CLINICAL PRACTICE

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Screening for Prostate Cancer

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.*

A 60-year-old patient asks whether he should undergo screening for prostate cancer and, if he undergoes screening and the results are positive, what his options would be with respect to further diagnostic testing and treatments. How would you respond?

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THE CLINICAL PROBLEM

Prostate cancer is currently the most diagnosed cancer (excluding nonmelanoma skin cancer) and the second leading cause of cancer death among U.S. men. Prostate cancer was diagnosed in an estimated 268,500 men in 2022, and approximately 34,500 died of it.[1] The disease occurs primarily in older persons, with the incidence greatest among men in their 70s and mortality highest among men in their 80s. The incidence among non-Hispanic Black men is 1.7 times as high as that among non-Hispanic White men, and mortality is 2.1 times as high; incidence and mortality are lower among Hispanic men and Asian men than among White men and non-Hispanic Black men.[1]

Measurement of prostate-specific antigen (PSA), a protein secreted by both normal and malignant prostate epithelial cells, was approved by the Food and Drug Administration (FDA) in 1986 for use in monitoring patients with known prostate cancer and later (in 1994) as an aid in the detection of prostate cancer in conjunction with digital rectal examination in patients 50 years of age or older.[2,3] Notably, this approval occurred in the absence of evidence that early detection of prostate cancer leads to improved patient outcomes. The onset of widespread PSA screening in the late 1980s is widely acknowledged to be the primary cause of the sharp increase in prostate cancer incidence that was observed in the next decade; rates later fell, beginning in approximately 2009 (Fig. S1A in the Supplementary Appendix, available with the full text of this article at NEJM.org).[1,4] From a peak in the early 1990s, prostate cancer mortality steadily decreased during the next two decades by approximately 50% and has subsequently remained essentially constant (Fig. S1B).[1]

The association between PSA screening and mortality is less clear than the association between screening and incidence, with various analyses undertaken to assess the relative contribution of screening (as compared with other factors, including treatment improvements) to the reduction in mortality.[5-8] An estimate with the use of a quantitative model showed that slightly less than half the reduction in mortality was as a result of screening.[8]

In the majority of prostate cancer cases currently diagnosed in the United States, the disease is localized, with only approximately 7% of patients presenting

KEY CLINICAL POINTS

SCREENING FOR PROSTATE CANCER

- Prostate cancer is the most diagnosed cancer (excluding nonmelanoma skin cancer) and is the cancer with the second highest mortality among men in the United States. Prostate cancer–specific survival at 10 years is 95% among men with localized disease.
- Prostate-specific antigen (PSA) screening should involve shared decision making with consideration of the risks and benefits of screening and patient preferences.
- Findings from randomized trials support a modest reduction in prostate cancer mortality with PSA screening; screening 1000 men may prevent deaths from prostate cancer in 1.3 men in the 13 years after initial screening.
- Persons with elevated PSA levels on screening may choose to undergo further tests to inform the need for biopsy, multiparametric magnetic resonance imaging (MRI) to identify biopsy targets, or both.
- Persons with low-risk or favorable intermediate-risk prostate cancer may choose to undergo active surveillance (periodic PSA tests and biopsies) over immediate curative treatment (surgery or radiation therapy).
- Surgery and radiation therapy generally provide excellent outcomes in prostate cancer but may result in harms, including urinary incontinence and erectile dysfunction with surgery, and bowel dysfunction and erectile dysfunction with radiation therapy.

with metastatic disease.[1] Localized disease is classified according to risk of progression or death on the basis of tumor stage, PSA level, and tumor grade.[9-11] Tumor grade has traditionally been summarized by the Gleason score but has more recently been reported in terms of grade group, which ranges from 1 (Gleason score, 6) to 5 (Gleason score, 9 or 10). The grade-group nomenclature classifies a Gleason score of 6 as the lowest grade of prostate cancer.[12] The Gleason score is composed of a primary (most predominant) grade plus a secondary (highest nonpredominant) grade. In persons with localized disease, clinically significant prostate cancer is usually defined as grade group 2 or higher (Gleason score, ≥3+4) or grade group 3 or higher (Gleason score, ≥4+3). For localized disease, 10-year prostate cancer–specific survival is approximately 95%.[1] In contrast, 5-year survival is approximately 35% for metastatic disease.

