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PSA cancer screening: A case for shared decision-making

Whether to screen for prostate cancer using PSA testing is a difficult decision for many men. Here's the information you need to help them make an educated choice.

PRACTICE RECOMMENDATIONS

› *Recommend individualized decision-making to men ages 55 to 69 years after discussing the potential benefits and risks of prostate-specific antigen (PSA)-based screening.* (B)

› *Do not use a PSA-based screening method for prostate cancer in men ages < 50 years or > 70 years or men with a life expectancy < 10 years.* (C)

› *Do not routinely recommend PSA-based screening to men with a family history of prostate cancer or to men who are African American.* (C)

Strength of recommendation (SOR)

(A) Good-quality patient-oriented evidence

(B) Inconsistent or limited-quality patient-oriented evidence

(C) Consensus, usual practice, opinion, disease-oriented evidence, case series

Prostate cancer is the most frequently diagnosed cancer in men and the third leading cause of cancer death in men worldwide.[1] An estimated 174,650 new cases are diagnosed each year in the United States; 31,620 American men die annually from the disease.[2] Although prostate cancer can be a serious disease, many men do not die from it. In fact, 2.9 million men who were diagnosed with prostate cancer at some point are alive today.[3]

Risk factors. Prostate cancer develops mainly in men ages ≥ 65 years and rarely occurs before age 40. In addition to age, family history and African American ethnicity are the major nonmodifiable risk factors for prostate cancer.[4] From the 1970s to the most recent statistical analysis of the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program, African American men have continued to have significantly higher incidence of, and mortality rates from, prostate cancer than their European American counterparts. African American men are also more likely than men of European ancestry to have aggressive prostate cancers.[5] Other risk factors include geographic location (higher risk in Northern Europe, North America, and Australia; lower risk in Asia, Africa, and South and Central America), mutations in the *BRCA*2 gene, and hereditary non-polyposis colon cancer syndrome.[4]

Prostate-specific antigen (PSA) was first used as a screening tool for prostate cancer in 1991.[6] Prostate cancer incidence, especially organ-confined disease, has dramatically increased since then.[7] PSA testing has a low sensitivity and specificity for the detection of prostate cancer, and there is no clear threshold at which biopsy can or should be offered. The most commonly used cutoff value of 4 ng/mL has a false-positive rate of about 70%.[8]

Benign prostatic conditions such as hypertrophy and infection can elevate PSA levels. In addition, the PSA test does not distinguish between aggressive and slow-growing cancers, and about 15% of patients with prostate cancer have a normal PSA level.[9]

TABLE 1

Recommendations for prostate cancer screening by various organizations[9,12-14]

Organization	Year updated	Screening age (y)	Screening of patients at high risk	Screening interval	PSA level for biopsy
US Preventive Services Task Force[14]	2018	Shared decision-making for patients 55-69	None specified	None specified	None specified
American Cancer Society[12]	2010	Begin at age 50 in those with life expectancy > 10 y	Begin at age 40 in those with life expectancy > 10 y	Annual if PSA > 2.5 ng/mL	Select patients if PSA > 2.5 ng/mL; most patients if PSA > 4 ng/mL
American Urological Association[13]	2013	55-69	40-69	Every 2 y	None specified
American College of Physicians[9]	2013	50-69	40-69	Annual if PSA > 2.5 ng/mL	None specified

PSA, prostate-specific antigen.

A word about the digital rectal exam. While PSA testing has been the mainstay of prostate cancer screening, a few studies have included digital rectal exam (DRE) in their protocols. Data from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial showed that DRE captured an additional 2% of men with prostate cancer in the setting of a normal PSA test result.[10] In the Rotterdam arm of the European Randomized Study of Screening for Prostate Cancer (ERSPC) trial, the overall detection rate for prostate cancer was found to be better when DRE was combined with PSA and prostate biopsy than when DRE was used alone (4.5% vs 2.5%).[11] Nevertheless, generally speaking, DRE can be omitted in the era of PSA screening.

