Clinical Policy Title: Prostate-specific antigen screening

Clinical Policy Number: 13.01.06

Effective Date: May 1, 2017
Initial Review Date: April 19, 2017
Most Recent Review Date: March 6, 2018
Next Review Date: March 2019

Policy contains:
- Prostate cancer.
- Prostate-specific antigen.

Related policies:

CP# 13.01.04 Enhanced cytoscopy for bladder cancer
CP# 13.01.01 Genetic tests for prostate cancer diagnosis

ABOUT THIS POLICY: AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas’ clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas’ clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas’ clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas’ clinical policies are not guarantees of payment.

Coverage Policy

An initial prostate-specific antigen (PSA) test is considered medically necessary for asymptomatic men after discussion of potential risks and benefits of prostate cancer diagnosis and treatment between the patient and provider, and the patient elects screening (Andriole, 2010; Brooks, 2010; Nam, 2013; Qaseem, 2013; Wolf, 2010). Such screening is only considered medically necessary:
- For average-risk males beginning at age 50 with a life expectancy at least 10 years.
- For African Americans beginning at age 45.
- For males with a father or brother diagnosed with prostate cancer at an early age beginning at age 40.

Annual follow-up PSA tests are considered medically necessary if the value is greater than or equal to 2.5 ng/ml; biannual tests are considered medically necessary if the value is less than 2.5 ng/ml.
An annual PSA test is considered medically necessary when used for surveillance after diagnosis and/or treatment of prostate cancer.

Limitations:

None.

Alternative covered services:

- Cystoscopy or bladder scope test.
- Digital rectal examination.
- Prostate ultrasound and biopsy.

Background

Prostate cancer is the third most commonly diagnosed cancer in the United States and has the highest incidence of any cancer among men. In 2016, an estimated 180,890 cases were diagnosed in the United States, with 26,120 deaths due to the disease. Incidence of prostate cancer has fallen by more than half since the early 1990s, largely due to less screening in men. The mortality rate has also fallen by just over 50 percent. African Americans have a 70 percent greater incidence rate of the disease than non-Hispanic whites; Hispanics, Asians, and American Indians have rates well below that of non-Hispanic whites (Howlader, 2016).

PSA is a protein found in prostate cells. In 1986, the U.S. Food and Drug Administration approved the PSA blood test to monitor the progress of males with prostate cancer and followed in 1994 with approval for a disease screening. PSA is a simple test that costs roughly $40. PSA levels are often elevated in males with prostate cancer, prostatitis, or benign prostatic hyperplasia (BPH). However, men with prostatitis or benign prostatic hyperplasia are not necessarily at higher risk for developing prostate cancer.

False positives and false negatives can occur in the test. A level of 4.0 ng/mL or less is considered normal. However, levels below 4.0 can exist in males with prostate cancer, and levels above 4.0 can occur in males without the disease (Thompson, 2004). False positives can lead to unnecessary biopsies with accompanying risks, while false negatives may delay needed treatment.

Prostate cancer is largely a disease affecting elderly men, raising the question of whether screening for an often slow-growing disease is needed in males with relatively short expected life spans. Autopsy studies have reported prostate cancer rates in undiagnosed and asymptomatic men between 18.5 and 38.5 percent (Loeb, 2014). The ability of frail elderly to tolerate treatments such as biopsy, surgery, and radiation is also called into question, leaving physicians to weigh risks and benefits of screening.
The false-positive rate of PSA tests has long been a concern. One early study estimated that 75 percent of men with PSA results over 4 ng/ml did not have prostate cancer after biopsy (Barry, 2001).

Even if a positive PSA test results in confirmation of a prostate cancer diagnosis, there is concern about whether or not to treat the disease. Surveillance of relatively small and slow-growing cancers has become more common in recent years, especially after a 2011 conference at the National Institutes of Health (NIH, 2011). One study of 290 men with prostate cancer who met criteria for active surveillance found that 65 percent remained on active surveillance after a median of 2.9 years, prompting authors to conclude that PSA results alone are less effective for monitoring than annual surveillance biopsy (Ross, 2010).

**Searches**

AmeriHealth Caritas searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on January 26, 2018. Search terms were: “prostate specific antigen” and “mortality.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

Numerous studies that showed insufficient evidence to determine if treatment after PSA screening improves outcomes more than treatment after clinical detection caused professional societies to alter their recommendations. The U.S. Preventive Services Task Force (USPSTF) recommended against PSA-based screening for prostate cancer, for all U.S. males, regardless of age (Moyer, 2012).