Definitive treatment for localized disease typically involves either radiation therapy or radical prostatectomy. In the past decade, active surveillance has emerged as an alternative to immediate, definitive therapy for persons with localized, low-risk disease and for selected persons with favorable, intermediate-risk disease.[13,14] Active surveillance includes periodic surveillance biopsies in addition to PSA monitoring, with a plan to initiate local therapy with curative intent if there is evidence of disease progression. Here, we review the current understanding of the benefits and harms of PSA screening.

STRATEGIES AND EVIDENCE

INTERPRETATION OF PSA LEVELS

In the United States, a PSA level of 4.0 ng per milliliter has been the generally accepted threshold at which providers recommend prostate biopsy; in Europe, a cutoff of 3.0 ng per milliliter has more commonly been used. However, there is no PSA level below which prostate cancer can be definitively ruled out. In the Prostate Cancer Prevention Trial, prostate cancer was detected in 15.2% of men whose PSA levels remained below 4.0 ng per milliliter throughout the 7-year trial and in 6.6% of men with a PSA level of 0.5 ng per milliliter or lower at the end of the trial.[15] However, only 2.3% of men with a PSA level of 4.0 ng per milliliter or lower had disease with a grade group score of 2 or higher as shown on the end-of-study biopsy. Data from the Physicians Health Study showed a cumulative risk of lethal prostate cancer of only 0.3% through 15 years among men 55 to 59 years of age with baseline PSA levels that were below the median of 1.0 ng per milliliter.[16]

RANDOMIZED, CONTROLLED TRIALS OF PSA SCREENING

The European Randomized Study of Screening for Prostate Cancer (ERSPC) was a multicenter,

randomized, controlled trial that was initiated in the early 1990s to assess the effect of PSA screening on prostate cancer mortality among 162,388 men 55 to 69 years of age.[17,18] Planned screening involved assessment of PSA every 4 years with a biopsy-recommendation threshold of 3.0 ng per milliliter, although there was some variation among the study centers; the control group was not offered screening as part of the trial (and screening rates were believed to be low, although rates were not rigorously assessed across the trial sites). Among men in the intervention group, the mean number of screens, positive results, and biopsies per participant was 1.9, 0.33, and 0.27, respectively. The positive predictive value of biopsy was 24.8%. Prostate cancer diagnoses were more common in the screening group than in the control group (rate ratio, 1.90 at 9 years and 1.41 at 16 years). At the 16-year follow-up, the rate ratio of prostate cancer mortality in the screening group was 0.80 (95% confidence interval [CI], 0.72 to 0.90); rate ratios were similar at 11 and 13 years. The risk differences per 1000 men were 1.28 at 3 years and 1.76 at 16 years, resulting in the numbers needed to invite to screening to prevent one prostate cancer death of 781 and 570, respectively. In an analysis adjusted for participants who were invited to undergo screening but did not accept, the rate ratio of prostate cancer mortality (through 16 years) was 0.75.[18]

In the Prostate, Lung, Colorectal and Ovarian (PLCO) trial, which began in 1993, a total of 76,683 men 55 to 74 years of age underwent randomization to screening (intervention) or usual care (control).[19] Screening involved six annual PSA measurements and four annual digital rectal examinations; the PSA biopsy-recommendation threshold was 4.0 ng per milliliter. Intervention-group adherence to PSA testing ranged from 85 to 89% across screening rounds. However, PSA testing was also common in the control group, with participants in that group undergoing approximately half as much testing as participants in the intervention group.[19] The incidence of biopsy after positive results on screening was substantially lower in the PLCO trial than in the ERSPC trial. The incidence of prostate cancer was modestly higher in the intervention group than in the control group (rate ratio, 1.12 at 13 years). At 15-year and 17-year follow-ups, rate ratios for prostate cancer mortality were 1.04 (95% CI, 0.87 to 1.24) and 0.93 (95% CI, 0.81 to 1.08), respectively[19,20]; the rate ratio for disease of grade groups 4 or higher at 17 years was 0.89 (95% CI, 0.80 to 0.99).

