Serum PSA for the Early Detection, Assessment and Monitoring of Prostate Cancer

Rational or Risky?

I recommend prostate cancer early detection to well informed, healthy men

1. Yes
2. No
3. Sometimes

- Yes: 56%
- No: 13%
- Sometimes: 31%
### Prostate Cancer - Then vs. Now

- Little formal screening
- Tumors advanced
- Often under-staged, -graded
- Natural history poorly predicted
- Limited treatment options
- One form of systemic therapy
- Higher death rate
- Widespread screening, re-screening
- Considerable stage/grade migration
- Natural history better predicted
- Less under-staging, grading
- Many options
- Mortality declining
- Increasing number of systemic therapies

### Prostate Cancer - Then and Now

- Great controversy on the risks and benefits of screening
- No consensus as to what constitutes the best form of treatment for virtually any stage and grade of disease
A Continuum of Controversy (and Opportunity)

- Early Detection - Rationale or Risky?
- Risk Assessment - Reasonably Good or Reasonably Bad?
- Treatment - Appropriate and Effective or Arbitrary, Morbid or Ineffective?

PROSTATE CANCER

Important Questions

- Should I Be Screened?
- If I Undergo Screening and I Have Cancer, Should I Be Treated?
- If I Want To Be Treated, How Should I Be Treated?
- If I Am Treated, What Can I Expect?
  - Cancer Cure
  - Side Effects
Rationale for Screening

- Burdensome disease when detected late
- No cure for very late stage disease
- PSA screening detects disease at earlier stage
- Such screening may account for reduction in mortality noted
- Screening in ERSPC associated with 20% reduction in disease specific mortality
- Treatment may reduce mortality


Why Not Discourage Screening Given PLCO Trial?

- Large Number Pre-screened
- Heavy Contamination of Control Group
- Follow-up Limited
- Used Single Cut-Point

Screening and Prostate-Cancer Mortality in a Randomized European Study

182,160 Subjects 50–74 yr old underwent randomization
162,387 Were in the core age group (55–69 yr old)

160 Subjects 50–74 yr old died
144 Were 55–69 yr old

82,816 Were assigned to the screening group
72,890 Were 55–69 yr old

99,184 Were assigned to the control group
89,333 Were 55–69 yr old

6830 Had prostate cancer
5970 Were 55–69 yr old

4781 Had prostate cancer
4107 Were 55–69 yr old

NEJM 360:1320-1328
ERSPC - Conclusions

- Reduction in mortality shown conclusively
- However, to save one man’s life
  - 1068 men screened
  - 48 treated
Prostate Cancer Mortality Reduction by Prostate-Specific Antigen–Based Screening Adjusted for Nonattendance and Contamination in the European Randomised Study of Screening for Prostate Cancer (ERSPC)

A Dilemma?

- Reduction in Mortality
- Over-detection/
- treatment

Risk Reduction

Eur Urol, 2009
PROSTATE CANCER

PSA - Concerns

- Most Men with PSA Values Between 4 and 10 ng/ml Do Not Have Cancer
- Prostate Biopsy Associated with Limited, but Significant, Resource Utilization (Psychological, Physical, and Monetary)
- Improvements in Specificity Would Decrease Resource Utilization
- Impact of Treatment Poorly Defined

Notable Revisions

- The age for obtaining a baseline PSA has been lowered to 40 years
- No longer recommends a single, threshold value of PSA, which should prompt prostate biopsy
- The decision to proceed to prostate biopsy should be based primarily on PSA and DRE results, but should take into account multiple factors
  - free and total PSA
  - patient age
  - PSA velocity and density
  - family history
  - ethnicity
  - prior biopsy history
  - comorbidities
2000 Guidelines - 2009 Changes

Candidates for early detection testing:
- Baseline PSA age 40 years with anticipated lifespan of 10 or more years
- Men age 50 or more with an anticipated lifespan of 10 or more years
- Men age 40-49 with a family history of prostate cancer or African-American ethnicity

Maintained DRE

What tests should be offered?
- Prostate-specific antigen (PSA)
- Digital rectal examination (DRE)

