diagnosis.[3]

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In the large RCTs, one-fourth to one-third of men offered PSA-based screening had at least 1 positive screening test result. In the PLCO trial, 13% of men had undergone at least 1 biopsy. In the ERSPC trial, nearly 28 biopsies were performed for every 100 men randomized to screening.[3] In the ProbE trial, 7.3% of men reported moderate or greater pain, 5.5% reported moderate to severe fever, and 26.6% reported troublesome hematospermia within the 35 days after biopsy.[28] Complications from transrectal prostate biopsy resulted in 1.3% of men in the UK cohort, 1.6% of men in the VA cohort, and 0.5% of men in the Rotterdam cohort requiring hospitalization.[30-32] In these studies, two-thirds to three-fourths of biopsies demonstrated that the PSA screening 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 overdiagnosis rate. Trial data suggest that 21% of cases of screen-detected cancer in the PLCO trial and 50% in the ERSPC trial were overdiagnosed.[3] Using a different type of methodology (ie, not estimates based directly on single trials), 3 decision analysis models produced by the Cancer Intervention and Surveillance Modeling Network estimated that between 1988 and 2000 in the United States, the overdiagnosis rate among cases of screen-detected prostate cancer was 22% to 42%.[24] Overdiagnosis increases with age; 1 study estimates that the overdiagnosis rate is more than 15-fold higher in men older than 85 years than in men aged 50 to 54 years.[24]

Men older than 70 years in the ERSPC trial had a higher rate of false-positive results than younger men (younger than 55 years) (20.6% vs 3.5% in the first screening round, respectively). In the VA cohort study, fewer older men were sent for biopsy for a PSA level greater than 4.0 ng/mL (50.5% of men aged 65-69 years vs 25.4% of men aged 75-79 years). Data from the PLCO trial suggest that older men may be more likely than younger men to experience biopsy complications (28.2 vs 17.7 complications per 1000 biopsies, respectively; OR, 1.4 [95% CI, 0.9-2.4]; $P = .06$).

The USPSTF reviewed studies evaluating psychological harms of screening and diagnosis. In 2 observational studies, men who had abnormal PSA screening results but benign biopsy results had significantly increased worry about prostate cancer at 6- to 8-week and at 1-year follow-up compared with men with normal PSA screening results.[33] After 1 year, one-third of men with a benign biopsy finding after an abnormal screening result thought about prostate cancer "a lot" or "some," compared with 18% of men who had a normal PSA level ($P = .005$). In a prospective cohort study embedded in the UK ProtecT trial (n = 7344), there was no increase in anxiety or depression and similar scores on the Mental Health Component of the 12-Item Short Form Health Survey compared with baseline among men who had abnormal PSA screening results.[34] In a cross-sectional US study (n = 210), men with benign biopsy findings after abnormal PSA screening results did not have significantly greater anxiety than men who had normal results.[35]

Potential Harms of Treatment

Men who undergo active surveillance may undergo repeated biopsies and be exposed to potential repeated harms from biopsies (as discussed above). In addition, a significant proportion of men will go on to have active treatment with surgery or radiation therapy, with resultant harms (as discussed below).

The USPSTF identified 3 good-quality and 1 fair-quality randomized trials and 7 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 (requiring daily use of pads or worse) for every 7.9 men who undergo radical prostatectomy rather than conservative management (95% CI, 5.4-12.2), and 1 man will experience long-term erectile dysfunction for every 2.7 men who undergo radical prostatectomy rather than conservative management (95% CI, 2.2-3.6).[3] In addition, more than 20% of men in the PIVOT trial had a perioperative complication and 5.3% of men in a large US cohort study required reintervention for a surgical complication.[3] A meta-analysis of the harms of radiation therapy found that 1 man will experience long-term erectile dysfunction for every 7 men treated with radiation therapy rather than conservative management (95% CI, 5.1-10.7).[3] Although 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 1 cohort study,[36] and these bowel complications were more common compared with conservative management in 2 trials and 3 cohort studies.[3]

After a median follow-up 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.[36] The older SPCG-4 trial had similar results after a median follow-up of 12 years when comparing men who received radical prostatectomy vs watchful waiting.[37] There was no evidence of an adverse effect of radical prostatectomy on generic quality-of-life measures compared with conservative management in cohort studies.

In several studies, men older than 70 years had a significantly increased risk of medical complications and perioperative mortality after radical prostatectomy compared with younger men.[3]

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. However, these strategies are also associated with more false positives, more biopsies, and higher rates of overdiagnosis.[24]

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. However, no strategy completely eliminates overdiagnosis. PSA-based screening for prostate cancer every 2 or 4 years instead of annually appears to provide a good trade-off between a reduction in overdiagnosis and a small reduction in mortality benefit.[24]

Decision analysis models confirm the USPSTF's conclusion that the overall benefit of PSA-based screening for prostate cancer is sensitive to the values of individual men. The magnitude of net benefit of PSA-based screening depends on how each man weighs the potential benefits and harms of screening, diagnosis, and treatment. The value a man places on potential benefits and harms may also

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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.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from April 11 to May 8, 2017. A number of comments suggested that because men are now living longer, they should be screened beyond 70 years of age. However, the USPSTF considered other evidence in addition to data on life expectancy when recommending against screening in men older than 70 years, including results from large screening trials that did not report a mortality benefit for men older than 70 years and evidence on the increased likelihood of harm from screening, diagnostic evaluation, treatment, overdiagnosis, and overtreatment. Several comments requested a recommendation for younger men and for baseline PSA-based screening in men 40 years and older or 50 years and older. The USPSTF found inadequate evidence that screening younger men or performing baseline PSA-based screening provides benefit.

