

Screening for Prostate Cancer: A Guidance Statement From the Clinical Guidelines Committee of the American College of Physicians

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Description: Prostate cancer is an important health problem in men. It rarely causes death in men younger than 50 years; most deaths associated with it occur in men older than 75 years. The benefits of screening with the prostate-specific antigen (PSA) test are outweighed by the harms for most men. Prostate cancer never becomes clinically significant in a patient's lifetime in a considerable proportion of men with prostate cancer detected with the PSA test. They will receive no benefit and are subject to substantial harms from the treatment of prostate cancer. The American College of Physicians (ACP) developed this guidance statement for clinicians by assessing current prostate cancer screening guidelines developed by other organizations. ACP believes that it is more valuable to provide clinicians with a rigorous review of available guidelines rather than develop a new guideline on the same topic when several guidelines are available on a topic or when existing guidelines conflict. The purpose of this guidance statement is to critically review available guidelines to help guide internists and other clinicians in making decisions about screening for prostate cancer. The target patient population for this guidance statement is all adult men.

Methods: This guidance statement is derived from an appraisal of available guidelines on screening for prostate cancer. Authors searched the National Guideline Clearinghouse to identify prostate cancer screening guidelines in the United States and selected 4

developed by the American College of Preventive Medicine, American Cancer Society, American Urological Association, and U.S. Preventive Services Task Force. The AGREE II (Appraisal of Guidelines, Research and Evaluation in Europe) instrument was used to evaluate the guidelines.

Guidance Statement 1: ACP recommends that clinicians inform men between the age of 50 and 69 years about the limited potential benefits and substantial harms of screening for prostate cancer. ACP recommends that clinicians base the decision to screen for prostate cancer using the prostate-specific antigen test on the risk for prostate cancer, a discussion of the benefits and harms of screening, the patient's general health and life expectancy, and patient preferences. ACP recommends that clinicians should not screen for prostate cancer using the prostate-specific antigen test in patients who do not express a clear preference for screening.

Guidance Statement 2: ACP recommends that clinicians should not screen for prostate cancer using the prostate-specific antigen test in average-risk men under the age of 50 years, men over the age of 69 years, or men with a life expectancy of less than 10 to 15 years.

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Although 1 in 6 men (16.7%) will receive a diagnosis of prostate cancer in their lifetime (1), only 2.9% will eventually die of the disease (2). The proportion of men who are diagnosed with prostate cancer but never have associated clinical symptoms is difficult to estimate, but it may range from 23% to 66% (3). Among cancer-related deaths in men, prostate cancer is the second-leading cause (4), representing 11.2% of such deaths (5). An estimated 2.3 million Americans have prostate cancer (5). In 2012, approximately 241 000 men are expected to be diagnosed with prostate cancer and 28 000 are expected to die of it (6).

The purpose of this guidance statement is to critically review the available guidelines developed in the United States to help guide internists and other clinicians in making decisions about screening for prostate cancer. The target patient population for this guidance statement is all adult men. The 2 tests generally used for screening and

discussed in this guidance statement include the prostate-specific antigen (PSA) test and digital rectal examination (DRE). The PSA test is more sensitive than DRE, and no screening trials have evaluated the utility of DRE alone. Clinical trials of PSA-based screening have focused on absolute PSA thresholds to guide biopsy decisions. Although various strategies can be used to try to improve the diagnostic performance of the PSA test, such as PSA velocity (change in PSA over time), PSA density (PSA per unit

See also:

Print

Summary for Patients. I-28

Web-Only

CME quiz

* This paper, written by Amir Qaseem, MD, PhD, MHA; Michael J. Barry, MD; Thomas D. Denberg, MD, PhD; Douglas K. Owens, MD, MS; and Paul Shekelle, MD, PhD, was developed for the Clinical Guidelines Committee of the American College of Physicians. Individuals who served on the Clinical Guidelines Committee from initiation of the project until its approval were: Paul Shekelle, MD, PhD (*Chair*); Roger Chou, MD; Molly Cooke, MD; Paul Dallas, MD; Thomas D. Denberg, MD, PhD; Nick Fitterman, MD; Mary Ann Forcica, MD; Robert H. Hopkins Jr., MD; Linda L. Humphrey, MD, MPH; Tanveer P. Mir, MD; Douglas K. Owens, MD, MS; Holger J. Schünemann, MD, PhD; Donna E. Sweet, MD; David S. Weinberg, MD, MSc; and Timothy Wilt, MD, MPH. Approved by the ACP Board of Regents on 16 April 2012.

volume of the prostate gland), or free PSA, these strategies have not been evaluated in clinical trials of screening and are not discussed in this guidance statement.