Test results
- One or more tests is high risk
  - Possible causes: prostate cancer, BPH, prostate
- Both results are low risk
  - Return regularly for PSA and DRE testing, depending on risk
- Biopsy negative

Biopsy positive
- For definite diagnosis: prostate biopsy

More Formally Acknowledge Risks Of Overdetection

Biopsy not done
- Biopsy done, extended, local anesthesia
  - Management discussion and risk assessment
  - Active surveillance or Treatment

Guidelines 2009

Candidates for early detection testing:
- Baseline PSA age 40 years with anticipated lifespan of 10 or more years

What tests should be offered?
- Prostate-specific antigen and Digital rectal examination

Family history, race, PSA history, prior biopsy

1. DRE abnormal/PSA low for age (consider possible causes: prostate cancer, BPH, infection, trauma, etc)
2. PSA high for age or
3. DRE abnormal and PSA high

Both tests are low/not suspicious
- Return regularly for PSA and DRE

Counsel patient regarding both risks and benefits of biopsy

Biopsy not done
- Biopsy positive

Active surveillance or Treatment
Rationale for Earlier Screening

- A baseline PSA level above the median for age 40 is a strong predictor of prostate cancer
- The age adjusted mortality rate for prostate cancer between ages 55 and 64 is significant. Such men may have been cured by earlier diagnosis and treatment
- Younger men are more likely to have curable cancer
- PSA is a more specific test for cancer in younger men
- Earlier and less frequent testing might reduce mortality and costs compared to annual testing beginning later
- Men at risk of, but do not have prostate cancer may be candidates for chemoprevention


Screening at Earlier Ages

Fig 2. Predicted probability of a prostate cancer diagnosis before age 75 years by population-based centiles of prostate-specific antigen (PSA) measured at age 44 to 50 years, with 95% CIs.

JCO 25:431
Where to Set Cut - Point?

- Do we use single cut-point, age-stratified cut-point?
- No PSA level that is not associated with some risk
- May view serum PSA as a continuum and over time
- Integrate with other risk factors

<table>
<thead>
<tr>
<th>Age</th>
<th>Race</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Caucasian</td>
</tr>
<tr>
<td>40-49</td>
<td>2.5</td>
</tr>
<tr>
<td>50-59</td>
<td>3.5</td>
</tr>
<tr>
<td>60-69</td>
<td>4.5</td>
</tr>
<tr>
<td>70-79</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Oesterling JE. JAMA 1993; 270:360
Morgan TO. NEJM 1996; 335:304

Results from Prostate Cancer Prevention Trial

<table>
<thead>
<tr>
<th>PSA</th>
<th># Positive</th>
<th># Biopsied</th>
<th>% +ve Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4.0</td>
<td>449</td>
<td>2950</td>
<td>15.2%</td>
</tr>
<tr>
<td>≤0.5</td>
<td>32</td>
<td>486</td>
<td>6.6%</td>
</tr>
<tr>
<td>0.6-1</td>
<td>80</td>
<td>791</td>
<td>10.1%</td>
</tr>
<tr>
<td>1.1-2.0</td>
<td>170</td>
<td>998</td>
<td>17.0%</td>
</tr>
<tr>
<td>2.1-3.0</td>
<td>115</td>
<td>482</td>
<td>23.9%</td>
</tr>
<tr>
<td>3.1-4.0</td>
<td>52</td>
<td>193</td>
<td>26.9%</td>
</tr>
</tbody>
</table>

### Gleason Score 7 and Above

<table>
<thead>
<tr>
<th>PSA</th>
<th># GS ≥7</th>
<th># Positive</th>
<th>% GS ≥7</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4.0</td>
<td>67</td>
<td>449</td>
<td>14.9%</td>
</tr>
<tr>
<td>≤0.5</td>
<td>4</td>
<td>32</td>
<td>12.5%</td>
</tr>
<tr>
<td>0.6-1.0</td>
<td>8</td>
<td>80</td>
<td>10.0%</td>
</tr>
<tr>
<td>1.1-2.0</td>
<td>20</td>
<td>170</td>
<td>11.8%</td>
</tr>
<tr>
<td>2.1-3.0</td>
<td>22</td>
<td>115</td>
<td>19.1%</td>
</tr>
<tr>
<td>3.1-4.0</td>
<td>13</td>
<td>52</td>
<td>25.0%</td>
</tr>
</tbody>
</table>

