Point-Counterpoint:

Early Detection of Prostate Cancer Is Not Valuable In a Lot of Men
~ E. David Crawford, MD

We Can't Go Backwards – Of Course Screening Has Saved Lives
~ Robert E. Donohue, MD

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

PLCO

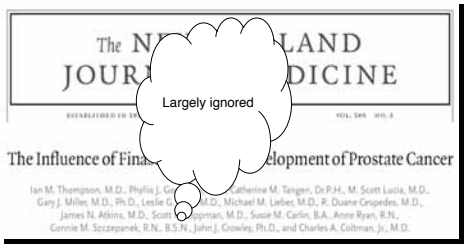
University of Colorado School of Medicine — Far Beyond The Ordinary

1989

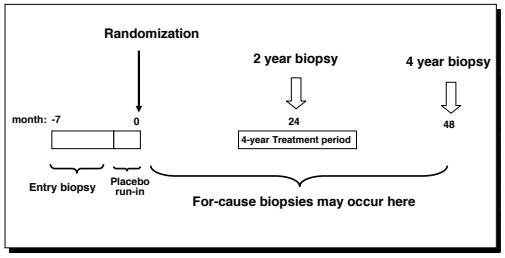
- Prostate cancer became the most common cancer in American Males
- And the second leading cause of death
- Options:
  - Do nothing
  - Prevention
  - Early detection
  - Improve outcome for advanced disease

1989-Fast forward, what happened?

Prevention: PCPT 25% reduction



REDUCE Schema to be presented



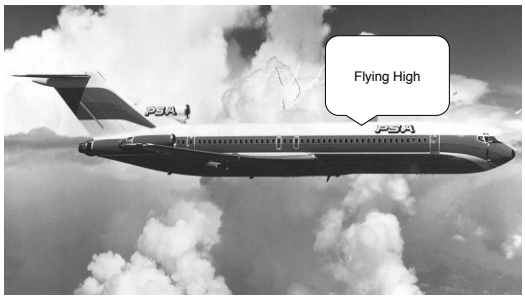
Andriole et al, J Urol 172:1314, 2004

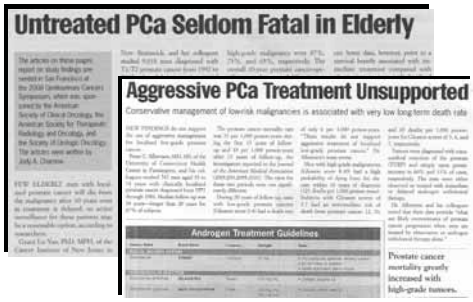
Optimism that Screening Is Associated with a Fall in Mortality

- Fall in mortality now seen
  - SEER
  - Olmsted County
  - Canada/Quebec
  - [illegible]
  - 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





Untreated PCa Seldom Fatal in Elderly

Aggressive PCa Treatment Unsupported

Conservative management of low-risk malignancies is associated with very low long-term death rate

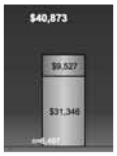
Androgen Treatment Guidelines

Prostate cancer mortality greatly increased with high-grade tumors.

Renal and Urology News June 2005, April 2008

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

Organization	Recommendation
American Urological Association (AUA)	Men who are in good health: annual PSA testing starting at age 50, or 40 if high-risk (AA, or with a father, brother or son with prostate cancer.)
American Cancer Society (ACS)	[illegible] life expectancy of another 10 years, and [illegible]
Centers for Disease Control and Prevention (CDC)	Considers evidence "insufficient to determine whether the benefits outweigh the harms".
U.S. Preventive Services Task Force (USPSTF)	Doctors should not screen men who are unlikely to live probably live 10 years or fewer. For men under 75, the evidence insufficient to determine whether the benefits outweigh the [illegible]
American College of Preventive Medicine (ACPM)	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.

Conflicting recommendations
Updates expected

PLCO Cancer Screening Trial

- Multi-center randomized screening trial for:
  - Prostate
  - Lung
  - Colo-rectal
  - 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

NATIONAL CANCER INSTITUTE
PLCO
Prostate, Lung, Colorectal & Ovarian CANCER SCREENING TRIAL

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"

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. Andriole, M.D., E. David Crawford, M.D., Robert L. Grubb, III, M.D., Saundra S. Buys, M.D., David Chia, Ph.D., Timothy R. Church, Ph.D., Mona N. Fouad, M.D., Edward P. Gelmann, M.D., Paul A. Kvale, M.D., Douglas J. Reding, M.D., Joel L. Weissfeld, M.D., Lance A. Yokochi, M.D., Barbara O'Brien, M.P.H., Jonathan D. Clapp, B.S., Joshua M. Rathmell, M.S., Thomas L. Riley, B.S., Richard B. Hayes, Ph.D., Barnett S. Kramer, M.D., Grant Izmirlian, Ph.D., Anthony B. Miller, M.B., Paul F. Pinsky, Ph.D., Philip C. Prorok, Ph.D., John K. Gohagan, Ph.D., Christine D. Berg, M.D., for the PLCO Project Team

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The NEW ENGLAND JOURNAL of MEDICINE