The U.K. Cluster Randomized Trial of PSA Testing for Prostate Cancer (CAP) trial was a primary care–based, randomized, controlled trial in which 419,582 men 55 to 69 years of age were assigned to receive an invitation to one-time PSA screening (with prostate biopsy recommended in persons with PSA levels >3.0 ng per milliliter) or to not be offered screening.[21] PSA screening was performed in 36% of participants in the intervention group, within the 35-to-50% range on which the power calculations were based. At the median 10-year follow-up, the rate ratio for prostate cancer diagnosis was 1.19 (95% CI, 1.14 to 1.25). Prostate cancer mortality did not differ significantly between the groups (0.30 in the intervention group vs. 0.31 in the control group per 1000 person years; rate ratio, 0.96; 95% CI, 0.85 to 1.08). An analysis that accounted for adherence to screening showed similar results (rate ratio, 0.93; 95% CI, 0.67 to 1.29).

Systematic reviews of PSA screening trials have noted a high risk of bias in the PLCO trial owing to contamination of the control group and in the CAP trial owing to low adherence to screening.[22,23] A review by the U.S. Preventive Services Task Force (USPSTF) also noted that there was uncertain applicability of results from the ERSPC trial in the United States owing to a lower PSA positivity threshold (3 ng per milliliter) and a higher incidence of biopsies than is customary in U.S. practice, and noted a greater use of radical prostatectomy in the intervention group than in the control group.[23] The USPSTF review resulted in an estimate, based on data from randomized, controlled trials, that screening 1000 U.S. men 55 to 69 years of age may prevent deaths from prostate cancer in 1.3 men in the 13 years after initial screening.[24]

RANDOMIZED, CONTROLLED TRIALS OF CONSERVATIVE MANAGEMENT OR CURATIVE TREATMENT

The Scandinavian Prostate Study Group (SPCG)–4 trial and the U.S. Prostate Intervention versus Observation Trial (PIVOT) randomly assigned men to undergo prostatectomy or to receive ob-

servation without curative intent.[25,26] Both trials showed a lower incidence of death from prostate cancer with surgery than with observation, although the difference between surgery and observation was not significant in the PIVOT trial (SPCG-4 rate ratio, 0.56; 95% CI, 0.41 to 0.77; and PIVOT rate ratio, 0.63; 95% CI, 0.36 to 1.09). The greater absolute difference in the incidence of death from prostate cancer between observation and surgery in the SPCG-4 trial as compared with the PIVOT trial (12 percentage points vs. 4 percentage points) reflected a higher risk at baseline among men in the SPCG-4 trial, among whom fewer cancers were detected by PSA screening (12% in the SPCG-4 trial vs. 75% in the PIVOT trial).

The Prostate Testing for Cancer and Treatment (ProtecT) trial enrolled only participants who had cancer that was diagnosed after screening revealed an elevated PSA, 77% of whom had disease that was grade group 1 (clinically insignificant disease).[27] Men in the ProtecT trial were randomly assigned to prostatectomy, radiation therapy, or active monitoring (i.e., serial PSA tests, with increases in the PSA level triggering consideration of biopsy). At median follow-up of 10 years, prostate cancer mortality per 1000 person years was low (1.5 in the prostatectomy group, 0.9 in the radiation therapy group, and 0.7 in the active monitoring group) and did not differ significantly among the groups. However, the rate of metastases per 1000 person-years was significantly higher with active monitoring (6.3) than with radical prostatectomy (2.4) or radiation therapy (3.0), and by the end of follow-up, 55% of the men in the active monitoring group had crossed over to active treatment. An updated report at a median of 15 years of follow-up similarly showed no significant difference in prostate cancer mortality among the groups; the percentage of men with metastatic disease was 9.4% in the active monitoring group as compared with 4.7% and 5.0% in the radical prostatectomy and radiation therapy groups, respectively.[28]