GS=Gleason Score

### The Impact of Multiple Factors

![Graph showing the impact of multiple factors on PSA levels](image-url)
Rationale for Including Multiple Risk Factors
*Single Cut Point/DRE vs. Calculator*

<table>
<thead>
<tr>
<th>Age</th>
<th>Race</th>
<th>PSA</th>
<th>DRE</th>
<th>Family History</th>
<th>Risk</th>
<th>Risk High Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>White</td>
<td>0.3</td>
<td>Pos.</td>
<td>Neg.</td>
<td>13%</td>
<td>1%</td>
</tr>
<tr>
<td>55</td>
<td>Black</td>
<td>2.4</td>
<td>Neg.</td>
<td>Pos.</td>
<td>31%</td>
<td>8%</td>
</tr>
<tr>
<td>73</td>
<td>Black</td>
<td>2.4</td>
<td>Neg.</td>
<td>Pos.</td>
<td>31%</td>
<td>13%</td>
</tr>
</tbody>
</table>

J Urol 180:1219

**TRUS - Guided Biopsy**
Detection Rates of Systematic Schemes

1990 - 2007

Number of Prostate Biopsies

<table>
<thead>
<tr>
<th>Year</th>
<th>&gt;12 cores</th>
<th>7-12 cores</th>
<th>&lt;7 cores</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990-1994</td>
<td>71.6%</td>
<td>28.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>1995-1999</td>
<td>56.7%</td>
<td>40.5%</td>
<td>2.8%</td>
</tr>
<tr>
<td>2000-2001</td>
<td>34.7%</td>
<td>54.5%</td>
<td>10.8%</td>
</tr>
<tr>
<td>2002-2003</td>
<td>22.8%</td>
<td>66.0%</td>
<td>11.2%</td>
</tr>
<tr>
<td>2004-2007</td>
<td>14.0%</td>
<td>73.3%</td>
<td>12.7%</td>
</tr>
</tbody>
</table>
PROSTATE CANCER
Improve PSA Performance

- PSA Density
- PSA Velocity
- Age-Specific Reference Ranges
- Molecular Forms of PSA (Free/Total/HK2)

PCA3 continuous score predicts positive repeat biopsy

PCA3 score more diagnostic than tPSA and was independent of number of previous biopsies, age, prostate volume and total PSA

Variations in testing

• PSA derivatives (i.e. PSAV, PSAD, PSADT) correlate with PSA and do not improve operating characteristics enough to likely replace PSA
• PSAC, AMACR, EPCA, EPCA - 2, HK2, hepsin, GSTPI are undergoing validation
• New approaches - autoantibody signatures, proteomic and genomic undergoing discovery and validation
• All require standardized evaluation and validation

Unresolved Issues

• Frequency of testing
• Impact of DRE
• Over - detection and resultant over - treatment
• Impact of hypersensitive PSA values; variation in cut - points for recurrence
Early Detection

- **Past**
  - Single PSA cutpoint (4 ng/dl)
  - Sextant biopsy
  - Understaging common
- **Recent Past**
  - Cutpoint lowered (2.5 ng/dl)
  - Extended core
  - Less understaging
- **Present**
  - No single cutpoint
  - More cores
  - Frequent testing and biopsy
  - Emerging markers (PCA - 3)
- **Future**
  - As above
  - Add germline or other risk factors

PSA alone as a mass screening tool

- Case control study
- PSA a robust marker
- AUC 0.84
- Sens., spec. at cutpoints of 3, 4 and 5 were 59, 44, 33% and 87, 92, 95%
- Pos. likelihood ratios of 10 and negative likelihood ratios of 0.1 normally accepted for mass screening

