Prostate Cancer
To Screen or Not To Screen - That is the Question

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Should either of these men be screened for prostate cancer using PSA?

• Mr. Jones is a 55 year old Caucasian who had a normal colonoscopy 5 years ago. He has never smoked and his LDL cholesterol is 120, HDL 55, triglycerides 135. His BMI is 26. He has no personal history of coronary artery disease.

• Mr. Smith is a 69 year old African American who has type 2 diabetes mellitus. He had an MI at age 60, with very successful bypass surgery. He is adherent to his medications, A1C is 7.0, LDL 80, HDL 40, triglycerides 150. He exercises regularly and has no angina.
Current USPSTF Recommendation

• Uncertain value for PSA
• Recommend against screening men age 75 and older


• The new recommendation published for public comment in November 2011 place PSA screening in category D.
• This recommendation is controversial and is under review for public comment.

The Evidence
European Study of Screening for Prostate Cancer

- Published 2009 in NEJM
- 162,387 men ages 55 to 69
- PSA every 4 years
- Cutoff of 2.5 to 4.0
- 20% relative risk reduction
- Needed to screen 1,410 to prevent one prostate cancer death
- 48 men treated to prevent one death
- No reduction in all cause mortality


US PLCO

- 76,693 men age 55 through 74
- Yearly screening PSA plus rectal exam
- PSA cut off of 4.0
- Prostate cancer mortality: 92 deaths in screened and 82 in the control group
- No significant difference in death rate
- BUT nearly 50% in control group had a PSA

Reconciling PLCO and European PSA Trials

• More cancers were detected in the screening arms of each trial.

• ERSPC had more power
  – 540 vs 174 CA deaths,
  – longer complete follow-up, 9 vs 7 years

• ERSPC: NNS = 1400, NNT = 48 for prostate cancer death

• PLCO: No benefit after 7 years follow-up; contamination reduced ability to detect benefit: 50% of controls had PSA

• Both: No reduction in all-cause mortality (RR 0.99 for ERSPC, RR 0.98 for PLCO) and no reduction in prostate CA deaths at 7 years

• Bottom Line: If there is benefit, it is small.

2010 Meta-analysis of PSA Screening

• 6 randomized trials comparing screening with no screening in asymptomatic men using several databases, including the Cochrane Registry of Controlled Trials.

• A single study provided 46% of the total number of patients.

• The diagnosis of prostate cancer was almost 50% more likely in the screened men.

• Study quality was only moderate for most of the studies. Four studies assessed the effect of screening on all-cause mortality, finding no benefit to screening when patients were followed up from 9 years to 14 years.

• Death from prostate cancer was also not decreased by screening, though there was heterogeneity among the studies.

• Bottom Line: In the past 4 years, the results from 4 randomized studies enrolling more than 350,000 men found that screening for prostate cancer with prostate-specific antigen testing in asymptomatic men does not decrease all-cause or prostate cancer-related mortality.
Prevention of Prostate Cancer

- Vitamin C, Vitamin E and selenium don’t work
  - 14,641 male physicians in the United States, 50 years or older, for the Physicians' Health Study II on the individual clinical effects of supplemental vitamins E and C.
  - Eligible men randomly received either (concealed allocation assignment) vitamin E (400 IU/day) and vitamin C (500 mg/d), either vitamin alone with a placebo, or double placebo.
  - Complete follow-up occurred for 98% of men at 8 years.
  - Neither vitamin E or C had any significant effect on the incidence of prostate cancer, total cancer, or all-cause mortality. Neither vitamin significantly reduced the individual incidence of colorectal, lung, bladder, or pancreatic cancer.
  - In secondary outcome analyses, vitamin E was associated with a significantly increased risk of hemorrhagic stroke.
  - A related article in the same journal (Lippman SM, et al. JAMA 2009;301:39-51) also reported that neither selenium nor vitamin E, alone or together, reduced the risk of prostate cancer.

Treatment of Symptomatic Prostate Cancer

- 695 men with localized prostate cancer
- Radical prostatectomy vs “watchful waiting”
- Followed up for median of 13 years
- All cause mortality benefit: 46.1% vs 52.7%, NNT = 13


Minimally Invasive vs. Open Radical Prostatectomy

- In the United States, the use of robotic-assisted MIRP has increased from 1% to 40% of all radical prostatectomies performed from 2001 to 2006.

- These investigators analyzed data from an observational cohort study from 2003 through 2007 using Medicare-linked information from men with prostate cancer undergoing either MIRP (n = 1938) or RRP (n = 6899).

- Various analyses were performed to control for baseline differences including urinary incontinence, erectile dysfunction, age, race, household income, and additional comorbid medical conditions.