METHODS

When several guidelines are available on a topic or existing guidelines conflict, ACP believes that it is more useful to provide clinicians with a rigorous review of the available guidelines rather than develop a new guideline on the same topic. Thus, the ACP Clinical Guidelines Committee developed this guidance statement by assessing current guidelines developed by other organizations on screening for prostate cancer.

We began by searching the National Guideline Clearinghouse for guidelines on screening for prostate cancer (August 2012). We reviewed the titles and abstracts of each document. We excluded those that restated guidelines from other organizations. We selected 4 prostate cancer screening guidelines developed in the United States: American College of Preventive Medicine (ACPM) (7), American Cancer Society (ACS) (8), American Urological Association (AUA) (9), and U.S. Preventive Services Task Force (USPSTF) (10). These guidelines were reviewed independently by 4 coauthors. We followed the AGREE II (Appraisal of Guidelines, Research and Evaluation in Europe) collaboration method to produce this guidance statement (11). The AGREE II instrument asks 23 questions in 6 domains: scope and purpose, stakeholder involvement, rigor of development, clarity and presentation, applicability, and editorial independence. The authors selected 1 guideline to calibrate their scores on the 6 domains of the AGREE II instrument. The authors then scored each guideline independently, and the scores were compared (Table 1). Although total quantitative scores varied, the qualitative assessment of guideline quality was consistent among the 4 reviewers; indeed, the overall rankings of the quality of the guidelines were similar.

Details of the ACP guidance statement development process can be found in ACP's methods paper (12).

SUMMARY AND EVALUATION OF REVIEWED GUIDELINES ACPM (2008)

ACPM concludes that there is insufficient evidence to recommend routine population screening with digital rectal examination or prostate-specific antigen.

ACPM concludes that clinicians caring for men, especially African American men and those with a family history of prostate cancer, should provide information about potential benefits and risks of prostate cancer screening, and the limitations of current evidence for screening in order to maximize informed decision-making. While the usual age for prostate cancer screening is between 50–70 years in average risk men, it has been suggested that those who are at high risk may

benefit from earlier screening beginning at age 45, while even higher risk men (those with two or more first-degree relatives with prostate cancer before age 65) should be screened at age 40.

Comments

The stated purpose of the ACPM guideline is to review the efficacy of DRE and the PSA test for prostate cancer screening. It includes a very helpful discussion on PSA screening criteria and cutoff PSA levels and acknowledges high false-positive and false-negative rates associated with the PSA test and weak evidence for DRE. The guideline emphasizes a shared decision-making approach for screening and discusses tools to support discussion with patients. However, many details about the literature review and guideline development process are not presented. In addition, the guideline was published before the PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial and ERSPC (European Randomized Study of Screening for Prostate Cancer) results were published. The guideline does not address the upper age limit for prostate screening or the issue of screening younger men in a high-risk group.

ACS (2010 Update)

ACS recommends that asymptomatic men who have at least a 10-year life expectancy have an opportunity to make an informed decision with their health care provider about screening for prostate cancer after they receive information about the uncertainties, risks, and potential benefits associated with prostate cancer screening.

ACS recommends that prostate cancer screening should not occur without an informed decision-making process. Men at average risk should receive this information beginning at age 50 years. Men in higher risk groups should receive this information before age 50 years. Men should either receive this information directly from their health care providers or be referred to reliable and culturally appropriate sources.

Comments

The stated goal of the ACS guideline is to focus on evidence related to the early detection of prostate cancer, test performance, harms of therapy for localized prostate cancer, and the importance of shared and informed decision making in prostate cancer screening. The ACS acknowledges the unclear role for DRE screening and recommends PSA screening with or without DRE, adding that the additional value of DRE is likely low. The guideline acknowledges the limitations of the evidence and describes a shared decision-making approach, which makes it very helpful for clinicians. It also has a clear cutoff age to start screening discussions with patients (age 50 years for average-risk men).