BMJ 2009; 339:b3537
Risk Assessment and Risk Migration

Prostate Cancer Risk Assessment

- **Goal**: inform physician-patient decisions about optimal initial treatment approach and timing

- Numerous existing instruments
  - D’Amico
  - Kattan
  - UCSF-CAPRA

- Treatment options:
  - Active surveillance
  - Early local therapy
  - Multimodal therapy
  - Systemic therapy
Objectives of Risk Assessment

- Predict
  - Biochemical Failure
    - *Indolent*
    - *Clinically Important*
  - Bone Metastases
  - Prostate Cancer Mortality
  - Overall Mortality

Prostate Cancer Assessment

- Gleason Grade
- TNM Stage (Volume)
- Serum PSA
**Risk Assessment: D’Amico / AUA**

- **Low**
  - PSA ≤10, GS ≤6, and stage T1-2a

- **Intermediate**
  - PSA 10-20, GS 7, or stage T2b

- **High**
  - PSA >20, GS ≥8, or stage T2c / T3a

D’Amico et al. JAMA 1998; 280:969

**Performance in CaPSURE**

Kattan Nomogram Values by Clinical Risk Group

### The UCSF-CAPRA

<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA</td>
<td>2.0-6</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>6.1-10</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>10.1-20</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>20.1-30</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>&gt;30</td>
<td>4</td>
</tr>
<tr>
<td>Gleason</td>
<td>1-3/1-3</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>1-3/4-5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>4-5/1-5</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-stage</td>
<td>T1/T2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>T3a</td>
<td>1</td>
</tr>
<tr>
<td>% pos bx</td>
<td>&lt;34%</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt;34%</td>
<td>1</td>
</tr>
<tr>
<td>Age</td>
<td>&lt;50</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>1</td>
</tr>
</tbody>
</table>

Sum of points from each variable for 0-10 score


### The UCSF-CAPRA: bRFS

![Graph showing Kaplan-Meier survival curves with CAPRA scores]

Cooperberg et al. Cancer 2006; 107:2384
## Validation: Early outcomes

<table>
<thead>
<tr>
<th></th>
<th>Positive Margins</th>
<th>Extracapsular Extension</th>
<th>Seminal Vesicle Invasion</th>
<th>Lymph Node Involvement</th>
<th>PSA Recurrence-Free Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>CaPSURE¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.5 (1.4-1.6)</td>
</tr>
<tr>
<td>SEARCH²</td>
<td>1.3 (1.1-1.5)</td>
<td>1.4 (1.2-1.5)</td>
<td>1.8 (1.6-2.0)</td>
<td>1.4 (1.3-1.5)</td>
<td>1.6 (1.5-1.7)</td>
</tr>
<tr>
<td>Berlin³</td>
<td>1.6 (1.3-1.9)</td>
<td>1.7 (1.6-1.9)</td>
<td>1.8 (1.7-1.9)</td>
<td>1.9 (1.8-2.1)</td>
<td></td>
</tr>
<tr>
<td>JHU⁴</td>
<td>1.4 (1.3-1.4)</td>
<td>1.7 (1.6-1.8)</td>
<td>1.8 (1.7-1.9)</td>
<td>1.9 (1.8-2.1)</td>
<td></td>
</tr>
</tbody>
</table>

- Each 2-point increase in CAPRA score indicates roughly a doubling of risk

3. May et al. J Urol 2007; 178:1957 (includes PSA 0-2 as 0 points)
4. Zhao et al. Urology 2008; epub ahead of print (no PPB data; CAPRA 0-9)