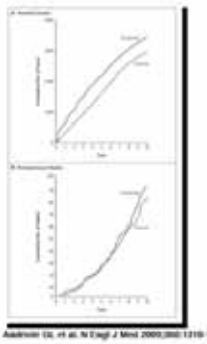
Characteristics of the Subjects at Baseline

The NEW ENGLAND JOURNAL of MEDICINE

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

~ E. David Crawford, MD

Number of Diagnoses of All Prostate Cancers (Panel A) and Number of Prostate-Cancer Deaths (Panel B)



Andriole GL, et al. N Engl J Med 2009;360:1310-1319

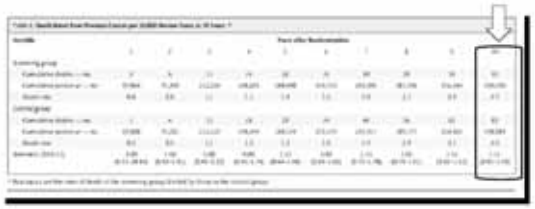
The NEW ENGLAND JOURNAL of MEDICINE

Tumor Stage, Histopathological Type, and Gleason Score for All Prostate Cancers at 10 Years, According to Method of Detection and Time of Diagnosis

Andriole GL, et al. N Engl J Med 2009;360:1310-1319

The NEW ENGLAND JOURNAL of MEDICINE

Death Rates from Prostate Cancer per 10,000 Person-Years at 10 Years



Andriole GL, et al. N Engl J Med 2009;360:1310-1319

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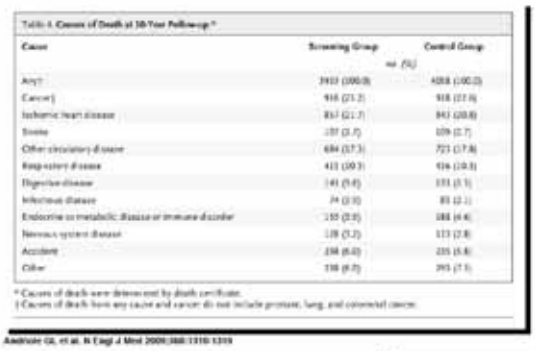
Causes of Death at 10-Year Follow-up



Cause	Screening Group	Control Group
	no. (%)	
Any†	3933 (100.0)	4238 (100.0)
Cancer‡	916 (23.3)	918 (27.9)
Ischemic heart disease	857 (21.7)	843 (20.0)
Stroke	107 (2.7)	109 (2.7)
Other circulatory disease	684 (17.5)	721 (17.0)
Respiratory disease	413 (10.5)	436 (10.3)
Digestive disease	141 (3.6)	151 (3.5)
Infectious disease	74 (1.9)	83 (2.1)
Endocrine or metabolic disease or immune disorder	155 (3.9)	188 (4.4)
Nervous system disease	128 (3.2)	123 (2.9)
Accident	238 (6.0)	255 (5.8)
Other	198 (5.0)	293 (7.1)

* Causes of death were determined by death certificate.
† Causes of death from any cause and cancer do not include prostate, lung, and colorectal cancer.

Andriole GL, et al. N Engl J Med 2009;360:1310-1319

The NEW ENGLAND JOURNAL of MEDICINE

PLCO Trial Conclusions:

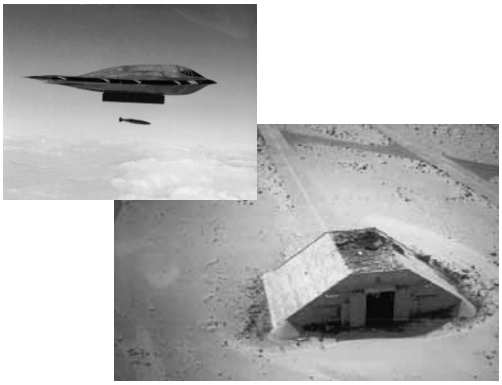
- 7-10 years, no difference in mortality
- Few CaP related deaths in either group- 92 screening and 82 control at 10 years
- Balance of benefits and harms unfavorable and does not support routine screening, at this time
- Even if mortality is shown to decrease, still significant harm to many men

PLCO Trial Conclusions:

- First report-planned follow for at least 13 years, more to come
- Contamination-as high as 50%, could be a contributing factor, improved therapy could also be a contributing factor-
- PSA not the best test, far from it
- Need a better test and marker of progression

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

Exam Cycle	Risk Factors	Usual Diet	Serum	Plasma	RBC	DNA	Viable Cells	Tumor Sample
Intervention Arm								
Baseline	X	X	X	X	X	X		
Year 1			X					
Year 2			X					
Year 3		X	X	X	X	X	X	
Year 4			X	X		X		
Year 5			X	X	X	X		
2004-2013								x
Comparison Arm								
	X	X				X		X

PLCO Prostate Subcommittee

Thanks to participants

Urologists
G. Andriole, Chair
C. Amling
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A. Miller
P. Pinksy
P. Prorok

Others
D. Chia
T. Church
D. Reding
B. Wilcox

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