Table 1. Mean Guideline Scores and Scaled Domain Scores Across Domains of AGREE II Instrument*

Domain	ACS	AUA	USPSTF	ACPM
Scope and purpose				
1. The overall objective(s) of the guideline is (are) specifically described.	6	5	6	5
2. The health question(s) covered by the guideline is (are) specifically described.	6	6	6	5
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	6	5	7	4
Domain score	18	16	19	13
Scaled domain score, %	83	71	88	57
Stakeholder involvement				
4. The guideline development group includes individuals from all relevant professional groups.	5	5	4	2
5. The views and preferences of the target population (patients, public, etc.) have been sought.	3	2	4	2
6. The target users of the guideline are clearly defined.	3	6	6	2
Domain score	11	13	14	6
Scaled domain score, %	44	54	61	15
Rigor of development				
7. Systematic methods were used to search for evidence.	5	2	7	2
8. The criteria for selecting the evidence are clearly described.	4	1	7	2
9. The strengths and limitations of the body of evidence are clearly described.	4	2	7	2
10. The methods for formulating the recommendations are clearly described.	4	4	6	2
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	6	5	7	6
12. There is an explicit link between the recommendations and the supporting evidence.	5	4	7	3
13. The guideline has been externally reviewed by experts prior to its publication.	5	5	6	2
14. A procedure for updating the guideline is provided.	2	2	6	1
Domain score	35	24	51	18
Scaled domain score, %	56	33	90	21
Clarity of presentation				
15. The recommendations are specific and unambiguous.	7	5	7	6
16. The different options for management of the condition or health issue are clearly presented.	6	6	6	5
17. Key recommendations are easily identifiable.	6	6	7	5
Domain score	19	16	20	16
Scaled domain score, %	88	74	92	71
Applicability				
18. The guideline describes facilitators and barriers to its application.	6	2	4	3
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	6	2	4	6
20. The potential resource implications of applying the recommendations have been considered.	1	1	2	3
21. The guideline presents monitoring and/or auditing criteria.	1	2	2	2
Domain score	14	7	11	13
Scaled domain score, %	43	10	30	36
Editorial independence				
22. The views of the funding body have not influenced the content of the guideline.	2	3	6	2
23. Competing interests of guideline development group members have been recorded and addressed.	6	6	6	4
Domain score	8	9	12	6
Scaled domain score, %	50	54	81	31
Overall guideline assessment				
1. Rate the overall quality of this guideline.	5	3	6	3
2. I would recommend this guideline for use (please respond: yes, yes with modifications, or no).	4 yes	4 yes with modifications	2 yes; 2 yes with modifications	1 yes, 3 no

ACPM = American College of Preventive Medicine; ACS = American Cancer Society; AGREE = Appraisal of Guidelines, Research and Evaluation in Europe; AUA = American Urological Association; USPSTF = U.S. Preventive Services Task Force.

* Mean guideline scores across domains of the AGREE II instrument. Each question was rated on a Likert scale with a maximum of 7 points. The scores were averaged for each of the 4 reviewers. The scaled domain score is calculated as follows: (obtained score – minimum possible score) ÷ (maximum possible score – minimum possible score).

AUA (2009 Update)

AUA recommends that the decision to use PSA for the early detection of prostate cancer should be individualized. Patients should be informed of the known risks and the potential benefits.

AUA recommends that men who wish to be screened for prostate cancer should have both a PSA test and a DRE.

AUA recommends that early detection and risk assessment of prostate cancer should be offered to asymptomatic men 40 years of age or older who wish to be screened and have an estimated life expectancy of more than 10 years.

Comments

In addition to discussing the management and treatment of patients with prostate cancer, the goals of the AUA

guideline are to help clinicians understand the evidence for using the PSA test to evaluate men at risk for prostate cancer and provide guidance about how to discuss the risks and benefits of early detection with patients. The guideline acknowledges that evidence is lacking about the proportion of clinically significant prostate cancer that is detected with PSA testing. The guideline emphasizes the sensitivity and specificity of PSA testing in addition to age-specific reference ranges that should be considered when evaluating the results for serum PSA. It discusses the association between elevated serum PSA levels with common prostatic diseases, such as prostatitis, benign prostatic hyperplasia, and prostate cancer. The guideline notes the harms of screening. The AUA's recommendation to begin baseline testing at age 40 years is not based on data from clinical trials. In addition, the guideline does not specify a threshold PSA level to initiate further evaluation, making this guideline challenging to implement. The AUA guideline focuses on PSA screening but suggests that the addition of DRE to PSA screening may enhance prostate cancer detection and, therefore, recommends DRE in addition to PSA tests.