HARMS OF SCREENING

Among the harms associated with PSA screening is the performance of unnecessary biopsies and the risks associated with those procedures.[29] The cumulative percentage of false positive PSA results is estimated to be between 10% and 15% over several (three to four) rounds of screening, with approximately a 5% risk of a false positive screen with a subsequent negative biopsy. According to data from a U.S. private insurer database, from 2008 through 2014, a mean of 1.8 biopsies were performed per 100 PSA tests, with a positivity percentage of 37%.[30] The major risk associated with prostate biopsy is infection, which occurs in 5 to 7% of patients and results in hospitalization in 1 to 3%.[31] Other complications include hematuria (incidence, <1%), rectal bleeding that leads to medical intervention (incidence, approximately 2.5%), and less commonly, urinary obstruction or retention, or transient erectile dysfunction. In addition, prostate biopsy can be associated with substantial discomfort.

Screening results in substantial overdiagnosis (defined as the identification of a case of prostate cancer that would not otherwise have been diagnosed during a patient's lifetime without screening). An analysis that was conducted with the use of three natural history models estimated that in the 1985–2000 period, 23 to 42% of prostate cancer cases detected by screening were overdiagnosed.[32] In light of this estimate, the risks associated with treatment are of particular concern. A meta-analysis showed that radical prostatectomy was associated with substantially elevated risks of both erectile dysfunction and urinary incontinence.[24] Although data were inconclusive as to whether the risk of these adverse events was greater after radiation therapy than with conservative management, there was some evidence of elevated risk of erectile dysfunction. In the ProtecT trial, radiation therapy, but not radical prostatectomy, was associated with worse bowel function than active monitoring.[33]

MANAGEMENT OF POSITIVE SCREENS

Figure 1 shows management strategies after a positive PSA screen. Initial steps include a repeat of the screening test to rule out laboratory error and assessment of the possibility of transient or treatable causes of PSA elevation (e.g., prostatitis, benign prostatic hyperplasia, recent ejaculation, or vigorous exercise). Antibiotic agents are not recommended for the treatment of increased PSA levels in the absence of symptoms.[29] After confirmation of an unexplained elevation in PSA level, further assessments that may reduce unnecessary biopsies include PSA kinetics (change