Screening guidelines vary

Recommendations for prostate cancer screening vary by organization and are summarized in **TABLE 1**.[9,12-14] In 2012, the US Preventive Services Task Force (USPSTF) recommended against PSA-based screening for prostate cancer (Category D).[15] In 2018, USPSTF provided an update with a new recommendation that clinicians inform men ages 55 to 69 years about the potential benefits and harms of PSA-based screening (Category C).[14] The USPSTF continues to recommend against PSA-based screening for men ages ≥ 70 years (Category D).[14]

Does PSA-based screening improve patient-centered outcomes?

Several randomized controlled trials (RCTs) such as the Quebec Prospective Randomized Controlled Trial,[16] the Norrköping Sweden Study,[17] ERSPC,[11] and PLCO[10] have been conducted to assess the benefits of PSA testing. PLCO and ERSPC have contributed significantly to our understanding of prostate cancer screening even though their 13-year follow-up results are conflicting (**TABLE 2**).[10,11,18]

In the ERSPC 13-year follow-up publication, the authors concluded that a substantial reduction in prostate cancer mortality is attributable to testing with PSA.[18] Despite limitations in the study design (eg, France entered after 2 years, screening intervals varied between 2 and 4 years, biopsy indications varied, and screening was discontinued at different times), PSA screening detected more prostate cancer than was detected in the control arm (10.2% vs 6.8%).

In the initial 11 years of follow-up, the study group experienced a 21% reduction in prostate cancer mortality, even though the absolute decrease ranged from only 0.6% (545 per 89,352) to 0.5% (355 per 72,891). The updated absolute risk reduction of death from prostate cancer at 13 years of follow-up showed a larger benefit: 0.11 per 1000 person-years or 1.28 per 1000 men randomized, which is equivalent to 1 prostate cancer death averted per 781 (95% confidence interval

TABLE 2

Follow-up results of the PLCO and ERSPC trials[10,11,18]

	PLCO	ERSPC
Number	76,685 men	182,000
Age (y)	55-74	55-69
Follow-up (y)	13	13
Enrollment	1993-2006	1993-2005
Contamination of control group	40%-52% during study + 45% prestudy (85%)	24% in Rotterdam cohort
PSA threshold	Community standard for biopsy was applied in various centers (in general > 4 ng/mL)	≥ 3 ng/mL
Screening interval	1 y (first 6 y)	4 y
Biopsy results	Mostly stage 2 in both arms	Mostly stage 1 in both arms
Mortality	Low mortality both arms 3.7 (intervention) and 3.4 (control)/10,000 person-years	21% reduction in screened group; Goteborg arm 44% with 14 years' follow-up

ERSPC, European Randomized Study of Screening for Prostate Cancer; PLCO, Prostate, Lung, Colorectal, and Ovarian (Cancer Trial); PSA, prostate-specific antigen.

TABLE 3

Mortality among participants in PIVOT[24]

	Radical prostatectomy 20-year follow-up	Observation 20-year follow-up	*P* value
Overall mortality	61.3%	66.8%	.06
Overall prostate cancer mortality	7.4%	11.4%	.06

PIVOT, Prostate Cancer Intervention vs Observation Trial.

[CI], 490-1929) men invited for screening, or 1 per 27 (17-66) additional prostate cancers detected.

The PLCO trial did not show any significant difference in prostate cancer detection (11.1% screened vs 9.9% control), and there was no improvement in prostate cancer mortality (3.7 vs 3.4 death per 10,000 person-years).[10] However, the PLCO trial suffered from issues of contamination, which may have influenced the overall results. About 52% of men in the control (usual care) group received a PSA test at some point during the study. And more than two-thirds of the men who had a prostate biopsy because of a positive PSA test did not have prostate cancer.

Community standards for the PSA threshold for biopsy were applied in various centers (> 4 ng/ml in general) in PLCO, whereas in ERSPC, a cut-off PSA value ≥ 3 ng/mL was used for biopsy. Because of the lower PSA threshold, ERSPC may have identified cancers that would have had good outcomes without any intervention.