USPSTF (2012 Update)

USPSTF recommends against PSA-based screening for prostate cancer.

Comments

The USPSTF recently updated its prostate cancer screening guideline in 2012. The purpose of the USPSTF guideline is to evaluate the evidence on the benefits and harms of detection and early treatment of prostate cancer to make recommendations about screening for prostate cancer using the PSA test. The guideline uses rigorous methods, evaluates evidence through a systematic literature review, and links the evidence and recommendations. The target population for the recommendation is all asymptomatic men regardless of age or risk factors. The guideline describes the primary benefit of prostate cancer screening being the reduction of deaths. It concluded that the benefits of PSA-based screening do not outweigh the harms and recommends against screening. The USPSTF states that physicians should not offer or order PSA screening unless they are prepared to engage in shared decision making that enables an informed choice by the patients with full understanding of the possible benefits and risk for harm. The harms of screening were identified as many false-positive results (80% when the PSA cutoff is between 2.5 and 4.0 $\mu\text{g/L}$); negative psychological effects, such as persistent worry; unnecessary biopsies; and overdiagnosis of tumors that may not become clinically significant in a patient's lifetime. The USPSTF also identified harms related to treatment of screen-detected cancer, such as surgery, radiation, and androgen-deprivation therapy. They also considered harms related to treatment of overdiagnosed cancer because the rate of treatment of screen-detected cancer is

high. The USPSTF did not address use of DRE in the guideline.

SUMMARY

In light of current evidence, making decisions about screening for prostate cancer is a complex issue. The 2012 USPSTF guideline concluded that the harms of prostate cancer screening outweigh the benefits for most men and recommended against screening using the PSA test. The other guidelines we evaluated concluded (at the time of the evidence review) that it is uncertain whether the benefits of routine screening using the PSA test outweigh the harms. In addition, all of the guidelines acknowledged that the benefits of early detection with the PSA test must be weighed against the serious harms, such as a false-positive rate of 70% for PSA levels greater than 4.0 $\mu\text{g/L}$ (8), and the harms associated with treating men with cancer that would not have become clinically evident in their lifetime. The ACPM, ACS, and AUA guidelines recommend using a shared decision-making approach. However, the recommendations about shared decision making vary among the guidelines. The ACS and AUA recommend not to screen unless an informed decision-making approach has been used. The ACPM does not explicitly emphasize shared decision making to the same extent as the ACS and AUA. Clinicians should help men understand the potential benefits of early detection; the strengths and weaknesses of the various screening tests, such as the PSA test; and the risks of treating cancer that is detected by screening. Although the USPSTF does not recommend screening with the PSA test, it does suggest that men who opt to be screened should only do so after being fully informed of the benefits and harms. Studies have shown that up to one third of men screened for prostate cancer were unaware that they were being tested, and many men who were aware that they were tested do not receive an adequate discussion of the benefits and harms of screening (13–15).

The primary benefit of reduction in mortality rates from PSA-based screening was assessed by 2 higher-quality trials, ERSPC and PLCO (16, 17). The ERSPC study, which used various screening intervals, showed an absolute reduction in deaths due to prostate cancer in men between 55 and 69 years of age (17), and an additional 2-year follow-up confirmed a reduction in deaths due to prostate cancer in the screened group (18). In the PLCO study, there was no mortality benefit because more deaths occurred in the screened group (50 deaths) than in the control group (44 deaths), but this difference was not statistically significant (16). A similar trend was seen after 13 years of follow-up (19). Both the ERSPC and PLCO trials included mostly white men, and hence, the results from these studies may not be as applicable to nonwhite men. PIVOT (Prostate Cancer Intervention Versus Observation Trial) (20) assessed treatment by randomly assigning men with local prostate cancer to radical prostatectomy or ob-

ervation. Many men treated for prostate cancer were screened with the PSA test. The trial found that prostatectomy did not reduce overall or prostate cancer deaths after 12-year follow-up. However, in a subgroup analysis, men with PSA levels greater than 10 $\mu\text{g/L}$ had a 13.2% reduction in all-cause mortality (hazard ratio, 0.67 [95% CI, 0.48 to 0.94]).