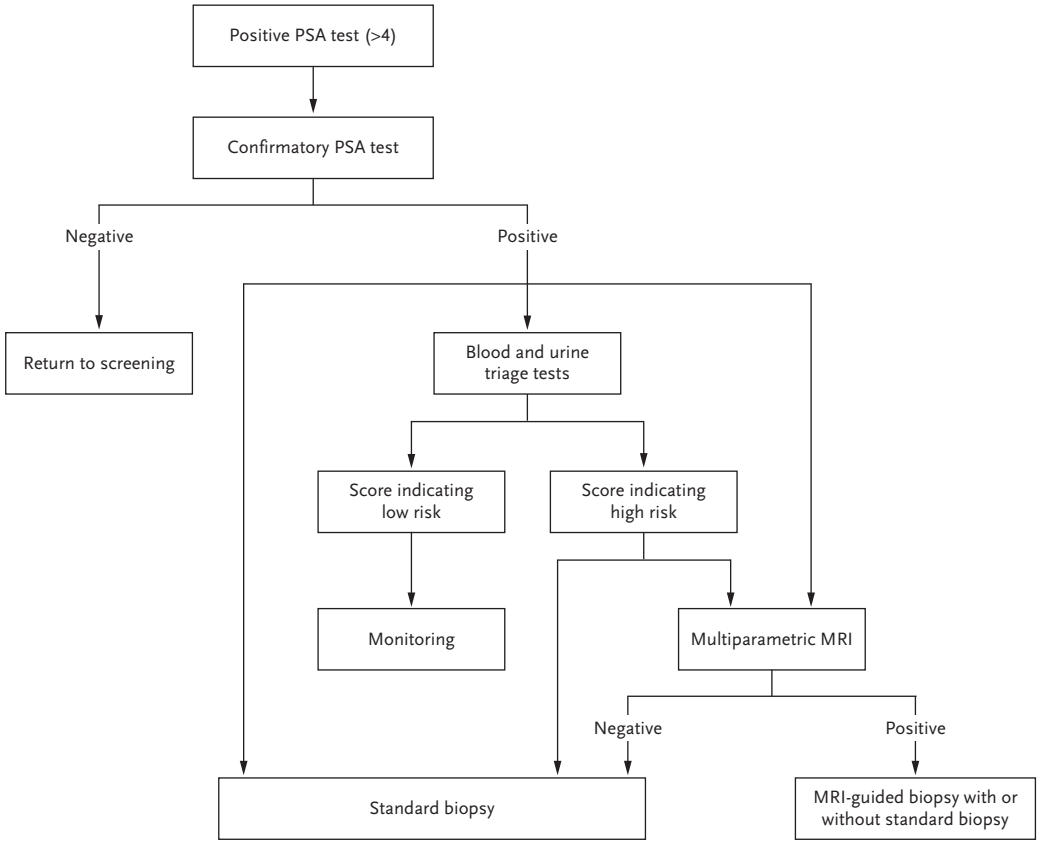

Figure 1. Follow-up after PSA Screening.

Blood and urine triage tests include the Stockholm-3 model, the Prostate Health Index, the 4Kscore Test, and the PCA3 test.[34] Depending on the triage test score and other factors, next steps may include standard biopsy, multiparametric magnetic resonance imaging (MRI), or monitoring. PSA denotes prostate-specific antigen.

over time) and urine- or blood-based molecular tests (Fig. 1); however, none of these assessments can definitively rule out prostate cancer.

A review article described six blood- or urine-based tests that were designed to assess the risk of disease of grade group 2 or higher in men with an elevated PSA level.[34] All the tests had similar performance; the area under the curve (AUC) ranged from 0.77 to 0.82 for the use of the test alone or in conjunction with clinical variables. For context, with a background incidence of disease of grade group 2 or higher of 36% among men referred for biopsy, an AUC of 0.81 translated to the avoidance of 22 to 37% of biopsies, depending on the cutoffs that were used, with corresponding chances of missed diagnoses of grade group 2 or higher in 1 to 5% of men.[35]

The standard method of tissue diagnosis of prostate cancer is the 12-core, ultrasonography-guided, systematic biopsy procedure. However, standard, ultrasonography-guided biopsies have been shown to underestimate tumor grade, as determined at prostatectomy, in 30 to 50% of men.[36] The use of multiparametric magnetic resonance imaging (MRI) platforms to guide biopsy has been shown to reduce the incidence of misclassification[37] and to increase the incidence of detection of clinically significant disease.[38] A score of 3 or higher on the Prostate Imaging Reporting and Data System (PI-RADS) scale (scores range from 1 to 5, with higher scores indicating higher cancer risk) for any lesion prompts an MRI-guided biopsy of the lesion. Systematic biopsy is also typically performed, although the additional yield appears to be very

low in persons with lesions with a score of 5 on the PI-RADS scale.[39] Questions remain regarding the safety of forgoing standard biopsies in persons who have not previously undergone biopsies and have an elevated PSA level and nonsuspicious results on MRI.[40]

A potential downside of the greater sensitivity of MRI in identification of small, higher-grade lesions is the risk of overdiagnosis.[41] For example, a study showed that among 999 men with negative standard biopsies, the addition of MRI-targeted biopsies led to the detection of grade group 1 and grade group 2 disease in 7.4% and 7.5% of the men, respectively, the vast majority of whom would have had clinically insignificant disease.[37]

SHARED DECISION MAKING AND DECISION AIDS

Decision making that involves sharing of information between the patient and the clinician and joint participation in the decision-making process should be an integral component of an offer of PSA screening.[29] The clinician should discuss with individual patients the potential benefits and harms of screening and review downstream options in the case of a positive screen, and the patients should share with the clinician their values and preferences. Table 1 describes recommended considerations for these discussions.[42-44]

