NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

SCREENING FOR PROSTATE CANCER

Guidelines

1. **American Cancer Society (ACS)**. Recommendations from the American Cancer Society Workshop on Early Prostate Cancer Detection, May 4-6, 2000 and ACS guideline on testing for early prostate cancer detection: update 2001. CA Cancer J Clin 2001 Jan-Feb;51(1):39-44 [181 references].
2. **American College of Preventive Medicine (ACPM)**. Screening for prostate cancer in U.S. men. Am J Prev Med 2008 Feb;34(2):164-70. [60 references]
3. **University of Michigan Health System (UMHS)**. Adult preventive health care: cancer screening. Ann Arbor (MI): University of Michigan Health System; 2004 May. 12 p. [4 references].
4. **United States Preventive Services Task Force (USPSTF)**. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2008 Aug 5;149(3):185-91. [19 references] PubMed

INTRODUCTION:

A direct comparison of the American Cancer Society (ACS), American College of Preventive Medicine (ACPM), University of Michigan Health System (UMHS), and the U.S. Preventive Services Task Force (USPSTF) recommendations for screening for prostate cancer is provided in the following tables.

The tables below provide a side-by-side comparison of key attributes of each guideline, including specific interventions and practices that are addressed. The language used in these tables, particularly that which is used in Table 3, Table 4, and Table 5 is in most cases taken verbatim from the original guidelines:

- Table 1 provides a quick-view glance at the primary interventions considered by each group and which make up the focus of this guideline synthesis.
- Table 2 provides a comparison of the overall scope of the included guidelines.
- Table 3 provides a more detailed comparison of the specific recommendations offered by each group for the topics under consideration in this synthesis, including:
  - Whom to Screen and Screening Modality
  - Screening Education/Counseling
- Table 4 lists the potential benefits and harms associated with the implementation of each guideline as stated in the original guidelines.
- Table 5 presents the rating schemes used by the guideline groups to rate the level of evidence and the strength of the recommendations.

A summary discussion of the areas of agreement and areas of differences among the guidelines is presented following the content comparison tables.

Abbreviations:

- ACPM, American College of Preventive Medicine
- ACS, American Cancer Society
- DRE, digital rectal examination
- PSA, prostate specific antigen
- UMHS, University of Michigan Health System
- USPSTF, United States Preventive Services Task Force (USPSTF)

TABLE 1: COMPARISON OF INTERVENTIONS AND PRACTICES CONSIDERED
("✓" indicates topic is addressed)

	ACS (2001 reviewed 2006)	ACPM (2008)	UMHS (2004)	USPSTF (2008)
Whom to Screen and Screening Modality	✓	✓	✓	✓
Screening Education/Counseling	✓	✓	✓	✓

TABLE 2: COMPARISON OF SCOPE AND CONTENT

	Objective and Scope
ACS (2001 reviewed 2006)	• To update the 1997 American Cancer Society guideline pertaining to prostate cancer screening • To offer recommendations to health care professionals and the public for informed decision-making related to early detection of prostate cancer
ACPM (2008)	To review the efficacy of DRE and PSA for prostate cancer screening found in the medical literature prior to July 2007
UMHS (2004)	To implement an evidenced-based strategy for cancer screening in adults
USPSTF (2008)	• To summarize the current USPSTF recommendations and supporting scientific evidence on screening for prostate cancer

	• To update the 2002 USPSTF recommendations on screening for prostate cancer
Target Population	
ACS (2001 reviewed 2006)	• Men aged 50 years and older who have a life expectancy of at least 10 years and younger men who are at high risk for prostate cancer • Men aged 45 years and older of Sub-Saharan African descent or with first-degree relative diagnosed at a young age • Men 40 and older with multiple first-degree relatives diagnosed with prostate cancer at an early age
ACPM (2008)	American men
UMHS (2004)	• Men >age 50 • Men with positive family history and for African Americans, consider starting PSA screening at age 40
USPSTF (2008)	Adult males
Intended Users	
ACS (2001 reviewed 2006)	Advanced Practice Nurses Allied Health Personnel Health Care Providers Health Plans Hospitals Managed Care Organizations Nurses Patients Physician Assistants Physicians Public Health Departments
ACPM (2008)	Physicians
UMHS (2004)	Physicians
USPSTF (2008)	Advanced Practice Nurses Allied Health Personnel Health Care Providers