Clinically significant harms are associated with prostate cancer screening and treatment, including infections and urine retention resulting from biopsies, overdiagnosis, overtreatment, and downstream harms and costs associated with overtreatment (21). False-positive results also lead to anxiety. Whether the harms associated with treatment can be reduced by more selective treatment of men with low-risk cancer is debatable. However, epidemiologic data indicate that nearly 90% of men with screen-detected cancer receive treatment aimed at a cure (such as prostatectomy and radiotherapy) (22, 23) rather than observation or active surveillance.

Although the evidence is unclear about which PSA levels should warrant a consideration of continuing with ongoing monitoring or biopsy, most of the guidelines we evaluated, as well as the PLCO study, used 4.0 $\mu\text{g/L}$ as a threshold. Bacterial prostatitis or asymptomatic prostatic inflammation may cause the elevated PSA levels that generally return to baseline 6 to 8 weeks after symptoms resolve. This guidance statement recognizes that as many as 15% of men with PSA levels less than 4.0 $\mu\text{g/L}$ will have prostate cancer on biopsy and as many as 15% of those with cancer will have high-grade cancer as assessed by pathology. However, although the ERSPC trial used PSA thresholds that ranged between 2.5 and 4.0 $\mu\text{g/L}$, no evidence indicated that a biopsy-and-treat strategy based on lower PSA thresholds (such as 3.0 $\mu\text{g/L}$ or even 2.0 $\mu\text{g/L}$) will produce more benefits than higher thresholds and using a lower threshold will definitely result in more false-positive results. Therefore, on the basis of the limited evidence from current studies, it is reasonable to continue using the current most widely accepted PSA thresholds of 4.0 $\mu\text{g/L}$ or greater.

Evidence is mixed on whether DRE is beneficial alone or in combination with PSA screening. Prostate screening using DRE was not addressed by the USPSTF, but it was recommended in addition to PSA screening in the AUA guideline and as an option to use with PSA testing in the ACS guideline. The sensitivity and specificity of DRE screening are dependent on the examiner, and therefore, considerable variability can occur with this test. The ACS suggests that DRE can be helpful in deciding whether to do a biopsy in men with PSA levels between 2.5 and 4.0 $\mu\text{g/L}$.

The current evidence does not provide direction about the frequency of screening with the PSA test. Although many clinicians in the United States screen annually, the PLCO trial, which screened annually, found no benefit. In the only trial to report a reduction in prostate cancer–

specific mortality, most patients were screened every 4 years (range, 2 to 7 years) (17). Therefore, no evidence supports annual screening for prostate cancer. A recent modeling study showed that an aggressive screening strategy is associated with reduction in prostate cancer mortality but also results in major harms, such as unnecessary biopsies, diagnoses, and treatments (24). Screening older men (age >69 years) substantially increases overdiagnosis even though life expectancy is not affected in this age group. On the basis of the guidelines we reviewed, PSA levels of 2.5 $\mu\text{g/L}$ or greater may warrant annual evaluation in men who seek early diagnosis.

Asymptomatic men older than 75 years or those who have a life expectancy less than 10 years should not be offered prostate cancer screening in light of the substantial harms associated with prostate cancer screening and treatment relative to questionable benefits.

GUIDANCE STATEMENTS

Guidance Statement 1: ACP recommends that clinicians inform men between the age of 50 and 69 years about the limited potential benefits and substantial harms of screening for prostate cancer. ACP recommends that clinicians base the decision to screen for prostate cancer using the prostate-specific antigen test on the risk for prostate cancer, a discussion of the benefits and harms of screening, the patient's general health and life expectancy, and patient preferences. ACP recommends that clinicians should not screen for prostate cancer using the prostate-specific antigen test in patients who do not express a clear preference for screening.