The use of decision aids, tools that help patients understand the benefits and harms of undergoing screening, may facilitate shared decision making. The results of a meta-analysis of randomized, controlled trials that assessed decision aids as compared with usual care without the use of decision aids showed modest improvements in patient knowledge and a small decrease in decisional conflict (i.e., personal uncertainty about which course of action to take), but no significant differences in the frequency of screening discussions with clinicians or in the proportion of patients who decided to undergo screening.[47] Another meta-analysis showed similar findings with respect to knowledge and decisional conflict but also showed a small reduction in the proportion of men who planned to undergo screening.[48] However, there was no significant effect on the number of patients who actually underwent PSA screening within the next year. Decision aids tailored specifically to Black patients also have been developed.[49,50]

AREAS OF UNCERTAINTY

Although numerous series have shown the safety of active surveillance with regard to prostate cancer mortality, uncertainties remain about appropriate patient selection criteria (e.g., which patients with grade group 2 disease can safely defer definitive therapy and the appropriate use of biomarkers), monitoring strategies (e.g., the frequency of surveillance biopsy and the need for PSA monitoring), and triggers for intervention (e.g., what extent of tumor-grade progression is acceptable). Whether the tailoring of screening according to race, polygenic risk scores, or other factors results in improved outcomes is unknown.

GUIDELINES

Table 2 summarizes the guidelines of several professional organizations with regard to prostate cancer screening.[25,29,51-56] Similar to the present recommendations, most recommend some form of shared decision making, although the recommendations vary in the suggested age range for screening and the frequency of screening.

CONCLUSIONS AND RECOMMENDATIONS

For the 60-year-old man in the vignette, shared decision making regarding prostate cancer screening should be pursued. Discussion is warranted regarding the benefits and risks of screening, the potential pathways after a positive screen (relating to both the biopsy and treatment, if the biopsy is positive), the patient's level of risk, and his attitudes and preferences.

We recommend the use of a decision aid to facilitate shared decision making; culturally tailored tools should be considered, especially for non-Hispanic Black men, given the higher prostate cancer mortality in that population and the inclusion of few Black men in major screening trials. He should receive counseling that screening, if pursued, is not a one-time test but instead

Table 1. Elements of Shared Decision Making in Screening for Prostate Cancer.[29,42-44]☆

Category and Components	Details
Screening test: PSA test positivity	Approximately 8% (with 4 ng per milliliter as the cutoff for positivity)[45]
Cancer risk: probability of prostate cancer diagnosis after positive screen	18% at baseline, 11% at postbaseline screen (diagnosis within 1 yr of screening; cutoff of 4 ng per milliliter)[45]
Potential benefits	
Prevention of death from prostate cancer	Among 1000 men invited to undergo screening, approximately 5 will die from prostate cancer and 1.3 will avoid death from prostate cancer owing to screening in the 13-year period after initial screening[24]
Reassurance regarding low risk	In men 55 to 59 years of age, a PSA level of <1 ng per milliliter is associated with an approximate 0.3% cumulative risk of lethal prostate cancer (death or metastatic disease) in the 15 years after screening[16]
Potential harms	
Overdiagnosis	In an 11-year period, prostate cancer will be diagnosed in approximately 96 of 1000 men, among whom overdiagnosis will occur in 23 to 42%[32,43]
Overtreatment and resulting complications	Of men in whom prostate cancer is diagnosed, approximately two thirds will initially receive active treatment (i.e., radical prostatectomy or radiation therapy) and approximately one third will receive active surveillance; of the latter, approximately half will progress to active treatment[24] Radical prostatectomy is associated with an elevated risk of erectile dysfunction and urinary incontinence[23] Radiotherapy is associated with an elevated risk of erectile dysfunction and impaired bowel function[23,33]
Likelihood of false positive test, further diagnostic testing (e.g., biopsy), and risk of biopsy complications	10–15% false positive rate after 3–4 screening rounds, including 5% rate of false positive screening results that lead to subsequent negative biopsy[29] Risk of bleeding and infection with biopsy and 1–3% risk of hospitalization[31]
Personal risk	
Age[1]	50–64 yr: incidence, 253 per 100,000 person-yr; mortality, 9 per 100,000 person-yr 65–74 yr: incidence, 735 per 100,000 person-yr; mortality, 54 per 100,000 person-yr ≥75 yr: incidence, 558 per 100,000 person-yr; mortality, 224 per 100,000 person-yr
Race	Incidence among Black men is 1.7 times as high as that among non-Black men, and mortality among black men is 2.1 times as high as that among non-Black men[1]
Family history of prostate cancer	Incidence among persons with a family history of prostate cancer is 2.5 times as high as that among those with no family history of the disease[46]
Attitudes and preferences: personal assessment of the relative importance of potential benefits and harms	Benefits: prostate cancer ruled out, risk of dying from prostate cancer reduced Harms: treatment or periodic surveillance testing for a cancer that may never have caused any symptoms, with possible associated complications; an unnecessary prostate biopsy in men without cancer, with possible associated complications
Next-step options after confirmed positive PSA test: decisions on biopsy and treatment	Triage tests may allow the patient to avoid or defer the need for biopsy, with a small risk of missed clinically significant disease[34] The use of MRI-guided biopsy can increase detection of clinically significant disease but with some risk of overdiagnosis[37] In low-risk disease, active surveillance, involving periodic PSA tests and biopsies, may provide for avoidance of or delay in the need for curative treatment, with a possible small increased risk of metastatic progression or death from prostate cancer[27]