	Nurses Physician Assistants Physicians

TABLE 3: COMPARISON OF RECOMMENDATIONS FOR PROSTATE CANCER SCREENING	
Whom to Screen and Screening Modality	
ACS (2001 reviewed 2006)	ACS recommends that both the PSA test and the DRE should be offered annually, beginning at age 50, to men who have a life expectancy of at least 10 years. Men at high risk, including men of African descent (specifically, sub-Saharan African descent) and men with a first-degree relative diagnosed at a younger age should begin testing at age 45. Men at even higher risk of prostate cancer due to multiple first-degree relatives diagnosed with prostate cancer at an early age could begin testing at age 40. However, if PSA is less than 1.0 ng/mL, no additional testing is needed until age 45. If PSA is greater than 1.0 ng/mL but less than 2.5 ng/mL, annual testing is recommended. If PSA is 2.5 ng/mL or greater, further evaluation with biopsy should be considered.
ACPM (2008)	**Recommendation of the ACPM** The ACPM concludes that there is currently insufficient evidence to recommend routine population screening with DRE or PSA, concurring with the USPSTF recommendation. Pending resolution of ongoing controversies, screening for prostate cancer among African-American men and those with a family history of prostate cancer has the potential to detect treatable forms of disease that are more likely to occur in these groups than in the general population. While the usual age for prostate cancer screening is between 50 to 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 higher-risk men (those with two or more first-degree relatives with prostate cancer before age 65) be screened at age 40. Granted that prostate cancer is more likely to be found in high-risk men, issues pertaining to tumor grade have yet to be resolved (that is, optimal grade of tumor that a screening test should detect to confer a benefit in survival or morbidity), and there is still no evidence establishing effectiveness of screening in high-risk men. In the meantime further studies are needed to establish the efficacy and optimal age at which prostate cancer screening should be initiated in these high-risk population

	groups.
UMHS (2004)	**Modality**. PSA and DRE. Both have specificity limitations. **Initiate**. Clinicians who screen for prostate cancer should share decision making with patients **[*A*]**, giving objective information about the potential risks and benefits of screening. • Average risk. For men >age 50, consider initiating PSA screen. • High-risk. For men with positive family history and for African Americans, consider starting PSA screening at age 40 **[*D*]**. **Frequency**. Annually **Terminate**. Stop when life expectancy is less than 10 to 15 years **[*C*]**. **Rationale for Recommendations** There is considerable controversy surrounding screening for prostate cancer. Early detection and treatment may avert future prostate cancer-related illness, but treatment includes some risk of sexual dysfunction and incontinence and a small risk of treatment-induced mortality. At this time, no trials of sufficient power are available to document the benefit of aggressive treatment (e.g., surgery, radiation) versus conservative management and hormonal therapy. Similarly, there is no conclusive evidence that routine screening for prostate cancer is beneficial, and there is no consensus concerning the role of DRE and PSA testing in screening.
USPSTF (2008)	**<u>Summary of Recommendations and Evidence</u>** • The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of prostate cancer screening in men younger than age 75 years. **This is an I statement**. • The USPSTF recommends against screening for prostate cancer in men age 75 years or older. **This is a grade D recommendation**. **<u>Clinical Considerations</u>** **Patient Population under Consideration** This recommendation applies to men in the general U.S. population. **Risk Assessment** Older men, African-American men, and men with a family history of

