Guidelines Being Compared:

1 American College of Physicians (ACP)

**Screening for prostate cancer: a guidance statement from the Clinical Guidelines Committee of the American College of Physicians.**

2013 Apr 01

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2 American Urological Association Education and Research, Inc. (Am Urol Assoc Edu Res)

**Early detection of prostate cancer: AUA guideline.**

2013 Apr 01

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# Areas of Agreement and Difference

A direct comparison of the recommendations presented in the above guidelines for prostate cancer screening is provided in the tables. The ACP guidance statement was developed from an appraisal of guidelines developed by other organizations on screening for prostate cancer. Additional details of this process are available in the **Methodology** section of this synthesis.

## Areas of Agreement

should not occur in the absence of an informed, shared decision-making process, and that the decision to initiate or continue PSA screening should reflect an explicit understanding of the possible benefits and harms, as well as patients' preferences and values.

## Areas of Difference

### Screening in Average-Risk, Asymptomatic Men

ACP and AUA take similar approaches to providing screening recommendations, with both providing guidance according to patient age. However, the age ranges for which screening is either not routinely recommended or explicitly recommended against differ somewhat. ACP recommends against PSA screening 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. The developer recommends that clinicians inform men between the **ages of 50 and 69 years** about the limited potential benefits and substantial harms of screening for prostate cancer, and that clinicians base the decision to screen for prostate cancer using the PSA 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 further recommends that clinicians should not screen for prostate cancer using the PSA test in men who do not wish to make the screening decision or do not express a clear preference for screening.

AUA also provides recommendations for screening according to age. The developer explicitly *recommends against* PSA screening in men under age 40 years, and does not recommend routine PSA screening in average-risk men aged 40 to 54, men aged 70 or older, or any man with a less than 10 to 15 year life expectancy. For men **ages 55 to 69 years who are considering PSA screening**, AUA strongly recommends shared decision-making, and proceeding based on men's values and preferences. In those men who have participated in shared decision-making and have decided on screening, AUA states that a routine screening interval of two years or more may be preferred over annual screening. As compared to annual screening, AUA continues, it is expected that screening intervals of two years preserve the majority of the benefits and reduce overdiagnosis and false positives. According to AUA, the guideline panel did not interpret the evidence from a public health perspective but rather from the perspective of the individual, with emphasis on the information—both benefit and harm—

# Comparison of Recommendations

## Screening for Prostate Cancer

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| ACP (2013) | ***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 PSA 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 PSA test in patients who do not express a clear preference for screening.*<br><br>**Benefits and Harms of Screening (PSA Test and DRE)**<br><br>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 European Randomized Study of Screening for Prostate Cancer (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. Evidence for the benefit of DRE screening is limited, and the Prostate, Lung, Colorectal, and Ovarian (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.<br><br>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 |

mortality), high false-negative rates, 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, 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 Prostate Cancer Intervention Versus Observation Trial (PIVOT) 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 would still prefer to be screened because they may put more value on the possible small benefit and less value on the harms. In 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 do PSA testing will not be diagnosed with prostate cancer and will die of something else.

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

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 in the original guidance statement document.

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%. 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**

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. 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 PSA 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 a person's 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.

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| | 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.<br><br>The figure in the original guidance statement document summarizes the recommendations and clinical considerations for prostate cancer screening. |
| AUA (2013) | **Age <40 years**<br><br>Guideline Statement 1. The Panel recommends against PSA screening in men under age 40 years. (***Recommendation; Evidence Strength Grade C***)<br><br>*In this age group there is a low prevalence of clinically detectable prostate cancer, no evidence demonstrating benefit of screening and likely the same harms of screening as in other age groups.*<br><br>**Age 40 to 54**<br><br>Guideline Statement 2. The Panel does not recommend routine screening in men between ages 40 to 54 years at average risk. (***Recommendation; Evidence Strength Grade C***)<br><br>*For men younger than age 55 years at higher risk (e.g., positive family history or African American race), decisions regarding prostate cancer screening should be individualized.*<br><br>**Age 55 to 69**<br><br>Guideline Statement 3. For men ages 55 to 69 years the Panel recognizes that the decision to undergo PSA screening involves weighing the benefits of preventing prostate cancer mortality in one man for every 1,000 men screened over a decade against the known potential harms associated with screening and treatment. For this reason, the Panel strongly recommends shared decision-making for men age 55 to 69 years that are considering PSA screening, and |

