PROSTATE CANCER SCREENING: AN UPDATE

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The U.S. Preventive Services Task Force (USPSTF)
Grade D: recommends against prostate-specific antigen (PSA)-based screening for prostate cancer

• …the reduction in prostate cancer mortality after 10 to 14 years is, at most, very small, even for men in what seems to be the optimal age range of 55 to 69 years…
• …no apparent reduction in all-cause mortality…
• …harms associated with the diagnosis and treatment of screen-detected cancer are common, occur early, often persist, and include a small but real risk for premature death…
• …more men in a screened population will experience the harms of screening and treatment of screen-detected disease than will experience the benefit…

- The USPSTF concluded that there is moderate certainty that the benefits of PSA-based screening for prostate cancer do not outweigh the harms.
Prostate Cancer in the United States

- Prostate cancer is the most commonly diagnosed life-threatening cancer in men (180,890 cases and 26,120 deaths in 2016)

- Small prostate cancers are present in 29% of men between ages 30 and 40 and 64% of men between ages 60 and 70

- The lifetime risk of a prostate cancer diagnosis is about 1 in 8

- The lifetime risk of dying from prostate cancer is about 1 in 37
PSA-Based Screening Recommendations of Other Organizations (American Cancer Society, American Urological Association, American Society of Clinical Oncology)

- PSA-based screening should be offered to all men beginning at age 50-55 years
- PSA-based screening should be considered before age 50 years for African-American men
- PSA-based screening should be considered before age 50 years for me with a strong family history of prostate cancer
- All men at risk for prostate cancer should participate in shared decision-making with physicians to ensure that the benefits and harms of screening are well understood before pursuing serum PSA testing
Prostate-Specific Antigen (PSA) is an Enzyme Normally Secreted into the Ejaculate that Appears in the Bloodstream of Men with Prostate Cancer.
The Rise of Serum (Blood) PSA Predicts Life-Threatening Prostate Cancer when Cure may be Possible*

*data from Baltimore Longitudinal Study of Aging (2005)

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European Randomized Study of Prostate Cancer Screening (ERSPC)*
(162,388 European men randomized to PSA testing every 4 years with a cut-off value of 3 ng/mL for biopsy)

Results:

• 40% reduction in metastatic prostate cancer
• 21% reduction in mortality at 13 years
• 781 men needed to be screened and 27 men diagnosed/treated to prevent one prostate cancer death
• Screening cost-effectiveness was $73,000 per quality-adjusted life-year gained
• Screening above age 63 not cost effective because of over-diagnosis

Prevalence of Prostate Cancer at Autopsy*

Unsuspected Prostate Cancers in Healthy Men Over Age 55 Years: Results of the Prostate Cancer Prevention Trial (PCPT)*

<table>
<thead>
<tr>
<th>Serum PSA level (at study entry)</th>
<th>Number of men biopsied from the placebo group</th>
<th>Number of men with prostate cancer**</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0-1.0 ng/mL</td>
<td>2196</td>
<td>357 (16.3%)</td>
</tr>
<tr>
<td>1.1-2.0 ng/mL</td>
<td>1647</td>
<td>457 (27.7%)</td>
</tr>
<tr>
<td>2.1-3.0 ng/mL</td>
<td>848</td>
<td>332 (29.3%)</td>
</tr>
<tr>
<td>3.1-4.0 ng/mL</td>
<td>1</td>
<td>1 (100%)</td>
</tr>
</tbody>
</table>

**63% of prostate cancer diagnoses made at end-of-study biopsy

Core Needle Biopsies of the Prostate
Random Sampling of the Peripheral Zone

biopsy #1: “positive” for cancer

biopsy #2: “negative” for cancer

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United States Food and Drug Administration Approval of a DNA (Methylation) Test for Prostate Cancer: Pivotal Registration Trial Data*

<table>
<thead>
<tr>
<th>Investigators</th>
<th>Study</th>
<th>Number of Men</th>
<th>Odd Ratio for Cancer on Second Biopsy</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steward GD et al. (2013)</td>
<td>MATLOC</td>
<td>498</td>
<td>3.17 (95% CI of 1.81-5.53)</td>
<td>90% (95% CI of 87-93)</td>
</tr>
<tr>
<td>Partin AW et al. (2014)</td>
<td>DOCUMENT</td>
<td>350</td>
<td>2.69 (95% CI of 1.60-4.51)</td>
<td>88% (95% CI of 85-91)</td>
</tr>
</tbody>
</table>

Prostate Cancer DNA, RNA, or Protein in Prostate Secretions/Urine: Can a New Molecular Test be Used for Prostate Cancer Screening/Early Detection?

* prostate cancer cell DNA, RNA, or protein
* urine test
* blood test

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Decline in Prostate Cancer Mortality: Result of PSA Screening?

- Prostate cancer mortality rates since 1995 are below those for 1986 when serum PSA testing was rare
- Mortality decline is attributable to a decrease in the incidence of advanced/metastatic prostate cancer
- Mortality rates are lowest in areas where the rates of advanced stage prostate cancer are lowest, and advanced stage prostate cancer is lowest in areas with highest PSA utilization
- 2 of 3 randomized clinical trials of prostate cancer screening have shown reductions in prostate cancer mortality
Active Surveillance of Low-Risk Prostate Cancer

Candidate men with prostate cancer for active surveillance
- low-risk (Gleason score ≤ 6) localized prostate cancer
- low-volume intermediate-risk (Gleason 3 + 4 = 7) prostate cancer

Active surveillance regimen
- serum PSA testing at 3-6 month intervals
- digital rectal examination (DRE) annually
- follow-up biopsies at 2-4 year intervals
- imaging and genomic tests were recommended only for discordant clinical and/or pathologic findings
- curative intervention reserved for men reclassified to a higher-risk category (Gleason score ≥ 7) and/or for men with an increase in the extent of low grade cancer on surveillance biopsies.

(Gleason score is the sum of the two most common grades)