Guidelines from other organizations resemble that of the USPSTF. The American College of Physicians recommends no PSA screening in average-risk men under age 50 or over age 69 or men with a life
expectancy less than 10 – 15 years, and suggests clinicians inform men age 50 – 69 of the risks and benefits of screening (Qaseem, 2013).

The American Society of Clinical Oncology discourages prostate cancer screening in males with a life expectancy under 10 years and recommends patients with a life expectancy over 10 years to discuss risks and benefits with physicians (Nam, 2013). The American Cancer Society recommendation is the same for men with life expectancy over 10 years, stipulating that those at average risk begin discussions at age 50 (Brooks, 2010), and those at high risk (from family history or being African American) receive this information at an earlier age (Wolf, 2010).

The American Urological Association (AUA) statement supports men first being informed of PSA screening risks and benefits, with routine screening not recommended for average-risk males age 40 to 54. For men under 55 who are African-American or have a family history of the disease, decisions to test should be individualized – as should decisions for all men ages 55 – 69. The AUA does not recommend PSA screening in men over age 70 or men with less than a 10 – 15 year life expectancy (Greene, 2009).

One review of the literature assessed whether separate screening guidelines were needed for African-American men. Authors who point out that studies often include small numbers of African Americans concluded separate guidelines were needed, due to elevated incidence and mortality rates, clinical course of the disease, genetic differences, and social barriers (Shenoy, 2016).

Studies of PSA screening effectiveness typically focus on reductions in prostate cancer-specific and all-cause mortality. Some studies address overdiagnosis of the disease leading to unneeded therapy. An estimate of overdiagnosis — 22 percent and 33 percent of screen-detected cases for white and black Americans (Telesca, 2008) — was matched (23, 28, and 42 percent) by estimates using three models (Draisma, 2009).

A consensus has formed supporting clinician-patient discussion of the pros and cons of PSA screening, and only performing the test for those men who express a preference for it (Hayes, 2014). In addition, a risk-based approach on decisions to perform the test has been suggested (Zhu, 2011). One search of five systematic reviews and six randomized controlled trials (RCTs) failed to show a significant reduction in prostate cancer mortality or overall mortality with PSA-based screening (Pron, 2015).

Two studies have played a major influence in professional opinion on PSA screening. One was the prostate component of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. A total of 76,685 American men ages 55 – 74 were either given an annual PSA screening for six years and an annual digital rectal examination (DRE) for four years, or not screened. After 13 years, prostate cancer deaths per 10,000 person years were 3.7 and 3.4 for the screening and control groups (Andriole, 2012). All-cause mortality in the screening group was a (non-significant) 3 percent lower than controls (Andriole, 2010).
The other large-scale study (European Randomized Screening for Prostate Cancer) consisted of 162,388 European men ages 50 – 74, who were offered PSA every four years, which 82 percent accepted, or no PSA (control). After nine years median follow-up, incidence of prostate cancer was higher (8.2 percent versus 4.8 percent), and prostate cancer mortality was 20 percent lower for the intervention group (Schroeder, 2009). All cause mortality was 1 percent lower for the screening group (18.2 versus 18.5 deaths per 1000 person-years — a non-significant difference (Schroeder, 2012).

In a study of 19,904 men ages 50 – 64 in Goteborg, Sweden, half were given the opportunity for a PSA test every two years, and screening was not discussed with the other half. After 14 years, the incidence was higher in the screening group (12.7 percent versus 8.2 percent). Forty-four percent fewer prostate cancer deaths occurred in the screening group, but non-prostate cancer death rates were higher in the screening group (9.6 versus 7.5 percent). The number of men invited to be screened needed to prevent one prostate cancer death was calculated to be 293 (Hugosson, 2010).

A systematic review and meta-analysis of five RCTs and 341,342 participants that updated 2006 and 2010 Cochrane reviews found that only the European study showed a significantly lower risk of prostate cancer deaths due to screening. Diagnosed prostate cancer cases were significantly (30 percent) greater in screening groups, and all-cause mortality was equal in both screening and control groups. Harm from overtreatment after screening included infection, blood loss requiring transfusion, pneumonia, erectile dysfunction, incontinence, bleeding, bruising, and short-term anxiety (Ilic, 2013).