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| | *The greatest benefit of screening appears to be in men ages 55 to 69 years.*<br><br>Guideline Statement 4. To reduce the harms of screening, a routine screening interval of two years or more may be preferred over annual screening in those men who have participated in shared decision-making and decided on screening. As compared to annual screening, it is expected that screening intervals of two years preserve the majority of the benefits and reduce overdiagnosis and false positives. (***Option; Evidence Strength Grade C***)<br><br>*Additionally, intervals for rescreening can be individualized by a baseline PSA level.*<br><br>**Age 70+**<br><br>Guideline Statement 5. The Panel does not recommend routine PSA screening in men age 70+ years or any man with less than a 10 to 15 year life expectancy. (***Recommendation; Evidence Strength Grade C***)<br><br>*Some men age 70+ years who are in excellent health may benefit from prostate cancer screening.* |

## Strength of Evidence and Recommendation Grading Schemes

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| ACP (2013) | Not applicable |
| AUA (2013) | **Body of Evidence Strength**<br><br>**Grade A**: Well-conducted and highly-generalizable randomized controlled trials (RCTs) or exceptionally strong observational studies with consistent findings |

**Grade C**: Observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data

**Note**: By definition, Grade A evidence is evidence about which the Panel has a high level of certainty, Grade B evidence is evidence about which the Panel has a moderate level of certainty, and Grade C evidence is evidence about which the Panel has a low level of certainty.

**AUA Nomenclature Linking Statement Type to Evidence Strength**

**Standard**: Directive statement that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be taken based on Grade A or B evidence

**Recommendation**: Directive statement that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be taken based on Grade C evidence

**Option**: Non-directive statement that leaves the decision regarding an action up to the individual clinician and patient because the balance between benefits and risks/burdens appears equal or appears uncertain based on Grade A, B, or C evidence

**Clinical Principle**: A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature

**Expert Opinion**: A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence

# Methodology

*Click on the links below for details of guideline development methodology*

| ACP | AUA | |
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The methods used to develop the two guidelines differ. The AUA guideline was developed from systematic reviews of the evidence, and the ACP guidance statement was derived from an appraisal of available guidelines on screening for prostate cancer. To develop the ACP guidance statement, authors searched the National Guideline Clearinghouse to identify prostate cancer screening guidelines developed by U.S.-based organizations, excluding any that restated the guidelines of other organizations (August 2012), and selected four, including the USPSTF Screening for Prostate Cancer guideline (2012) and the previous (2009) version of the AUA guideline included in this synthesis. The AUA guideline was developed by the American College of Preventive Medicine (2008) and the American Cancer Society (2010). The AGREE II (Appraisal of Guidelines, Research and Evaluation in Europe) instrument was used to independently evaluate the selected guidelines by four coauthors. Expert consensus was used to formulate the recommendations based on the results of the critical appraisal and on the evidence. The guidance statement was validated using an internal peer review process and an independent peer-review process before publication.

With regard to the methods used to develop the AUA guideline, the developer performed searches of electronic databases and hand-searches of published literature (primary and secondary sources) to collect/select the evidence, and provide details regarding the process, including date ranges, search terms and inclusion/exclusion criteria. AUA commissioned an independent group to conduct a systematic review of the

scheme. To analyze the selected evidence, the guideline developer performed a systematic review with evidence tables and also reviewed published meta-analyses. The AUA also commissioned an independent group to conduct a meta-analysis of the published literature. Methods used to formulate the recommendations included using expert consensus (Delphi technique was used). AUA rates the strength of the recommendations according to a scheme. To validate their guideline, the developer sought some form of peer review.