Benefits and Harms of Screening (PSA Test and DRE)

The modest potential mortality benefit in 1 prostate cancer screening trial with the PSA test was limited to men between the age of 55 and 69 years. Data were insufficient to reach a conclusion about the benefits or harms of screening in men aged 50 to 54 years. However, because this group has a longer life expectancy, they have more potential for long-term net benefit. The ERSPC study, which screened men mostly with the PSA test, showed that 1410 men would need to be screened to prevent 1 death from prostate cancer (17). Evidence for the benefit of DRE screening is limited, and the PLCO trial, which included both PSA testing and DRE, showed no benefit. As far as mortality benefit is concerned, the evidence is inconsistent about whether screening reduces cancer-related death, and any absolute mortality risk reduction is probably small to none.

The harms of prostate cancer screening are substantial and include false alarms (suggesting that a patient may have cancer when he does not) related to high false-positive rates associated with DRE and especially the PSA test, overdiagnosis (that is, detecting cancer that will not cause future morbidity and mortality), high false-negative rates, anxiety, and discomfort. Positive screening results may lead to further testing, such as biopsies, which not only can be

Table 2. Free Decision Aids for Prostate Cancer Screening

Developer	Web Site
American Cancer Society	www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-024618.pdf
American Society of Clinical Oncology	www.asco.org/ASCOv2/Department%20Content/Cancer%20Policy%20and%20Clinical%20Affairs/Downloads/Guideline%20Tools%20and%20Resources/PSA/PSA%20PCO%20Decision%20Aid%207.16.12.pdf
The Prostate Cancer Research Foundation and European Randomized Study of Screening for Prostate Cancer	www.prostatecancer-riskcalculator.com
Mayo Clinic	www.mayoclinic.com/health/prostate-cancer/HQ01273

painful but can also lead to complications, such as infections, as well as overtreatment and the harms associated with it. In addition, currently available treatments are associated with harms, such as urinary, gastrointestinal, and sexual problems, as well as potential cardiovascular events and death. Data from PIVOT (20) showed that men who had radical prostatectomy had an 11% increased risk for urinary incontinence and a 37% increased risk for erectile dysfunction. Harms specific to DRE include discomfort and rectal bleeding.

Shared Decision-Making Approach

Clinicians should not screen for prostate cancer in men who do not wish to make the screening decision or do not express a clear preference about screening. However, some men still prefer to be screened because they may put more value on the possible small benefit and less value on the harms. Under these circumstances, shared decision making is important in making choices about prostate cancer screening. Clinicians should elicit patient preferences for screening during the shared decision-making process and document them in the medical record. It is important to educate the patient about the following points and document the conversation in the medical record:

1. Prostate cancer screening with the PSA test is controversial.
2. Screening with the PSA test can detect prostate cancer, but for most men, the chances of harm from screening with the PSA test outweigh the chances of benefit.
3. A small number of prostate cancer cases are serious and can cause death; however, the vast majority of prostate cancer is slow-growing and does not cause death.
4. Most men who choose not to have PSA testing will not be diagnosed with prostate cancer and will die of something else.
5. Patients who choose PSA testing are much more likely than those who decline testing to be diagnosed with prostate cancer.
6. The PSA test often does not distinguish between serious cancer and nonserious cancer. However, men with markedly elevated PSA levels (>10 µg/L) may have a reduced chance of dying from prostate cancer by having surgical treatment.
7. The small potential benefit of prostate cancer screening corresponds to preventing, at most, 1 death

caused by prostate cancer per 1000 men screened after 11 years of follow-up.

8. There are many potential harms of screening. There may be problems in interpreting test results: The PSA test result may be high because of an enlarged prostate but not because of cancer, or it may be low even though cancer is present. Prostate biopsy, if needed is also not free from risk. It involves multiple needles being inserted into the prostate under local anesthesia, and there is risk for infection or clinically significant bleeding and hospitalization (1.4%). If cancer is diagnosed, it will often be treated with surgery or radiation, which are associated with risks. There is a small risk for death with surgery, loss of sexual function (approximately 37% higher risk), and loss of control of urination (approximately 11% higher risk) compared with no surgery. These risks may vary depending on patient and surgeon characteristics and treatment method.

9. The PSA test is not “just a blood test.” It is a test that can open the door to more testing and treatment that a man may not actually want and that may actually harm him. A man’s chances of being harmed are much greater than his chances of benefiting from the PSA test. Thus, each man should have the opportunity to decide for himself whether to have the PSA screening test.