- Men undergoing MIRP experienced shorter length of stay, less need for blood transfusion, lower risk of postoperative respiratory complications, and stricture formation. However, the men undergoing MIRP also experienced more genitourinary complications, including postoperative incontinence and erectile dysfunction.

- The need for additional cancer therapy was similar with either surgical approach, suggesting no difference in survival benefit.

New USPSTF Prostate Cancer Screening Guidelines

- Proposed October, 2011

- D Recommendation – against screening

- Why?
USPSTF Press Release

LeFevre said that for every 1,000 men treated for prostate cancer, five die of perioperative complications; 10-70 suffer significant complications but survive; and 200-300 suffer long-term problems, including urinary incontinence, impotence or both.

"That's a lot of harm for a cancer that didn't need to be treated in the first place," he said.

The task force acknowledged in its recommendation that there is convincing evidence that PSA-based screening results in the detection of many cases of asymptomatic prostate cancer.

However, the USPSTF noted, the majority of men who have asymptomatic cancer detected by PSA screening have a tumor that meets histological criteria for prostate cancer, but that tumor either will not progress or is so indolent and slow-growing that it will not affect the men's lifespans or cause adverse health effects because the men are likely to die of other causes first.

"The evidence is convincing that for men aged 70 years and older, screening has no mortality benefit," the task force wrote. "For men aged 50 to 69 years, the evidence is convincing that the reduction in prostate cancer mortality 10 years after screening is small to none. Ninety-five percent of men with PSA-detected cancer who are followed for 12 years do not die from that cancer, even in the absence of definitive treatment."

LeFevre said the recommendation likely won't stop some physicians from offering screening, and it won't stop some patients for asking for it.

"While the USPSTF discourages screening tests for which the benefit does not outweigh the harms, we certainly understand this test is in wide use," he said. "If an individual man asks me for it, I'll respond with a balanced discussion about what we don't know, which is whether there is any benefit, and what we do know, which is that there are significant harms. I'll still order the test if a man who knows the evidence says he still wants it."

Young, Healthy Men Might Benefit?

- Re-analysis of the US PLCO trial
  - Purpose. Estimates of prostate cancer–specific mortality (PCSM) were similar for men randomly assigned to intervention compared with usual care in the PLCO study. However, results analyzed by comorbidity strata are unknown.
  - Patients and Methods. Between 1993 and 2001, of 76,693 men who were randomly assigned to usual care or intervention at 10 US centers, 73,378 (96%) completed a questionnaire that inquired about comorbidity and prostate-specific antigen (PSA) testing before random assignment. Fine and Gray's multivariable analysis was performed to assess whether the randomized screening arm was associated with the risk of PCSM in men with no or minimal versus at least one significant comorbidity, adjusting for age and prerandomization PSA testing.
  - Results. After 10 years of follow-up, 9,565 deaths occurred, 164 from prostate cancer. A significant decrease in the risk of PCSM (22 v 38 deaths; adjusted hazard ratio [AHR], 0.56; 95% CI, 0.33 to 0.95; P = .03) was observed in men with no or minimal comorbidity randomly assigned to intervention versus usual care, NNT of 5 to prevent one PC death at 10 years. Among men with at least one significant comorbidity, those randomly assigned to intervention versus usual care did not have a decreased risk of PCSM (62 v 42 deaths; AHR, 1.43; 95% CI, 0.96 to 2.11; P = .08), a possible increase in PCSM.
  - Conclusion. Selective use of PSA screening for men in good health appears to reduce the risk of PCSM with minimal overtreatment. Use in high risk men might cause harm.

Comorbidity and Mortality Results From a Randomized Prostate Cancer Screening Trial Journal of Clinical Oncology. February 1, 2011 vol. 29 no. 4 355-361
Discussing PSA Screening with Patients

- The Ask-Tell-Ask Method
  - Based on some of the concepts and techniques of motivational interviewing and allows for eliciting and using the patient’s stage of change during the discussion of prostate cancer screening.
  - Ask: Have you thought about whether you want to be screened?
    - What have you heard about screening?
    - What would you like to know before making a decision?
  - Tell: The PSA test results may be less clear than other tests we do. Many positive test results are actually false positive, which can cause anxiety and lead to unnecessary biopsies. Some men die of prostate cancer, but sometimes this type of cancer is slow growing and does not cause any symptoms. Treatment can remove the cancer, but may lead to long-term side effects.
  - Ask: So, does screening for prostate cancer sound like something you’d be interested in? Based on what you’ve told me, it sounds like we should (test/not test). Does that sound right to you?

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