## Benefits and Harms

### Benefits

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| ACP (2013) | 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. |
| AUA (2013) | • Appropriate use of prostate cancer screening<br>• An approach to PSA based prostate cancer screening has to take into account the controversies surrounding available data and the fact that over a decade the benefits are modest in terms of prostate cancer deaths averted; 1 death per 1,000 men screened in the European Randomized Study of Screening for Prostate Cancer. However the relative benefit (20% reduction in disease-specific deaths) could be very meaningful at the population level. The potential benefits of screening could extend beyond survival as a primary outcome, and will depend on the relevant time horizon for an individual. Further, disconnecting screening from automatic treatment will significantly impact the risk benefit ratio. |

## Harms

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| ACP (2013) | • 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.<br>• 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, 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 Prostate Cancer Intervention Versus Observation Trial (PIVOT) 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. |
| AUA (2013) | **Harms from Screening**<br>• Prostate cancer screening itself is associated with a number of potential harms, both psychological and physical.<br>• The transrectal or transperineal prostate biopsy has risks of hematuria, hematochezia, hematospermia, dysuria and retention, pain, and infection. Hematuria and hematospermia are the most frequently observed side effects with wide variation in observed rates. Hematospermia after biopsy occurs in 10% to 70% of patients while hematuria is seen 14% to 50% of the time. While the risk of hospitalization due to bleeding complications remains low, infectious complications are increasing steadily over time, possibly due to fluoroquinolone resistance. The 30-day risk of hospitalization after biopsy for any cause has been estimated to be approximately 4%, of which three in four are for infections. The use of routine fecal culture and sensitivity tailored |

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| | periprocedural prophylaxis. Since prostate biopsies are also an important part of some active surveillance programs, understanding these risks and communicating them to patients is not only integral to informed consent for prostate cancer screening but also for consideration of treatment options.<br>• Once diagnosed with prostate cancer, a man is faced with the risk of overtreatment of indolent disease due to the assumption that diagnosis with a malignancy must necessarily result in treatment of this malignancy. Estimates of overdiagnosis vary widely from less than 5% to more than 75% depending upon the population used with lead times of 5 to 15 years.<br>• Although prostate cancer specific mortality and the need for related palliative care is decreased by screening, quality of life may be impaired as a result due to lasting impairment in urinary, bowel, and sexual function.<br>• There is considerable distress involved in the decision making process, the biopsy, and deciding among treatment options. Along with the stress due to PSA screening and unnecessary biopsies, the diagnosis of prostate cancer alone may incite severe psychological stress with one study showing an increased rate of suicide and cardiovascular events in newly diagnosed men.<br>• Even when men select active surveillance rather than curative therapy, anxiety may continue and trigger intervention in men who would never have needed treatment in their lifetime; although it would appear that anxiety remains low for most men on surveillance in the short term.<br>Refer to the "Harms" section in the original guideline document for additional discussion. |

## Abbreviations

ACP, American College of Physicians

AUA, American Urological Association Education and Research, Inc.

DRE, digital rectal examination

PSA, prostate specific antigen

## Status

This synthesis was prepared by ECRI Institute on December 28, 1998. This synthesis was updated in 2005 to add recommendations from UMHS and to remove recommendations from AUA and SMOH. The information was verified by UMHS on August 23, 2005. This synthesis was updated on December 6, 2007 to remove recommendations from USPSTF. This synthesis was revised on June 13, 2008 to add ACPM recommendations. The information was verified by ACPM on July 17, 2008. This synthesis was revised in October 2008 to add USPSTF recommendations in March 2009 to remove recommendations from ACS and in March 2010 to remove UMHS recommendations and add AUA recommendations. The information was verified by AUA on April 12, 2010. This synthesis was revised in December 2011 to add recommendations from ACS. The updated information was verified by ACS on January 19, 2012. This synthesis was revised in March 2013 to update recommendations from USPSTF and remove recommendations from ACPM. The information was verified by USPSTF on April 1, 2013. This synthesis was revised in May 2013 to remove AUA recommendations. This synthesis was revised in February 2014 to add updated recommendations from AUA. The information was verified by AUA on February 17, 2014. This synthesis was revised most recently in October 2015 to add recommendations from ACP and remove recommendations from ACS. The information was verified by ACP on October 22, 2015. The information was updated to remove USPSTF recommendations on April 30, 2018.