Several comments asked for clarification about what new evidence led to the change from a D to a C grade. The new evidence included longer-term follow-up of the ERSPC trial and new data on reductions in risk of metastatic disease with screening. Although the added benefit reported from the additional follow-up to 13 years (from 10 years) in the ERSPC trial increased the number of lives saved from 1.07 to 1.28 (a small amount, according to some comments), these results gave the USPSTF more confidence that the benefit of screening could be greater over a 20- to 30-year period. Evidence newly considered since the draft recommendation statement was posted for comment includes the CAP trial, evidence on psychological harms, and longer-term follow-up of the PIVOT trial. This evidence led the USPSTF to continue to conclude that there is a small amount of benefit for some men. The USPSTF recognizes the importance of the potential harms of screening and treatment, including psychological harms and harms from active surveillance, and has added information about this evidence to the Rationale, Clinical Considerations, and Discussion sections. New evidence from the recently published CAP trial was added. Given the limitations of the CAP trial, including that it only examined 1-time PSA-based screening and the small difference between the percentage of men in the control and intervention groups (approximately 10%-15% vs 34%, respectively) who received PSA-based screening, the results of this trial did not change the USPSTF's overall assessment of the evidence and its recommendation.

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

Effect	No. of Men
Men invited to screening	1000
Men who received at least 1 positive PSA test result	240
Men who have undergone 1 or more transrectal prostate biopsies	220[b]
Men hospitalized for a biopsy complication	2
Men diagnosed with prostate cancer	100
Men who initially received active treatment with radical prostatectomy or radiation therapy	65
Men who initially received active surveillance	30
Men who initially received active surveillance who went on to receive active treatment with radical prostatectomy or radiation therapy	15
Men with sexual dysfunction who received initial or deferred treatment	50
Men with urinary incontinence who received initial or deferred treatment	15
Men who avoided metastatic prostate cancer	3
Men who died of causes other than prostate cancer	200
Men who died of prostate cancer despite screening, diagnosis, and treatment	5
Men who avoided dying of prostate cancer	1.3

Abbreviation: PSA, prostate-specific antigen.

[a] Estimates based on benefits observed in the ERSPC trial for men aged 55 to 69 years and on treatment harms derived from pooled absolute rates in the threatment groups in the 3 treatment trials (ProtecT, PIVOT, SPCG-4).

[b] 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.

Update of Previous USPSTF Recommendation

This recommendation replaces the 2012 USPSTF recommendation[38] on PSA-based screening for prostate cancer. In 2012, the USPSTF concluded that, although 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 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 follow-up of the ERSPC trial and from some ERSPC trial sites found that PSA-based screening for prostate cancer prevents 1.28 men from dying of prostate cancer for every 1000 men screened. In addition, a subset of ERSPC trial sites have since reported that screening 1000 men aged 55 to 69 years may prevent approximately 3 men from developing metastatic prostate cancer. Longer-term, 12.7-year results of the PIVOT trial became available since the posting of the draft recommendation statement and are similar to the 10-year results. Studies continue to demonstrate the harms of PSA-based screening, including false-positive results, complications from transrectal prostate biopsies, overdiagnosis (which may occur in 20%-50% of cases of screen-detected cancer, based on estimates from trial data), psychological harms, and harms of treatment, including urinary incontinence and erectile dysfunction. 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. For the C recommendation for men aged 55 to 69 years, the USPSTF's intention is to convey that each man's values may shift

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the balance to a net benefit of screening and to promote the importance of informed decision making prior to screening. The USPSTF continues to find that the benefits of screening do not outweigh the harms in men 70 years and older and recommends against screening in these men.

Recommendations of Others

The American Academy of Family Physicians[39] and the Canadian Task Force on Preventive Health Care[40] recommend against PSA-based screening for prostate cancer. The American College of Physicians[41] recommends that clinicians discuss the benefits and harms of screening with men aged 50 to 69 years and only recommends screening for men who prioritize screening and have a life expectancy of more than 10 to 15 years. The American Urological Association[42] recommends that men aged 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 decision making with their clinicians, taking into account each man's values and preferences. It notes that to reduce the harms of screening, the screening interval should be 2 or more years. The American Urological Association also notes 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[43] adopted detailed screening recommendations in 2016 that highlight the importance of shared decision making 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.

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