## Validation: 5-year bRFS

<table>
<thead>
<tr>
<th>CAPRA score</th>
<th>CaPSURE¹ N=1439</th>
<th>SEARCH² N=1346</th>
<th>Berlin³ N=1296</th>
<th>Hopkins⁴ N=6737</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>85 (73-92)</td>
<td>86 (80-91)</td>
<td>97 (91-100)</td>
<td>94 (93-95)</td>
</tr>
<tr>
<td>2</td>
<td>81 (69-89)</td>
<td>75 (68-80)</td>
<td>92 (88-96)</td>
<td>87 (86-89)</td>
</tr>
<tr>
<td>3</td>
<td>66 (54-76)</td>
<td>65 (57-71)</td>
<td>76 (70-82)</td>
<td>79 (76-82)</td>
</tr>
<tr>
<td>4</td>
<td>59 (40-74)</td>
<td>60 (51-69)</td>
<td>67 (59-75)</td>
<td>56 (50-61)</td>
</tr>
<tr>
<td>5</td>
<td>60 (37-77)</td>
<td>52 (40-63)</td>
<td>42 (33-52)</td>
<td>53 (46-59)</td>
</tr>
<tr>
<td>6</td>
<td>34 (12-57)</td>
<td>29 (17-41)</td>
<td>37 (25-49)</td>
<td>38 (30-47)</td>
</tr>
<tr>
<td>≥7</td>
<td>8 (0-28)</td>
<td>20 (10-32)</td>
<td>31 (21-39)</td>
<td>26 (16-37)</td>
</tr>
</tbody>
</table>

C-index: 0.66 0.68 0.81 0.76

3. May et al. J Urol 2007; 178:1957 (includes PSA 0-2 as 0 points)
4. Zhao et al. Urology 2008; epub ahead of print (no PPB data; CAPRA 0-9)
Face validity: treatment by CAPRA

Bone metastases

C-index = 0.78
Cancer-specific survival

C-index = 0.80

Overall survival

C-index = 0.71

Cooperberg et al. AUA 2008, abstract #321
PROSTATE CANCER
Where Has PSA Gotten Us?

- Detection Rates
- Stage Migration
- Cost
  - Psychological
  - Physical
  - Monetary
- Mortality

Trends in PSA at diagnosis
Trends in clinical T stage

Trends in % of biopsies +
Risk Migration

Cooperberg et al. J Urol

Excess Diagnoses - Younger Men

JNCI Online August 31
Excess Diagnoses - Younger Men

Decreasing Prostate Cancer Specific Mortality
Prostate Cancer
Treatment Options

Why are there so many and how is a man to choose?

Treatment Options

- Radical Prostatectomy
  - Open, laparoscopic or robotic
  - With/without lymph node dissection
- Radiation
  - External, IMGT
  - Protons
  - Brachytherapy
  - Combinations
- Ablative Therapy
  - Focal or whole gland
  - Cryotherapy, HIFU, radiofrequency
- Active Surveillance
- Androgen Deprivation
- Chemotherapy
- Novel Therapy
- Complementary Therapy
Radical Prostatectomy vs. Watchful Waiting

Bill-Axelson, A. et al. Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer. NEJM, 2005

- CaP specific mortality in WW group <65 yrs highest at ~ 19.2%
- Only 5% men diagnosed from screening
- Significant number of intermediate and high risk disease

Treatment - the basics

- Prostate cancer is an androgen sensitive disease - treatment with LHRH agonists alone or combination with anti - androgens indicated in -
  - Men with metastatic disease (or at near risk of it)
  - Men with intermediate and high risk, non - metastatic disease treated with radiation
- Many radiation techniques available - brachytherapy, protons, IMGRT
- Patients with low stage disease are candidates for a variety of treatments
- All treatments have side effects - often under estimated
  - Bowel, bladder, sexual
Side Effects of ADT

- Hot flashes\(^1\)
- Loss of libido\(^1\)
- Decreased sexual performance\(^1\)
- Weight gain\(^1\)
- Decreased muscle mass\(^1\)
- Anemia
- Accelerated osteoporosis\(^1\)
- Decreased cognitive function\(^2\)
- Increased DM\(^1\)
- Altered lipid profile\(^1\)
- Increased CV risk\(^1\)


Treatment Trends
Treatment Trends
Risk - Stratified

RADICAL PROSTATECTOMY
Technique
Increased Incidence of Very Low Risk Prostate Cancer

- Lead Time Bias
- Rates of Prostate Cancer Detected on Autopsy Decreasing*
- Increasing Percentage of Men Identified on Screening to Have Very Low Risk Disease
- Increasing Treatment of Men with Very Low Risk Disease

J Urol 174: 1785
Use of Active Surveillance

Lowrisk Treatment: Age ≥75
Evolution of Watchful Waiting
Active Surveillance

- Old
  - Less well assessed
  - Usually more advanced
  - Monitoring not rigid/planned
  - Treatment delayed until clinically significant, symptomatic disease noted
  - Managed with androgen deprivation

- New
  - Patients well assessed
  - Early stage disease
  - Monitored closely
  - Treatment at first sign of progression
  - Treated based on risk; local therapy

Treatment - free Survival
Less of a Dilemma?