A systematic review of seven RCTs with 571,594 participants found screening had no significant effect on prostate cancer and all-cause mortality (12 percent and 10 percent lower), even though screening detected 81 percent more localized prostate cancers (Lumen, 2011).

A systematic review and meta-analysis of six RCTs with 387,286 participants found a 46 percent higher probability of diagnosing prostate cancer in the screening group, with no significant effect of death from prostate cancer and all causes (12 percent and 1 percent lower) in the screening groups. The authors conclude that routine screening is not supported (Djulbegovic, 2010). A systematic review of six RCTs found prostate cancer and all-cause mortality were not significantly reduced (7 percent and 1 percent lower) for the screening group, but detection of prostate cancer was significantly (45 percent) higher (Lee, 2013).

Prostate cancer screening was included in a systematic review of six diseases for which screening evaluation is available from the U.S. Preventive Services Task Force. The research team from Stanford University School of Medicine concluded that for all available screening for high-mortality disease, reductions in disease-specific mortality are uncommon, and reductions in all-cause mortality are very rare or non-existent (Saquib, 2015).

A cost effectiveness analysis of PSA screening found that, compared to outcomes for a screened 40 year old man, the incremental cost from screening men ages 55 – 69 every four years was $36,300 per life year gained, a figure that rose to $588,300 per life year gained for screening men ages 40 – 74 every two
years. However, these figures were based on the large European study, the only large review that found significant reductions in prostate cancer mortality from PSA screening (Pataky, 2014).

Policy updates:

In January, 2018, two publications (one guideline and one peer-reviewed article) were added to the reference list. The guideline was also added to the Summary of clinical evidence.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mottet (2017)</td>
<td>Key points:</td>
</tr>
<tr>
<td>EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: Screening, diagnosis, and local treatment with curative intent</td>
<td>Systematic screening is discouraged. Instead, strategy should be based on individual risk after a detailed discussion between patient and physician and should take into account the patient's wishes as well as life expectancy.</td>
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<tr>
<td>Pataky, 2014</td>
<td>Key points:</td>
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<td>Cost-effectiveness of PSA prostate cancer screening</td>
<td>A modeling of cost-benefit in British Columbia, based on results from the European Study of Randomized Screening for Prostate Cancer.</td>
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<tr>
<td>Ilic, 2013</td>
<td>Key points:</td>
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<tr>
<td>Review of PSA screening ability to reduce prostate cancer and all-cause mortality</td>
<td>Cochrane review of five RCTs with 341,342 participants.</td>
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<tr>
<td>Andriole, 2012</td>
<td>Key points:</td>
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<tr>
<td>PSA screening ability to reduce prostate cancer mortality</td>
<td>Prostate component of Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.</td>
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<tr>
<td>Schroeder, 2012</td>
<td>Key points:</td>
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<tr>
<td>Follow up study on effect of PSA screening on prostate</td>
<td>Large European study of 162,388 men ages 50 – 74 in screening and controlled groups.</td>
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### Citation

<table>
<thead>
<tr>
<th>Cancer mortality</th>
<th>Screening groups.</th>
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<tr>
<td>Schroeder, 2009</td>
<td>1,055 men would need to be screened to prevent one death from prostate cancer.</td>
</tr>
</tbody>
</table>

### Study on effect of PSA screening on prostate cancer mortality

**Key points:**
- Study of 162,243 European men ages 55 – 69, randomly assigned to a group offered PSA every four years versus a group who was not.
- In the screening group, 82% accepted at least one offer of screening.
- After a median follow-up of nine years, incidence of prostate cancer higher in screening group (8.2% vs. 4.8%).
- Prostate cancer mortality 20% lower in screening group (significant, p < .04).

### References

**Professional society guidelines/other:**


**Peer-reviewed references:**


**CMS National Coverage Determinations (NCDs):**

Prostate cancer screening tests (210.1). CMS website: [https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDid=268&ncdver=2&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=prostate+cancer+screening&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAAA%3d%3d&](https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDid=268&ncdver=2&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=All&KeyWord=prostate+cancer+screening&KeyWordLookUp=Title&KeyWordSearchType=And&bc=gAAAAA%3d%3d&). Accessed January 26, 2018.

**Local Coverage Determinations (LCDs):**

No LCDs identified as of the writing of this policy.

**InterQual**

InterQual 2013. Clinical Evidence Summaries. Prostate Cancer.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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