10. Studies are ongoing, so clinicians expect to learn more about the benefits and harms of screening, and recommendations may change over time. Men are also welcome to change their minds at any time by asking for screening that they have previously declined or discontinue screening that they have previously requested.

Although ACP did not evaluate the evidence on the reliability, validity, or benefits of using available decision aids, some examples are listed in Table 2.

It is important for clinicians to convey to patients who may want to be screened that evidence indicates, at best, small benefits as well as substantial harms. Men who do not have a clear preference for screening should not be screened, and this should be documented. Clinicians should help men judge the balance of benefits and harms and discuss whether the harms outweigh the potential reduction in prostate cancer mortality in their particular cases. To frame the discussion, clinicians can inform patients that the PSA test will increase their lifetime risk for prostate cancer from approximately 9% to 16% (5, 25).

Figure. The American College of Physicians guidance statement on screening for prostate cancer.



Summary of the American College of Physicians Guidance Statement on Screening for Prostate Cancer

Disease or Condition	Prostate cancer
Target Audience	Internists, family physicians, other clinicians
Target Patient Population	All men
Screening Tests	PSA and DRE
Interventions	Strategies to manage prostate cancer
Outcomes	Mortality and morbidity
Indications for Discussing Screening	Men between the age of 50 and 69 y Earlier age in men who are at increased risk for prostate cancer (African American race and a first-degree relative [father or brother] diagnosed with prostate cancer, especially before age 65 y)
Frequency of Screening	No clear evidence guides the periodicity or frequency of screening No clear evidence that PSA screening more frequently than every 4 y produces any additional benefit PSA levels of 2.5 µg/L or greater may warrant yearly evaluation
Benefits of Screening	Reduction in mortality
Harms of Screening	False alarms related to number of high false-positive results associated with DRE and especially PSA High false-negative rates Overdiagnosis (detection of cancer that is not destined to cause future morbidity and mortality) Overtreatment and associated harms, including bleeding, pain, and hospitalization Anxiety and discomfort Positive screening results may lead to further testing, such as biopsies, which not only can be painful but can also lead to complications, such as infections
Recommendations	<i>Guidance Statement 1: ACP recommends that clinicians inform men between the age of 50 and 69 years about the limited potential benefits and substantial harms of screening for prostate cancer. ACP recommends that clinicians base the decision to screen for prostate cancer using the prostate-specific antigen test on the risk for prostate cancer, a discussion of the benefits and harms of screening, the patient's general health and life expectancy, and patient preferences. ACP recommends that clinicians should not screen for prostate cancer using the prostate-specific antigen test in patients who do not express a clear preference for screening.</i> <i>Guidance Statement 2: ACP recommends that clinicians should not screen for prostate cancer using the prostate-specific antigen test in average-risk men under the age of 50 years, men over the age of 69 years, or men with a life expectancy of less than 10 to 15 years.</i> Prostate cancer screening with the PSA test is controversial.
Talking Points With Patients	PSA screening can detect prostate cancer, but for most men, the chances of harm from screening with the PSA test outweigh the chances of benefit. A small number of prostate cancer cases are serious and can cause death; however, the vast majority of prostate cancer is slow-growing and does not cause death. Most men who choose not to have PSA testing will not be diagnosed with prostate cancer and will die of something else. Patients who choose PSA testing are much more likely than those who decline PSA testing to be diagnosed with prostate cancer. The PSA test often does not distinguish between cancer cases that are serious and those cases that are not serious. However, men with markedly elevated PSA levels (>10 µg/L) may have a reduced chance of dying from prostate cancer by having surgical treatment. The small potential benefit of prostate cancer screening corresponds to preventing, at most, 1 death caused by prostate cancer per 1000 men screened after 11 y of follow-up. The potential harms of screening include: Problems interpreting test results: The PSA test result may be high because of an enlarged prostate but not because of cancer, or it may be low even though cancer is present. If a prostate biopsy is needed, it, too, is not free from risk—the biopsy involves multiple needles being inserted into the prostate under local anesthesia, and there is a risk for infection or significant bleeding as well as risk for hospitalization (1.4%). If cancer is diagnosed, it will often be treated with surgery or radiation, which are associated with risks. There is a small risk for death with surgery, loss of sexual function (approximately 37% higher risk), and loss of control of urination (approximately 11% higher risk) compared with no surgery. These risks may vary depending on patient and surgeon characteristics and treatment method. The PSA test is not “just a blood test.” It is a test that can open the door to more testing and treatment that a man may not actually want and that may actually harm him. A man's chances of being harmed are much greater than his chances of benefiting from the PSA test. Thus, each man should have the opportunity to decide for himself whether to have the PSA screening test. Studies are ongoing, so clinicians expect to learn more about the benefits and harms of screening, and recommendations may change over time. Men are also welcome to change their minds at any time by asking for screening that they have previously declined or discontinue screening that they have previously requested.