The harms of PSA screening

While it is unclear whether PSA screening results in any improvement in patient-centered outcomes, it does lead to downstream intervention due to overdiagnosis, which precipitates unnecessary anxiety, biopsies, and overtreatment (eg, excess radiation, overuse of androgen deprivation therapy).[19] Biopsies carry the risk of hematuria (22.6%), hematospermia (50.4%), and urinary tract infection.[20] Data from SEER-Medicare showed that prostate biopsy was associated with a 2.65-fold increased risk of hospitalization within 30 days of the procedure compared to a control population.[21]

Overdiagnosis leads to overtreatment of low-risk prostate cancer. Both traditional treatment options for prostate cancer—radical prostatectomy and radiotherapy—are associ-

TABLE 4

Treatment outcomes among participants in the SPCG-4 trial[25]

	Radical prostatectomy 18-year follow-up (%)	Watchful waiting 18-year follow-up (%)
Anxiety	43	43
Erectile dysfunction	84	80
Urinary leakage	41	11
Death	56.1	68.9
Number needed to treat	8	

SPCG-4, Scandinavian Prostate Cancer Group Study Number 4.

TABLE 5

Adverse effects among participants in ProtecT[22]

	At 12 months of follow-up (%)			At 72 months of follow-up (%)		
	Active monitoring	**Surgery**	**Radiotherapy**	**Active monitoring**	**Surgery**	**Radiotherapy**
Erectile dysfunction (Baseline 33%)	51	85	62	70	83	73
Urinary incontinence (Baseline 1%)	4	26	4	8	17	4

ProtecT, Prostate Testing for Cancer and Treatment Trial.

ated with urinary incontinence, erectile dysfunction, and issues with bowel function.[22,23]

The Prostate Cancer Intervention vs Observation Trial (PIVOT),[24] the Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4),[25] and the Prostate Testing for Cancer and Treatment (ProtecT) trial,[22,23] are the major RCTs that looked at the outcomes of treatment modalities for localized prostate cancer in the modern era of PSA testing.

PIVOT compared passive observation with radical prostatectomy.[24] After 20 years of follow-up on 731 patients, the researchers concluded that radical prostatectomy did not reduce all-cause or prostate cancer–related mortality (**TABLE 3**).[24]