	prostate cancer are at increased risk for diagnosis and death from prostate cancer. Unfortunately, the previously described gaps in the evidence regarding potential benefits of screening also apply to these men. **Screening Tests** The PSA test is more sensitive than the DRE for detecting prostate cancer. The conventional PSA screening cut-point of 4.0 micrograms/L detects many prostate cancer cases; however, some early cases of prostate cancer will be missed by this cut-point. Using a lower cut-point to define an abnormal PSA detects more cases of cancer. The proportion of cancer cases detected by lower cutpoints that would ever become clinically apparent is unknown; lower cut-points would label many more men as potentially having cancer. For example, lowering the PSA cut-point to 2.5 micrograms/L would more than double the number of U.S. men between 40 and 69 years of age with abnormal results. Variations of PSA screening, including the use of age-adjusted PSA cut-points, free PSA, PSA density, PSA velocity, PSA slope, and PSA doubling time, have been proposed to improve detection of "clinically important" prostate cancer cases. However, no evidence suggests that any of these testing strategies improves health outcomes. **Screening Intervals** The yield of screening in terms of cancer cases detected declines rapidly with repeated annual testing. If screening were to reduce deaths, PSA screening as infrequent as every 4 years could yield as much of a benefit as annual screening.
Screening Education/Counseling	
ACS (2001 reviewed 2006)	Information should be provided to all patients about the benefits and limitations of testing. Specifically, prior to testing, men should have an opportunity to learn about the benefits and limitations of testing for early prostate cancer detection and treatment so that they can make an informed decision with the clinician's assistance. Men who ask the clinician to make the testing decision on their behalf should be tested. A policy of not discussing testing, or discouraging testing in men who request early prostate cancer detection tests, is inappropriate.
ACPM (2008)	**Recommendation of the ACPM** The College is in agreement with the American College of Physicians (ACP) that men should be given information about the potential

	benefits and harms of screening and limits of current evidence in order to make an informed decision about screening. Discussion about screening should occur annually, during the routine periodic examination, or in response to a request by the patient. The effectiveness of prostate cancer screening is questionable in elderly men with competing co-morbidities and men with life expectancies of less than 10 years. Ultimately, a man should be allowed to make his own choice about screening, in consultation with his physician, taking into consideration personal preferences and life expectancy. If the patient prefers to defer to the clinician or is unable to make a decision regarding screening, then testing should not be offered as long as the patient understands the benefits, potential limitations, and adverse effects associated with screening. Key points that should be communicated during the patient encounter regarding prostate cancer screening are listed in Table 1 of the original guideline document.
UMHS (2004)	**Initiate**. Clinicians who screen for prostate cancer should share decision making with patients [***A***], giving objective information about the potential risks and benefits of screening. **High risk groups**. First-degree relatives of men with prostate cancer and African-American men have been shown to have a higher lifetime risk for developing prostate cancer. These men should be informed that they are at higher risk for developing prostate cancer.
USPSTF (2008)	**Clinical Considerations** **Suggestions for Practice** Given the uncertainties and controversy surrounding prostate cancer screening in men younger than age 75 years, a clinician should not order the PSA test without first discussing with the patient the potential but uncertain benefits and the known harms of prostate cancer screening and treatment. Men should be informed of the gaps in the evidence and should be assisted in considering their personal preferences before deciding whether to be tested.

TABLE 4: BENEFITS AND HARMS	
Benefits	
ACS (2001 reviewed 2006)	Prostate cancer screening may result in the diagnosis of earlier-stage disease in younger men, which may decrease prostate cancer mortality rates.

	However, no direct evidence exists to show that prostate-specific antigen (PSA) screening decreases prostate cancer mortality rates.
ACPM (2008)	Benefits of screening include early detection and treatment of potentially curable stage of prostate cancer (i.e., better chances of survival with localized disease) and reassurance of being at low risk of cancer. **Subgroups Most Likely to Benefit** Men with a first-degree relative (e.g., father, brother) with prostate cancer and African-American men are at higher risk of both developing and dying from prostate cancer.
UMHS (2004)	Early detection and treatment may avert future cancer-related illness.
USPSTF (2008)	**Benefits of Detection and Early Treatment** • In men younger than age 75 years, the USPSTF found inadequate evidence to determine whether treatment for prostate cancer detected by screening improves health outcomes, compared with treatment after clinical detection. • In men age 75 years or older, the USPSTF found adequate evidence that the incremental benefits from treatment for prostate cancer detected by screening are small to none.
Harms	
ACS (2001 reviewed 2006)	Since prostate-specific antigen is prostate-tissue specific and not prostate-cancer specific, there is no absolute value that is applicable to all men. The range of "normal" prostate-specific antigen levels has conventionally been considered to be between zero and 4.0 ng/dl. A lower cut-off value of 2.5 ng/dl has been shown to improve the early detection of organ-confined prostate cancers; however, this also increases the number of men undergoing biopsy in whom no cancer is detected.
ACPM (2008)	Both screening and treatment can be harmful: • A false positive result may lead to increased anxiety and having to experience the discomfort and possible complications associated with biopsy (e.g., pain, hematospermia/hematuria, and infection) • Prostate cancer may be slow growing and may never advance or progress to cause significant disease or death. Treatment can cause both short- and long-term side effects (e.g., pain, urinary incontinence, and impotence). • Men who received false-positive PSA test results reported