Reduction in Mortality

Over - detection/Selective - treatment

Variation in CaP Treatment

Figure 5.1. Profiles of Surgical Variation for Ten Common Surgical Procedures (1986-96)

Treatment Variation in CaPSURE

[Graph showing treatment variation with different colors representing various treatment methods.]

Mean CAPRA score among low-risk patients per site
Sites with at least 30 patients

[Graph showing mean CAPRA score distribution.]
Variation due to site (provider)

Prostate Cancer Treatment
Evolution or Revolution?

- Smaller, lower volume cancers - more focal disease
- Rapid advances in molecular characterization and in imaging
- More selective treatment
Systemic Therapy - ASCO Themes

- More agents, alone or in combination
- Novel agents, often pathway specific
- Greater understanding of biology

New Therapeutic Agents for Prostate Cancer (cont)

Bone Targeted Agents
- Isotopes: alpharadin* (radium-223)
- RANK ligand/OPG: denosumab*
- ER-alpha: toremifene*

Endothelin antagonist
- Atrasentan* and ZD4054*

Stem cell targeted
- Anti-Prostate stem cell antigen (PSCA)
- Sonic hedgehog (eg, cyclopamine

Prostate specific surface targets
- Anti-PSMA (eg, J591, 7E11, MLN2704)

Chemotherapeutic resistance and apoptotic regulator
- Anti-Clusterin (OGX-11* or custirsen)

HDAC inhibitors
- Multiple compounds from multiple companies (eg, vorinostat, panobinostat)

*In phase III study.
New Therapeutic Agents for Prostate Cancer

Vaccines and Immune Stimulants
- GM-CSF transduced tumor cells (GVAX)*
- Sipuleucel-T (Provenge)*
- GM-CSF (Leukine)
- Anti-CTLA4 (MDX-010)

Angiogenesis Inhibitors
- Lenalinomide (Revlimid)
- Bevacizumab (Avastin)*
- VEGF TRAP (Aflibercept)*
- Anti-VEGF receptor targeted drugs (multiple)

Chemotherapeutics
- Epothilones and other anti-tubular agents (XRP6258)*
- Satraplatin*

Newer Androgen-Signaling Targeted Therapies
- HSP90 inhibitors (eg, geldanamycin, 17-AAG, IPI-504)
- Androgen synthesis (abiraterone)*
- AR blockade (MDV3100, BMS 641988)

Newer Signal Transduction Inhibitors
- PI3 Kinase (Exelexis XL147, Novartis BEZ235, Genentech GDC-0941, Semafore SF 1126)
- p60src and other kinases (dasatinib)*
- Multi-kinase inhibitor (sunitinib)*
- mTOR (RAD001, temsirolimus)

*In phase III

Perspective

- PSA is a valuable marker for assessment of prostate cancer risk
- PSA is a valuable tool to help select initial treatment, assess response and guide secondary treatment
- New technology/markers under development are likely to refine and may replace PSA
- Guidelines may change rapidly
- Screening decreases prostate cancer mortality
- Early treatment in some men decreases the risk of prostate cancer mortality
- The biggest risks to screening are over detection and resultant over treatment
- Refinement of initial treatment (or non-treatment) strategies is urgently needed
- More transparency and emphasis on quality, appropriateness and efficacy
Acknowledgements

• Matt Cooperberg, MD, MPH
• GSEPS - CaPSURE
  – Jenny Broering, RN, MPH
  – Janet Cowen
  – Natalia Sadesky, MD
  – June Chan, DSc
• UCSF Prostate Cancer Program