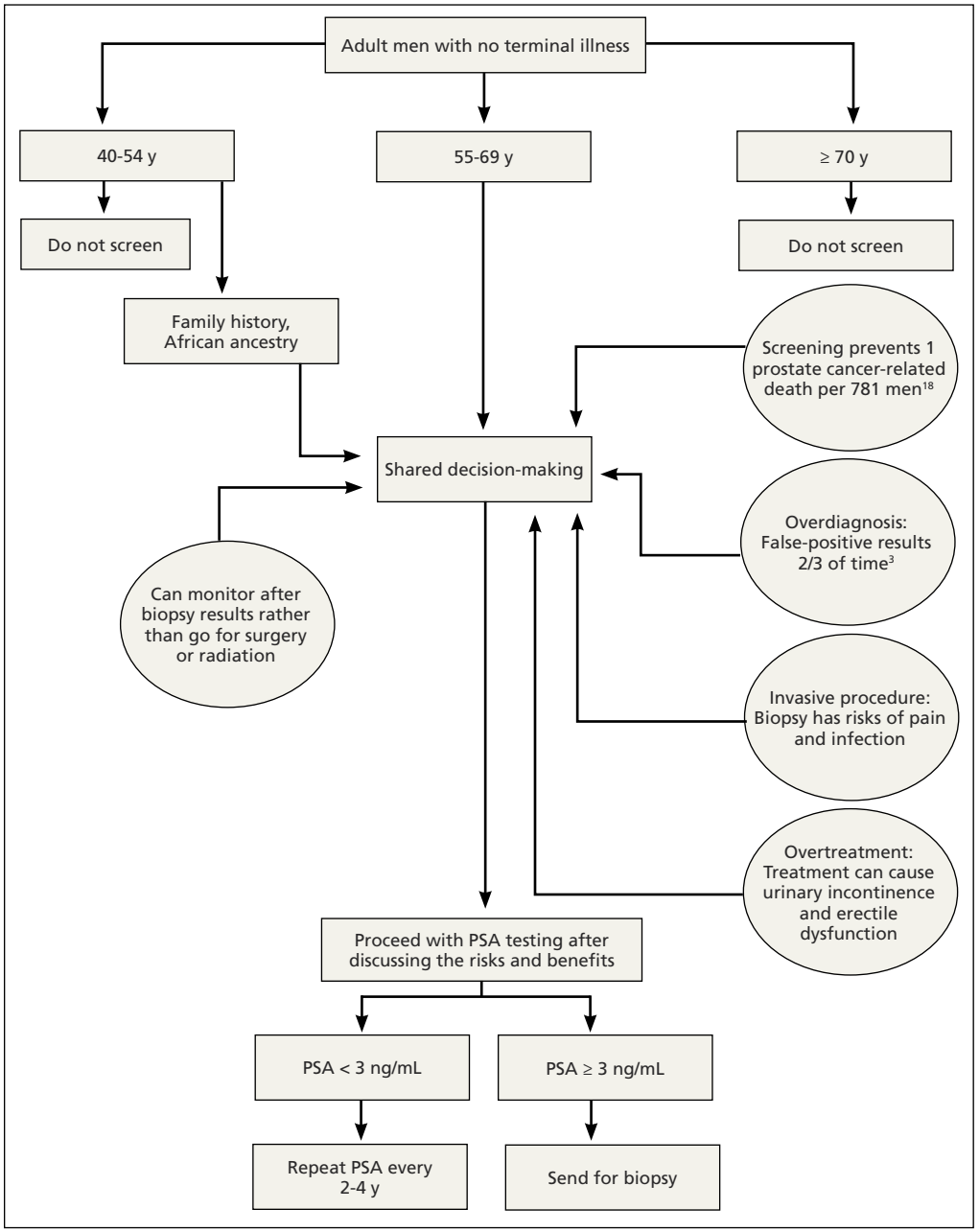
SPCG-4 showed survival benefits for men who underwent radical prostatectomy compared with men in a watchful waiting group, but only 5% of the study cohort had cancer detected by PSA screening (**TABLE 4**).[25] The rest had either palpable tumors or symptoms of a tumor.

ProtecT, which followed patients with localized prostate cancer for more than 10 years, compared the outcomes and adverse effects of active surveillance, radical prostatectomy, and radiotherapy.[23] Prostate cancer–specific mortality was low irrespective of the treatment,[23] and there was no significant difference in all-cause mortality or prostate cancer–specific mortality between the 3 treatment groups.[23] The active surveillance group had considerably fewer adverse events.[22,23] The incidence rates of erectile dysfunction and urinary incontinence at the 1- and 6-year follow-up marks are outlined in **TABLE 5**.[22]

The purpose of active monitoring is to minimize overtreatment by avoiding immediate radical intervention. Radical treatments with curative intent can be undertaken at any point while patients are being actively monitored. It is important to note that the active monitoring that took place in ProtecT[23] was very different from the passive surveillance of PIVOT[24] and SPCG-4.[25] In ProtecT, once an elevated serum PSA level was noted, PSA levels were monitored every 3 months in the first year and every 6 to 12 months thereafter.[23] Triggers to reassess patients and consider a change in clinical management were based largely on changes in PSA levels. Participants with an increase of at least 50% in PSA level during the previous 12 months were offered either continued monitoring or treatment after further testing.

FIGURE 1

Using shared decision-making when considering PSA screening[3,18]



PSA, prostate-specific antigen.