DRE = digital rectal examination; PSA = prostate-specific antigen.

Currently, the tradeoff between harms and benefits beyond 11 to 13 years of follow-up is unknown. Alternatively, although 3 in 100 men will die of prostate cancer (or 5 in 100 for African American men), this means that 97 in 100 men (or 95 in 100 African American men) will die of something else. Finally, although some men may avoid pain and discomfort commonly associated with advanced disease, this must be balanced against the possibility of incontinence, erectile dysfunction, and other side effects that result from certain forms of aggressive treatment.

The goal of screening for any disease is to identify an undiagnosed condition for which an effective treatment is available, and timely treatment can lead to improved clinical outcomes. Although the best treatment approach for prostate cancer is unknown, current management for prostate cancer includes active surveillance, radical prostatectomy, external beam radiation therapy, and brachytherapy. Research is needed to better identify cancer that is more likely to benefit from curative treatments, in which case benefits are more likely to outweigh harms.

High-Risk Patients

Screening in high-risk men has not been demonstrated to be associated with different outcomes than screening in average-risk men. Risks for prostate cancer include African American race and a first-degree relative diagnosed with prostate cancer, especially before age 65 years. Patients with such risks should receive information about the uncertainties, risks, and potential benefits associated with prostate cancer screening beginning at age 45 years. Shared decision making is important in making choices about prostate cancer screening in high-risk men as well. Men at appreciably higher risk (multiple family members diagnosed with prostate cancer before age 65 years) should receive this information beginning at age 40 years.

Frequency of Screening

Currently, no clear evidence is available to guide decisions about the periodicity or frequency of the evaluation of risk for prostate cancer or discussion about the benefits and harms. Considering the harms of screening and modest mortality benefit, increasing the interval between screening tests may reduce harms (10). The PLCO trial, which screened annually, found no benefit, whereas the ERSPC trial, in which most participants were screened every 4 years (range, 2 to 7 years), did find benefit, suggesting that longer intervals may be indicated.

Guidance Statement 2: ACP recommends that clinicians should not screen for prostate cancer using the prostate-specific antigen test in average-risk men under the age of 50 years, men over the age of 69 years, or men with a life expectancy of less than 10 to 15 years.

Increasing age or the presence of a chronic comorbid illness that affects life expectancy substantially limits the potential benefits of prostate cancer screening compared with harms. Evidence presented in the guidelines shows

substantial harms associated with prostate cancer screening and treatment relative to questionable benefits. Any benefit is even smaller in men older than 69 years because the cancer may not become clinically significant in their lifetime. For men younger than 50 years, the harms, such as erectile dysfunction and urinary incontinence, carry even more weight relative to any potential benefit. Hence, the harms of screening for prostate cancer outweigh the benefits in average-risk men younger than 50 years, men older than 69 years, or men who have a life expectancy less than 10 to 15 years. Therefore, clinicians should not screen men younger than 50 years, those aged 70 years or older, or men with substantial comorbid conditions and a life expectancy less than 10 to 15 years.

The **Figure** summarizes the guidance statements and clinical considerations for prostate cancer screening.

ACP HIGH-VALUE CARE ADVICE

High-value care reflects care for which the benefits are likely to outweigh the harms and costs associated with delivering such care. Screening with the PSA test is low-value care. The value of screening for prostate cancer in most cases is low, given that the chances of harm with screening outweigh the chances of benefit for most men and that the direct and indirect costs associated with biopsy, repeated testing, aggressive therapy, patient anxiety, and missed work are significant.

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Note: Clinical guidance statements are “guides” only and may not apply to all patients and clinical situations. Thus, they are not intended to override clinicians’ judgment. All ACP clinical guidance statements are considered automatically withdrawn or invalid 5 years after publication, or once an update has been issued.

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