As of May 2012, the USPTF gave a “D” recommendation for PSA screening, meaning that PSA screening of US males was not recommended.

Most randomized studies failed to show that PSA screening of asymptomatic men significantly prolonged life. (PSA is sensitive but not specific)

Prostate cancer detected by PSA is often (80%) indolent and not likely to cause death within a ten year interval. (length time bias)
The majority of US adult men are aware of and concerned about prostate cancer

- In 2012, 1 in 6 US men will be diagnosed with prostate cancer (240,000) (NCCN)
- It is the second leading cause of cancer death in US males (28,000/yr die of prostate cancer) (NCCN)

PSA is the most sensitive way to detect it

- Seer data analysis suggests that the number of US men presenting with metastatic disease would rise 300% if no PSA testing was done. (Messing et al., Cancer, 2012)
- Risk management issues have been reported when a patient requests a PSA and it is not done and advanced prostate cancer is subsequently found.
The only useful test to diagnose prostate cancer and predict death from it, is a biopsy, to determine Gleason Score. (GRADE)

Prostate biopsies carry the risk of pain, bleeding, possible infection, and death.

In US men aged 50 – 65 with Gleason less than 8: 20% risk of dying of prostate cancer, but Gleason greater than 8 yields a 60-70% risk of dying of prostate cancer. (CaEpidemBiomPrev 5/11)

Over 80% of biopsies done for elevated PSA show a Gleason less than 8. (Prost.Ca.Res.Inst.)

Gleason score of 6 is no guarantee of indolence, as all cancer eventually dedifferentiates.

Surveillance re-biopsies of Gleason 6 prostate cancer patients, at 12-18 month intervals, has been shown to detect an increase in Gleason score in 30% of these patients within 5 years. (JNCCN)

NCCN recommends consideration of active surveillance based on careful consideration of the patient’s prostate cancer risk, profile, age and health. (PCPT)
The PSA Controversy – Defining It, Discussing It and Coping With It

- NCCN guidelines state that serial PSA testing is likely to be optimal when used for early (start at age 40) detection in high risk populations, if in otherwise good general health. (greater than 10 year survival)

- High risk groups include African American, patients with first degree relations with prostate cancer.

- Patients on 5Alpha reductase inhibitors who fail to achieve a significant PSA decrease can also indicate a heightened risk for cancer.

How to Cope with the PSA Controversy

1. Shared decision making on the part of patient and physician, acknowledging risks and benefits.

2. Dedicated W.H. Multidisciplinary GU tumor board including urology, radiotherapy, oncology, pathology and radiology.

3. Nurse navigator helps patients obtain appropriate opinions.
Case Presentations

- 75 yo asymptomatic man presenting with a request for CaP screening
- 55 yo asymptomatic man presenting with a request for advise on whether or not he should be screened for CaP

Willet Whitmore MSKCC 1973

- For men in whom cure is possible it may not be necessary, while for men in whom cure is necessary, it may not be possible
- 2013: the way forward CaP risk stratification not all prostate cancer are created equal
- Shared decision making
What is PSA?

- A reproductive glycoprotein produced by prostatic acini
- Most PSA is released in the semen
- A small percentage is released into the bloodstream
- Serum PSA levels are reflective of prostate gland activity
- PSA levels are NOT CaP specific
What Clinical Circumstances Can Lead to PSA Elevation??

- Benign enlargement of the prostate
- Infection in the urinary tract (weeks)
- Urinary retention with instrumentation (weeks)
- Prostate biopsy (months)
- TURP (months)
- Ejaculation low level elevation (48hrs)
- No significant elevation post DRE

PSA History 1986

- FDA approved 1986 for monitoring of CaP progression
- Later approved for the detection of disease in symptomatic men
Ongoing Trials

- PLCO
- ERSPC
- PIVOT US Prostate Intervention vs Observation 5/11
- ProtecT UK Prostate testing for cancer and treatment trial
Overdiagnosis/Overtreatment
What are the Numbers??

- Since 1986 >1.3 million men dx
- Since 1986 >1.0 million men treated
- Assume that all of the 40% decline in US CaP mortality rate since 93 is attributable to screening
- For each man who experienced the presumed benefit more than 20 had to be diagnosed with CaP


What are the Recommendations?

Consider the varying viewpoints: What are the recommendations?