Although current guidelines regarding PSA screening differ by organization, generally speaking, PSA screening should be offered only to men with a life expectancy > 10 years.

Making individualized decisions about prostate cancer screening

Traditionally, the goal of cancer screening has been to maximize the number of people screened. Generally, the information provided to patients about cancer screening emphasizes the benefits and minimizes the harms. Recently, however, there has been a shift in communication about cancer screening with the emphasis now being placed on informed decision-making and encouraging patients to

make individual decisions about screening participation.[26]

The treatment option of active surveillance, with its lower incidence of adverse outcomes, is an important reason for patients to make individualized decisions about prostate cancer screening.

Another reason relates to 5-alpha-reductase inhibitors. Although their role in the management of prostate cancer is currently not well defined, a reduction of almost 25% in the risk of prostate cancer and improvement in the performance of PSA has been reported.[27]

And yet another reason is that there are alternate strategies to manage the majority of patients who have been diagnosed with low-risk disease through transrectal ultrasound biopsy. The ERSPC study mentions multiparametric magnetic resonance imaging combined with targeted biopsy to identify high-grade disease.[28,29] Genetic and epigenetic assays of the biopsied tissue can help grade disease based on aggressiveness.[30] Transperineal mapping biopsy using a mapping software program can identify specific disease sites within the prostate gland, so that patients can be offered the option of targeted therapy.[30]

The PSA test has low sensitivity and specificity and lacks a clear cut-off value that warrants prostate biopsy.

Applying shared decision-making to prostate cancer screening

Balancing errors of omission with errors of commission is challenging. Shared decision-making (SDM) is an approach whereby clinicians and patients share the best available evidence when faced with the task of medical decision-making and in which patients are supported while they consider their options and achieve their preferences.[31] SDM is well supported by evidence from a number of RCTs and results in increased knowledge, involvement, and confidence on the part of patients.[32] An individualized approach using the schematic diagram (**FIGURE 1**[3,18]) may be helpful.

Barriers to SDM success. Many factors can interfere with the success of SDM including limited or poor communication; lack of time during busy office visits; and patients' cultural, informational, and/or emotional needs. To improve patient-centered communication, we can: (1) make information understandable and available to patients and families; (2) prioritize training in communication; (3) use decision aid tools to facilitate communication; and (4) work to improve the payment model to incentivize patient-centered communication. Tools that facilitate SDM include videotapes, patient group discussions, brief scripts read to patients, and informational pamphlets. One such tool is the American Society for Clinical Oncology's decision aid tool for PSA testing.[33]

Limited knowledge among patients. Decisions regarding treatment among men diagnosed with localized prostate cancer can be difficult because there are several treatment options with similar prognoses, but there are differences in adverse effects. One population-based cohort study of men with newly diagnosed localized prostate cancer found that most men had significant knowledge deficits regarding the survival benefits of the 2 major treatment options—surgery and radiation.[34] In a large population-based study, 38% of men with localized prostate cancer reported receiving help from their primary care providers in the decision-making process for treatment.[35]

Learning to employ SDM. Elwyn et al proposed a 3-step model to incorporate SDM into clinical practice.[31] They described key steps that include: choice talk (making sure patients are informed about the reasonable options), option talk (providing more detailed information about the options), and decision talk (supporting the work of patients considering their preferences and deciding what is best). Properly employing these methods requires training using simulations.[31]

The bottom line

Although current guidelines regarding PSA screening differ by organization, generally speaking PSA screening should be offered only to men with a life expectancy > 10 years. The PSA test has low sensitivity and specificity and lacks a clear cut-off value that warrants prostate biopsy. Men who choose to have PSA testing increase their chances of detecting prostate cancer, but most prostate cancers are slow growing and do not cause

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death. The decision to undergo PSA screening should be made by both the provider and the patient, after a discussion of the limited benefits and associated harms. The interval of follow-up screening may vary from 2 to 4 years depending on patient age, level of PSA, and whether a patient is taking medications such as 5-alpha-reductase inhibitors. JFP

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