	having thought and worried more about prostate cancer despite receiving a negative follow-up (prostate biopsy) result. Thus screening may cause undesirable mental health consequences. • False reassurance from a normal test (false negative), leading to a delayed diagnosis of prostate cancer.
UMHS (2004)	**DRE** Although DRE can successfully detect some prostate cancers, it is less effective in detecting tumors deep within the prostate gland, and its impact on prostate cancer mortality has been shown to be limited. DRE has a significant subjective component that is manifested by only fair inter-examiner agreement. In addition, it has been suggested that 25 to 35% of prostate cancers occur in areas of the prostate not accessible to the examining finger. The sensitivity of DRE ranges from 18 to 68% with significantly lower specificity. **PSA** PSA is generally specific to prostate tissue; however, it is not specific to only prostate cancer. Older men may develop benign prostatic hyperplasia which often elevates PSA, and hence, the specificity of PSA decreases with age.
USPSTF (2008)	**Harms of Detection and Early Treatment** • The USPSTF found convincing evidence that treatment for prostate cancer detected by screening causes moderate- to-substantial harms, such as erectile dysfunction, urinary incontinence, bowel dysfunction, and death. These harms are especially important because some men with prostate cancer who are treated would never have developed symptoms related to cancer during their lifetime. • There is also adequate evidence that the screening process produces at least small harms, including pain and discomfort associated with prostate biopsy and psychological effects of false-positive test results.

TABLE 5: EVIDENCE RATING SCHEMES AND REFERENCES	
ACS (2001 reviewed	Not applicable

<table>
<tr><td>2006)</td><td></td></tr>
<tr><td>ACPM (2008)</td><td>Not applicable</td></tr>
<tr><td>UMHS (2004)</td><td>Levels of Evidence Reflect the Best Available Literature in Support of an Intervention or Test

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel</td></tr>
<tr><td>USPSTF (2008)</td><td>What the United States Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

<table>
<tr><th>Grade</th><th>Grade Definitions</th><th>Suggestions for Practice</th></tr>
<tr><td>A</td><td>The USPSTF recommends the service. There is high certainty that the net benefit is substantial.</td><td>Offer or provide this service.</td></tr>
<tr><td>B</td><td>The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.</td><td>Offer or provide this service.</td></tr>
<tr><td>C</td><td>The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is moderate or high certainty that the net benefit is small.</td><td>Offer/provide this service only if there are other considerations in support of the offering/providing the service in an individual patient.</td></tr>
<tr><td>D</td><td>The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.</td><td>Discourage the use of this service.</td></tr>
<tr><td>I Statement</td><td>The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor</td><td>Read "Clinical Considerations" section of USPSTF Recommendation Statement (see "Major Recommendations" field). If offered, patients should understand the</td></tr>
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		quality or conflicting, and the balance of benefits and harms cannot be determined.	uncertainty about the balance of benefits and harms.

GUIDELINE CONTENT COMPARISON

The American Cancer Society (ACS), American College of Preventive Medicine (ACPM), University of Michigan Health System (UMHS), and the United States Preventive Services Task Force (USPSTF) present recommendations for screening men for prostate cancer and provide explicit reasoning behind their judgments.

In addition to prostate cancer screening, the UMHS guideline provides screening recommendations for breast cancer, cervical cancer, ovarian cancer, and colorectal cancer (see related cancer screening Syntheses).

Areas of Agreement

Screening in Average-Risk, Asymptomatic Men

All four organizations emphasize the considerable controversy surrounding screening due to the lack of conclusive evidence that screening can reduce mortality from prostate cancer. All four groups also address the clear potential that screening may increase treatment-related morbidity. Nonetheless, ACS and UMHS agree that screening should be offered annually to average-risk, asymptomatic men beginning at age 50. UMHS does note, however, that there is no conclusive evidence that routine screening for prostate cancer is beneficial. The groups also agree that men to be screened should generally have a life expectancy of at least ten years. Refer to Areas of Differences below for ACPM and USPSTF screening recommendations in this population.

