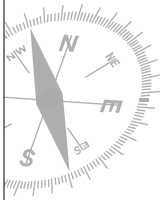


# PSA Controversy

David Fiore  
Angelo Kanellos



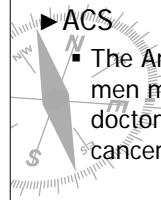
# CURRENT PROSTATE CANCER SCREENING GUIDELINES

## ► USPSTF\*\*

- Evidence is **insufficient** to assess the benefits and harms in men <75 yo. Recommends **against** screening men >75 yo.

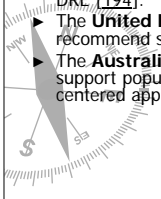
## ► ACS

- The American Cancer Society recommends that men make an informed decision with their doctor about whether to be tested for prostate cancer.



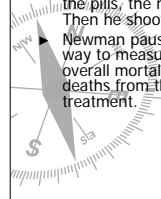
# Recommendations from others

- The **American College of Physicians (ACP)** recommendation states that "Rather than screening all men for prostate cancer as a matter of routine, physicians should describe the potential benefits and known harms of screening, diagnosis, and treatment; listen to the patient's concerns; and then individualize the decision to screen" The **Canadian Task Force on Preventive Health Care** recommends against screening for prostate cancer with PSA or TRUS and states that there is insufficient evidence to recommend for or against screening with DRE [194].
- The **United Kingdom National Screening Committee** does not recommend screening for prostate cancer [195].
- The **Australian Cancer Council** states that the evidence does not support population-based screening and recommends a patient-centered approach that individualizes the decision [196].



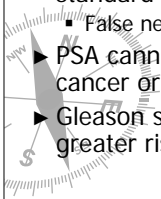
# Savior or killer?

- "Imagine you are one of 100 men in a room," he says. "Seventeen of you will be diagnosed with prostate cancer, and three are destined to die from it. But nobody knows which ones." Now imagine there is a man wearing a white coat on the other side of the door. In his hand are 17 pills, one of which will save the life of one of the men with prostate cancer. "You'd probably want to invite him into the room to deliver the pill, wouldn't you?" Newman says.
- Statistics for the effects of P.S.A. testing are often represented this way — only in terms of possible benefit. But Newman says that to completely convey the P.S.A. screening story, you have to extend the metaphor. After handing out the pills, the man in the white coat randomly shoots one of the 17 men dead. Then he shoots 10 more in the groin, leaving them impotent or incontinent.
- Newman pauses. "Now would you open that door?" He argues that the only way to measure any screening test or treatment accurately is to examine overall mortality. That means researchers must look not just at the number of deaths from the disease but also at the number of deaths caused by treatment.



# Problems with the PSA Test

- Most men with normal prostate numbers do not have their prostates biopsied
  - Overestimates sensitivity and underestimates specificity
- Transrectal needle biopsy is not a perfect gold standard
  - False negative rate is 10-20 percent
- PSA cannot tell the difference between a bad cancer or an indolent cancer
- Gleason score > 6 or volumes > 0.5 cm<sup>3</sup> have greater risk of progression



# European Randomized Study of Screening for Prostate Cancer (ERSPC)

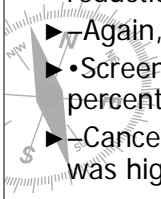
- •182,160 men between 50 and 74 years old
- •Multiple centers across multiple countries with multiple different protocols
- Average interval was every 4 years
- PSA cutoff was 3.0 (in most centers)
- The PSA screening rate in the control group was not reported
- Mortality from prostate cancer was 20 percent lower in the study group
- NNS 1410 men to prevent one cancer death over 9 years
- 48 additional cases of prostate cancer needed to be treated to prevent one death of prostate cancer

N Engl J Med. 2009 Mar 26;360(13):1310-9.

# United State Prostate, Lung, Colorectal and Ovarian Cancer (PLCO) Screening Trial

- •76,693 men between ages 55 and 74 assigned to annual screening
- •After seven years of follow up, no reduction in prostate cancer mortality
- •Again, not a very long follow up
- •Screening in the control group was 52 percent
- •Cancer detection in the screening group was higher than in the control group

•N Engl J Med. 2009 Mar 26;360(13):1320-8



# Problems with Both Studies

- •Control groups had a high percentage of PSA tracking
- •Study time may not have been long enough to effectively assess the benefits of PSA screening



## Randomised prostate cancer screening trial: 20 year follow-up

- ▶ Swedish trial of 9026 men 50 – 69yo, 1494 screened q 3 yrs. Initial DRE, PSA added in 1993 (<4ug/L)
- ▶ 5.7% vs 3.9% of men had prostate cancer detected.
- ▶ The risk ratio for death from prostate cancer was 1.16 (95% confidence interval 0.78 to 1.73), adjusted for age: 1.58 (1.06 to 2.36).

BMJ 2011;342: Mar2011

## Screening for prostate cancer: systematic review and metaanalysis of randomised controlled trials

- ▶ Six randomized trials, 387,286 participants.
- ▶ Screening increased probability of diagnosis of prostate CA RR 1.46
- ▶ No effect on death from prostate CA
- ▶ All studies has significant methodological limitations.
- ▶ No studies on quality of life.

BMJ. 2010 Sep 14;341

## Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer

- ▶ Swedish study of 695 men, <75yo, localized well differentiated tumor, PSA<50.
- ▶ Radical prostatectomy vs watchful waiting.
- ▶ cumulative incidence of death from prostate cancer at 15 years of 14.6% and 20.7%, and a relative risk with surgery of 0.62
- ▶ The survival benefit was confined to men younger than 65 years of age. The number needed to treat to avert one death was 15 overall and 7 for men younger than 65 years of age.
- ▶ Problem: only 5.2% of cancers were detected by screening.

N Engl J Med;364:1708-17.May 5 2011

## Can Screening be Harmful?

- ▶ Risk of biopsy
  - Anxiety over the possibility of diagnosing cancer
  - Often does not go away due to the higher false negative rate
- ▶ Overdiagnosis
  - Lifetime risk of being diagnosed with prostate cancer has increased from 1 in 11 to 1 in 6
  - Risk of dying from prostate cancer has remained at 1 in 34
  - Estimates of overdiagnosis from modeling studies range from 23 to 42 percent
- ▶ Used data from the ERSPC trial

## What about Treatment Harms?

- ▶ Radical Prostatectomy
  - 0.5% mortality rate
  - 45% decrease in sexual function (range 20 –70%)
  - 33% in urinary incontinence (range 15 –50%)
- ▶ External beam radiation
  - 32% decrease in sexual function (range 20-45%)
  - 8% urinary incontinence (range 2-16%)
  - 21% in bowel dysfunction (range 6-25%)

## Putting it all together

- ▶ We keep waiting for THE study that will give us THE answer (and rejecting negative studies)
- ▶ Prostate cancer is very common
- ▶ Prostate cancer death is still too common
- ▶ Metastatic prostate cancer can be terrible
- ▶ What to do
  - Discuss screening with men >50 (40 if high risk)
  - Probably makes sense to screen every 3 – 4 years
  - Stop screening if < 10 – 15 years of life expectancy, or after 70 - 75
  - Be involved in treatment decisions