Screening does not impact mortality rates!

E. David Crawford, MD
Professor of Surgery (Urology and Radiation Oncology)
Head, Urologic Oncology
E. David Crawford Endowed Chair in Urologic Oncology
University of Colorado Health Sciences Center
Denver, Colorado

1989

- Prostate cancer became the most common cancer in American Males
- And the second leading cause of death
- Options:
  - Do nothing
  - Prevention
  - Early detection
  - Improve outcome for advanced disease

1989-Fast forward, what happened?

Prevention: PCPT 25% reduction
Optimism that Screening Is Associated with a Fall in Mortality

- Fall in mortality now seen
  - SEER
  - Olmsted County
  - Canada/Quebec
  - DoD (US)
  - Tyrol, Austria
- Mortality fall not seen where PSA screening not performed
  - Mexico—where little to no PSA screening is performed

Evidence is conflicting, not strong enough to support public policy

PSA

Flying High
Point-Counterpoint: Early Detection of Prostate Cancer Is Not Valuable In a Lot of Men

~ E. David Crawford, MD

The Clinical and Economic Burden of Prostate Cancer

- Number 1 cancer, 16% men, 3-4% death
- Cost 8 billion 11.2%
- First year of treatment cost $40,873.20

PROSTATE SCREENING 2009

<table>
<thead>
<tr>
<th>Organization</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Urological Association (AUA)</td>
<td>Men who are in good health: annual PSA testing starting at age 50, or 40 if high-risk (AA, or with a father, bother or son with prostate cancer.)</td>
</tr>
<tr>
<td>American Cancer Society (ACS)</td>
<td>Offer to men &gt; 50 who expect to live another 10 years, and high risk if they're age 45 and older.</td>
</tr>
<tr>
<td>Centers for Disease Control and Prevention (CDC)</td>
<td>Considers evidence &quot;insufficient to determine whether the benefits outweigh the harms.&quot;</td>
</tr>
<tr>
<td>U.S. Preventive Services Task Force (USPSTF)</td>
<td>Do not screen &gt; 75 and older, or in men who will probably live 10 years or fewer. For men under 75, the evidence insufficient to determine whether the benefits outweigh the harms. (Am J Prev Med 2008;34(2):164)</td>
</tr>
<tr>
<td>American College of Preventive Medicine (ACPM)</td>
<td>Discuss risks/benefits. The need for screening questionable in elderly men with other chronic illnesses and men with life expectancies of less than 10 years.</td>
</tr>
</tbody>
</table>

Conflict recommendations

Updates expected
PLCO Cancer Screening Trial

- Multi-center randomized screening trial for:
  - Prostate
  - Lung
  - Colorectal
  - Ovarian
- 155,000 men and women aged 55-74
- Recruitment: 1993-2001
- Screening: 1993-2006
- Follow-up until 2015 by annual survey and mortality search

PLCO Screening Centers

Screening Interventions in PLCO Trial

- Prostate – Annual DRE x 4 and PSA x 6
- Lung – Annual Chest Xray x 4
  - Spiral CT for smokers
- Colon – FSG at years 1 and 6
- Ovary – TVU x 4 and CA125 x 6

PLCO Screening Follow-up

- Intervention Arm:
  - Screening results reported to patient and PCP
  - “Community standard of care” applied to biopsy and treatment decisions
- Comparison Arm:
  - “Community standard of care”
Point-Counterpoint: Early Detection of Prostate Cancer Is Not Valuable In a Lot of Men

~ E. David Crawford, MD

PLCO
Study Endpoints

- Cause-specific mortality
- Outcomes of screening exams
- Incident and prevalent cancers

Original Article
Mortality Results from a Randomized Prostate-Cancer Screening Trial

Gerald L. Andrieux, M.D., E. David Crawford, M.D., Robert L. Grob, III, M.D., Sandra S. Burns, M.D., David Chia, Ph.D., Timothy R. Church, Ph.D., Mona N. Fouad, M.D., Edward P. Goldmann, M.D., Paul A. Knoke, M.D., Douglas J. Feinberg, M.D., Joel L. Weissfield, M.D., Lance A. Yokochi, M.D., Barbara O'Blen, M.P.H., Jonathan O. Claiborn, D.S., Jonathan W. Haber, M.D., Thomas L. Hill, M.D., Richard G. Hayes, Ph.D., Barrett S. Kramer, M.D., Grant Ermiljan, Ph.D., Anthony B. Miller, M.E., Paul F. Persky, Ph.D., Philip C. Prorok, Ph.D., John K. Schrag, Ph.D., Christine D. Berg, M.D., for the PLCO Project Team

N Engl J Med
Volume 360(13):1313-1319
March 26, 2009

Characteristics of the Subjects at Baseline
Point-Counterpoint: Early Detection of Prostate Cancer Is Not Valuable In a Lot of Men

~ E. David Crawford, MD
PLCO Trial Conclusions:
- 7-10 years, no difference in mortality
- Few CaP related deaths in either group- 92 screening and 82 control at 10 years
- Balance of benefits and harms unfavorable and does not support routine screening, at this time
- Even if mortality is shown to decrease, still significant harm to many men

Thoughts
- Screening doesn’t work for all cancers: Lung, neuroblastoma, and not all breast cancers
- Need to separate diagnosis from treatment, clearly over treating men
- But, need to remember that 28,000 men died in 2008 of CaP
- We need to figure out who needs to be diagnosed and effectively treated.
There are a lot of exciting things happening in the PLCO Trial Biorepository: More than 2.7 million specimens

<table>
<thead>
<tr>
<th>Exam Cycle</th>
<th>Risk Factors</th>
<th>Dietary Factors</th>
<th>Serum</th>
<th>Plasma</th>
<th>RBC</th>
<th>DNA</th>
<th>Cells</th>
<th>Tumor Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 2</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 3</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Year 4</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 5</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Comparison Arm**

| X | X | X |

---

**PLCO Prostate Subcommittee**

Thanks to participants

- G. Andriole, Chair
- C. Berg
- C. Amling
- R. Hayes
- D. Crawford, V. Chair
- G. Izmerlian
- R. Grubb
- B. Kramer
- D. Levin
- A. Miller
- P. Pesey
- P. Prorok
- D. Carrick
- P. Pinksy
- D. Levin
- A. Miller
- P. Pesey
- P. Prorok
- T. Riley
- D. Chia
- T. Church
- D. Reding
- IMS
- T. Church
- D. Reding
- B. O’Brien
- L. Regard
- T. Riley
- IMS
- P. Pesey
- B. Wilcox
- B. Lake
- J. Mabie

A special thanks to Barry Kramer and Phil Prorok for their leadership and guidance during the past 15 years.