Screening in High-Risk Men

ACS and UMHS agree that screening should be offered to high-risk men at an earlier age than average risk men. UMHS recommends that screening be offered African American men and men with a positive family history of prostate cancer at age 40. ACS similarly recommends that men of African descent and men with a first-degree relative diagnosed at a younger age begin testing at age 45.

ACS continues to note that men at even higher risk of prostate cancer due to multiple first-degree relatives diagnosed with prostate cancer at an early age could begin testing at age 40. They then provide subsequent testing recommendations according to the patient's PSA level obtained during screening.

While ACPM falls short of making an explicit recommendation, they acknowledge that screening for prostate cancer among African-American men and those with a family history of prostate cancer has the potential to detect treatable forms of disease that are more likely to occur in these groups than in the general

population. They add that while the usual age for prostate cancer screening is between 50 to 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 higher-risk men (those with two or more first-degree relatives with prostate cancer before age 65) be screened at age 40. They continue to note, however, that further studies are needed to establish the efficacy and optimal age at which prostate cancer screening should be initiated in these high-risk population groups.

Similar to ACPM, USPSTF makes no formal recommendation regarding screening in high-risk populations. They acknowledge that older men, African-American men, and men with a family history of prostate cancer are at increased risk for diagnosis and death from prostate cancer, but note that unfortunately, the gaps in the evidence regarding potential benefits of screening also apply to these men.

Screening Education/Counseling

All four organizations assert that men should make an informed decision regarding prostate cancer screening with the help of their physicians. There is overall agreement that clinicians should share decision making regarding screening with the patient, providing the patient with clear information regarding the benefits and risks of screening. ACPM notes that discussion about screening should occur annually, during the routine periodic examination, or in response to a request by the patient. They also provide a listing of key points that should be communicated during the patient encounter regarding prostate cancer screening.

Screening Tests

When the decision to screen is made, there is agreement among the groups that PSA and DRE are the primary screening tests for prostate cancer.

Areas of Differences

Screening in Average-Risk, Asymptomatic People

In contrast to ACS and UMHS, ACPM concludes that there is currently insufficient evidence to recommend routine population screening with DRE or PSA. This conclusion is in agreement with the previous (2002) USPSTF recommendation. In its current (2008) guideline (included in this Synthesis), USPSTF provides screening recommendations according to age group, concluding that the current evidence is insufficient to assess the balance of benefits and harms of prostate cancer screening in men younger than age 75 years. USPSTF is the only group to explicitly recommend against screening for prostate cancer in a particular age group, which is men age 75 years or older.

Screening Education/Counseling

While both ACS and ACPM recommend that men make an informed decision regarding prostate cancer screening with the help of their physicians, their recommendations pertaining to men who defer the decision to screen to their physicians differ. ACS states that men who ask the clinician to make the testing decision on their behalf should be tested. ACPM, on the other hand, states that if

the patient prefers to defer to the clinician or is unable to make a decision regarding screening, then testing should not be offered as long as the patient understands the benefits, potential limitations, and adverse effects associated with screening.

Screening Tests

Although there is agreement among the groups that PSA and DRE are the primary screening tools for prostate cancer, ACS explicitly recommends combining the two to improve accuracy. UMHS' formal recommendation, in contrast, only addresses PSA, which they recommend be initiated in average risk men over the age of 50. UMHS notes that the combined use of DRE and PSA will decrease the rate of false positives (e.g., when both PSA and DRE are suspicious), but at the expense of reduced sensitivity (ability of the combined tests to identify patients with prostate cancer). USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of prostate cancer screening in men younger than age 75 years, and they therefore do not provide a formal recommendation regarding the use of PSA or DRE, but they do note that the PSA test is more sensitive than the DRE for detecting prostate cancer.

This Synthesis was prepared by NGC on December 28, 1998 and has been revised a number of times. The most current version of this Synthesis incorporates new guidelines from UMHS and removes recommendations of the American Urological Association (2000) and Singapore Ministry of Health (2000). 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 most recently in October 2008 to add USPSTF recommendations.

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