* PSA denotes prostate-specific antigen.

Table 2. U.S. and Selected Other Guidelines on Screening for Prostate Cancer.*

Organization and Recommendations	Population	Screening Interval	Comment
U.S. Preventive Services Task Force[24]			
Discuss the harms and benefits of PSA screening with patient	Age 55–69 yr	Not addressed	Grade C recommendation (at least moderate certainty that the net benefit is small)
No screening	Age ≥70 yr	NA	Grade D recommendation
National Comprehensive Cancer Network[51]			
Discuss risks and benefits to early detection of prostate cancer	Average risk, age 45–75 yr; high risk, age 40–75 yr†	2–4 yr with PSA level of <1 ng/ml); 1–2 yr with PSA level of ≥1 ng/ml	
No screening	Age >75 yr	NA	
American Urological Association[29]			
Shared decision making	Age 55–69 yr	2 yr	Moderate strength of evidence
No routine screening	Age 40–54 yr or ≥70 yr	NA	Weak strength of evidence
American Academy of Family Physicians[52]			
Shared decision making	Age 55–69 yr	≥2 yr	Grade C recommendation (selective offering based on professional judgment and patient preferences)
No screening	Age ≥70 yr	NA	
American Cancer Society: discuss screening[53]	Age ≥50 yr‡; age ≥45 yr for non-Hispanic Black men or men with a first-degree relative with prostate cancer that was diagnosed by age 65 yr‡	2 yr with PSA level of <2.5 ng/ml; 1 yr with PSA level of ≥2.5 ng/ml	
EAU–EANM–ESTRO–ESUR–SIOG[56]			
Individualized, risk-adapted strategy for screening	Life expectancy at least 10–15 yr	2 yr for men at elevated risk according to PSA level and age; 8 yr for men at lower risk	Weak recommendation
No screening without counseling regarding potential risks and benefits	NA	NA	Strong recommendation
Canadian Task Force on Preventive Health Care: no screening[54]	NA	NA	Strong recommendation for men <55 yr or ≥70 yr of age; weak recommendation for men 55–69 yr of age
Japan Urological Association: screening[55]	Age ≥50 yr; age ≥40 yr with family history	3 yr with PSA level of <1 ng/ml; 1 yr with PSA level of ≥1 ng/ml	Recommendation that fact sheets be provided that include important issues regarding prostate cancer

* EANM denotes European Association of Nuclear Medicine, EAU European Association of Urology, ESTRO European Society for Therapeutic Radiology and Oncology, ESUR European Society of Urogenital Radiology, NA not applicable, and SIOG International Society of Geriatric Oncology.
† The high-risk population includes non-Hispanic Black men and men with either a family history suggestive of prostate cancer or with certain germline mutations.
‡ Recommendation applies to men with a life expectancy of at least 10 years.

should be performed periodically (but generally not more frequently than every 2 years).

The opinions expressed by the authors in this article are their own, and this material should not be interpreted as representing the official viewpoint of the Department of Health and Human Services, the National Institutes of Health, or the National Cancer Institute.

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