<table>
<thead>
<tr>
<th>Organization</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Urological Association (AUA)</td>
<td>The AUA recommends that doctors offer a baseline PSA test to men who wish to be screened at age 40. It also encourages men who expect to live at least another 10 years to discuss the risks and benefits of PSA testing with their doctors.</td>
</tr>
<tr>
<td>American Cancer Society (ACS)</td>
<td>The ACS recommends that men consult with their doctors to make a decision about PSA testing. According to the ACS, men should explore the risks and benefits of the PSA test starting at age 50 if they are at average risk of prostate cancer, at age 45 if they are at high risk and at age 40 if they are at very high risk (those with several first-degree relatives who had prostate cancer at an early age).</td>
</tr>
<tr>
<td>Centers for Disease Control and Prevention (CDC)</td>
<td>The CDC recommends against PSA-based screening for men who do not have symptoms, but supports discussions between men and their doctors to make informed decisions about screening based on individual risks and preferences.</td>
</tr>
</tbody>
</table>
What are the Recommendations?

U.S. Preventive Services Task Force (USPSTF)

The USPSTF recommends against PSA-based screening, regardless of age. The USPSTF states that there is moderate to high certainty that PSA testing has no net benefit or that harms outweigh benefits.

American College of Preventive Medicine (ACPM)

The ACPM recommends that a man decide about whether to have PSA testing after discussing the risks and benefits with his doctor. The ACPM considers the need for screening questionable in older men with other chronic illnesses and men with life expectancies of fewer than 10 years.

Institute for Clinical Systems Improvement (ICSI)

The ICSI states that, while there is good evidence that PSA screening can detect early-stage prostate cancer, there is mixed or inconclusive evidence to clearly determine whether early detection improves health outcomes. It recommends that a man decide what’s right for him based on talking with his doctor.

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Pros and Cons of PSA Screening

Pros of PSA screening

PSA screening may help you detect prostate cancer early.

Cancer is easier to treat and is more likely to be cured if it’s diagnosed in the early stages of the disease.

PSA testing can be done with a simple, widely available blood test.

For some men, knowing is better than not knowing. Having the test can provide you with a certain amount of reassurance — either that you probably don’t have prostate cancer or that you do have it and can now have it treated.

The number of deaths from prostate cancer has gone down since PSA testing became available.

Cons of PSA screening

Some prostate cancers are slow growing and never spread beyond the prostate gland.

Not all prostate cancers need treatment. Treatment for prostate cancer may have risks and side effects, including urinary incontinence, erectile dysfunction or bowel dysfunction.

PSA tests aren’t foolproof. It’s possible for your PSA levels to be elevated when cancer isn’t present, and to not be elevated when cancer is present.

A diagnosis of prostate cancer can provoke anxiety and confusion. Concern that the cancer may not be life-threatening can make decision making complicated.

It’s not yet clear whether the decrease in deaths from prostate cancer is due to early detection and treatment based on PSA testing or due to other factors.
Virginia Lawsuit 03

- Family medicine resident during routine annual physical exam 53 yr old presented and documented risks/benefits of PSA screening
- Later PSA ordered by another MD eventually high risk GS 8/10 dx diagnosed
- 2 yr after first visit patient deceased
- Resident and residency program sued
- Plaintiff’s atty attacked the concept of evidence based medicine claimed EBM used solely as a means of “cost cutting”
- Residency program liable for $1 million
- JAMA 2004 Jan 7; 291(1):15-16

Male Life Expectancy from Birth 2009
US Census Bureau, International Data Base

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<thead>
<tr>
<th>Country</th>
<th>Male Life Expectancy (Years)</th>
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<tr>
<td>Australia</td>
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<tr>
<td>New Zealand</td>
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<tr>
<td>Ireland</td>
<td>75.6</td>
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</tbody>
</table>
CaP Prevention

- Low fat diet
- More plant based proteins/fats than animal
- Increase fruit and vegetable intake
- Eat fish
- Reduced dairy product intake
- Add soy to diet
- Drink green tea
- Maintain a healthy weight
- Exercise most days of the week

PCPT Prostate Ca Risk Calculator

Individualized Risk Assessment of Prostate Cancer

[Formula or calculator interface]
What is needed 2013??

- Better biomolecular and genetic markers that will separate the indolent CaPs from the virulent/biologically significant ones!!!!!!
- mRNA products in the urine
- Likely an array of multiple biomolecular marker and genetic markers
Active Surveillance with Curative Intent

- Favorable risk patients = cT1c, Gleason’s grades 6 or less, < 4/12 cores involved, no core > 40% involved, PSA < 10, PSADT > 2 yrs
- Repeat bx at least within 1 yr of dx
- Intervention for increasing grade or lowering of PSADT
- Delayed surgical intervention does not appear to compromise curability (Carter, JNCI 3/06)
- Americans in general have had a hard time accepting this management plan!!

WH CaP Last 100 Cases 2012

- 40 low risk (very favorable plus favorable)
- 39 intermediate risk
- 21 high risk
- 6 presenting with mets
WH CaP Last 100 Cases 2012

- 45 active surveillance
- 12 robotic lap radical prostatectomy
- 18 some form of radiation +/- ADT
- 6 androgen deprivation tx (ADT) alone
- 2 undecided or homeopathic
- 17 left the institution