PSA Screening: The Science Behind the Controversy

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What is the Prostate Cancer Stage Migration?

• Before PSA (circa 1985):
  – ~100,000 new cases per year, ~35,000 deaths per year
  – ~25% Advanced (metastatic disease) when diagnosed

• After PSA (2012):
  – ~220,000 new cases per year, ~28,000 deaths per year
  – 2-3% Advanced disease when diagnosed
The Changing Face of Prostate Cancer

Risk distribution by year of diagnosis

- Low
- Intermediate
- High
- Advanced
“Not all prostate cancer is created equally”

- **Turtles**: ~50% → Unlikely to harm (even if no treatment)
- **Rabbits**: ~35% → Unpredictable outcome
- **Birds**: ~15% → Most aggressive, lowest chance of cure

Approx 95% are treated
Side Effects of Treatment and Biopsy

Surgery
- Impotence
- Urethral stricture
- Incontinence

Radiation
- Proctitis
- Cystitis

Hormone Therapy
- Hot Flashes
- Bone Loss
- Metabolic Syndrome

Prostate Biopsy
- Bleeding
- Infection
<table>
<thead>
<tr>
<th>PSA level</th>
<th>Prevalence of Prostate Cancer</th>
<th>High-Grade Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 - 4.0</td>
<td>24%</td>
<td>25%</td>
</tr>
<tr>
<td>2.1 - 3.0</td>
<td>21%</td>
<td>19%</td>
</tr>
<tr>
<td>1.1 - 2.0</td>
<td>17%</td>
<td>12%</td>
</tr>
<tr>
<td>0.6 - 1.0</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>&lt;0.5</td>
<td>7%</td>
<td>13%</td>
</tr>
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</table>
PSA Modifications

• Age-adjusted PSA
  – Younger men: Normal PSA = 0.0 – 2.5
  – Older men: Normal PSA = 0.0 – 5.5

• PSA Velocity
  – How much or how fast your PSA changes per year

• Free PSA
PSA Screening Trials

- **European Randomized Study of Screening for Prostate Cancer (ERSPC):**
  - 162,387 men, 9 year follow-up

- **Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial:**
  - 76,693 men, 13.0 year follow-up

- **Göteborg randomized screening trial:**
  - 20,000 men, 15 year follow-up
• **ERSPC**: 162,387 men, 9 yr f/u
  - Screening reduced rate of prostate cancer death by 20%
  - Number needed to screen to prevent one death = 1410
  - Number needed to treat to prevent one death = 48
Prostate Cancer Screening in the Randomized Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial: Mortality Results after 13 Years of Follow-up


- **PLCO: 76,693 men, 13 yr f/u**
  - No difference in death rates between screening and control
  - **Issues:**
    - 52% of men in “control group” underwent screening during the study (“contamination”)
      - No stage migration in the control group
    - 44% of all men were “pre-screened” (i.e. had a PSA checked) before entering trial
Mortality results from the Göteborg randomised population-based prostate-cancer screening trial

- 20,000 men
  - Age 50-64 on 12/31/1994
  - Screening versus no screening

- Planned analysis after 15 yrs
32,298 men in Göteborg Age 50-64 in 12/1994

20,000 randomized

9,952 invited for PSA screening (screening group)

7,578 attendees (76%)

1,046 with PCa
27 died from PCa

2,374 non-attendees

92 with PCa
17 died from PCa

9,952 not invited (control group)

718 with PCa
78 died from PCa
### Stage/Risk of Cancer in Göteborg

<table>
<thead>
<tr>
<th>Tumour Grouping (%)</th>
<th>Control group (n=9952)</th>
<th>Screening group (n=9952)</th>
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<tbody>
<tr>
<td></td>
<td>All (n=9952)</td>
<td>Attendees (n=7578)</td>
</tr>
<tr>
<td>Number of men with prostate cancers diagnosed (%)</td>
<td>718 (7.2%)</td>
<td>1138 (11.4%)</td>
</tr>
<tr>
<td>Low risk*</td>
<td>199 (2%)</td>
<td>604 (6.1%)</td>
</tr>
<tr>
<td>Moderate risk†</td>
<td>249 (2.5%)</td>
<td>363 (3.6%)</td>
</tr>
<tr>
<td>High risk‡</td>
<td>126 (1.3%)</td>
<td>96 (1%)</td>
</tr>
<tr>
<td>Advanced disease§</td>
<td>87 (0.9%)</td>
<td>46 (0.5%)</td>
</tr>
<tr>
<td>Unknown¶</td>
<td>57 (0.6%)</td>
<td>29 (0.3%)</td>
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Clear stage migration with screening
Results: Prostate Cancer Deaths

- Control arm: 78 deaths
- Screening arm: 44 deaths
- Number needed to screen = 293
- Number needed to treat = 12
Discussion

- Why are results different than PLCO and ERSPC?
  - Longer follow-up
  - Younger men
  - Lower rates of previous PSA screening
  - Less contamination
  - Men had biopsies at low PSA
• Analysis of PLCO data based on other health problems

• Minimal or no other health problems:
  – Number needed to screen = 723
  – Number needed to treat = 5
• European trial data adjusted for longer follow-up time

<table>
<thead>
<tr>
<th>Follow-up Time (yrs)</th>
<th>Number needed to screen</th>
<th>Number needed to treat</th>
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<tbody>
<tr>
<td>9</td>
<td>1,254</td>
<td>43</td>
</tr>
<tr>
<td>10</td>
<td>837</td>
<td>29</td>
</tr>
<tr>
<td>12</td>
<td>503</td>
<td>18</td>
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## Screening “Truths”

### On one hand…
- Screening = ↑ overall diagnoses and ↑ overdiagnosis
- We overtreat prostate cancer
- Treatments have substantial side effects
- Trials show no conclusive evidence of benefit at this time

### On the other hand…
- Screening = stage migration
- Screening trials are relatively immature
- Prostate cancer deaths have decreased in PSA era, (in part due to screening)

### What to do?
- Selective screening (e.g. young, healthy)
- ‘Smarter’ screening (e.g. frequency of screening)
- Selective intervention (i.e. active surveillance)
- Improved biomarkers
- Informed and shared decision-making

### What we should NOT do?
- Stop PSA Screening!