# We can't go backwards: Screening has helped!

Robert E. Donohue M.D.

Denver V.A. Medical Center

University of Colorado



# **Prostate Biopsy**

"Is cure necessary; when it is possible?"

"Is cure possible; when it is necessary?" Willet F. Whitmore Jr.

# **Prostate Biopsy**

What is the most dangerous weapon in the world today?

Willet F. Whitmore Jr.

# **Prostate Biopsy**

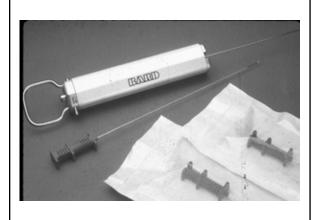
A prostate biopsy needle device in the hands of a Urologist!

Willet F. Whitmore Jr.

# **Prostate Biopsy**

A prostate biopsy needle device in the hands of a Urologist!

Willet F. Whitmore Jr.



#### **Prostate Cancer**

prevalence disease in a population

incidence disease diagnosed in a population

## Prostate Cancer Prevalence

210 patients		4696 patients
· 0	20-29	.0
0	30-39	0.2%
0	40-49	3.8%
29%	50-59	6.4%
30%	60-69	12.5%
40%	70-79	17.4%
67%	80-89	26.1%
100%	90+	
Franks 1954		Scott 1968

## Prostate Cancer Prevalence

violent death series

Detroit

Caucasian Afro-American

**Sakr 1993** 

# Prostate Cancer Prevalence

PSA	% positive	G 8, 9
< 0.5	32/486 6.6%	4/ 32 12.5%
0.6-1.0	80/791 10.1%	8/ 80 10%
1.1-2.0	170/998 17.0%	20/170 11.8%
2.1-3.0	115/482 23.9%	22/115 19.1%
3.1-4.0	52/193 26.9%	13/52 25%

Thompson NEJM 350:2239, 2004

# Screening

**AIMs** 

identify asymptomatic men with aggressive, localized tumors, treat them, reduce morbidity, LUTs, reduce metastases, [painful] reduce mortality,

???? rectal exam1936 acid phosphatase1941 DRE + acid p'tase1966 human semino-protein

1979 Prostate Specific Antigen 1930s perineal; 1937 rectal bx

# **Screening**

prostate specific antigen
Free / Total PSA; cPSA [2-6]
PSA velocity
PSA density
PSA age specific

**PSA** doubling time

# PSA - Age specific

40 – 44 1.8 ng/ml

45 – 49 2.0 ng/ml

50 – 54 2.6 ng/ml

55 – 59 3.6 ng/ml

60 - 64 4.3 ng/ml

65 – 69 5.0 ng/ml

70 - 75 5.5 ng/ml

**Crawford PCAW** 

## PSA – Age specific

40 – 44	1.8 ng/ml	Cau	AA
45 – 49	2.0 ng/ml	2.5	2.0
50 – 54	2.6 ng/ml		
55 – 59	3.6 ng/ml	3.5	4.0
60 - 64	4.3 ng/ml		
65 – 69	5.0 ng/ml	3.5	4.5
70 – 75	5.5 ng/ml	3.5	5.5
Crawford PCAW			Moul

#### **Prostate Cancer**

indications for biopsy; biopsy number of cores / lobe number of cores containing cancer % of tumor in all cores Gleason patterns one and two Gleason sum, biopsy 3+2+4 = 3+4 prostatectomy Gleason sum 3+2+4

#### **Tumors 2009**

incidence	mortality

#### **Tumors 2009**

	incidence	mortality
prostate	192,280	27,360
lung	103,350	88,900
colo/	52,010	25,240
rectal	23,580	
bladder	52,810	18,030p
non Hodgkin'	s 35,990	12,0901
melanoma	39,080	0,1801b

#### **Tumors 2009**

1992 325,000 + patients prostate cancer; 40,000 deaths 180,000 to 220,000 patients/year deaths down to 27,000 to 31,000 breast cancer; same incidence, death rate; 40,000 patients/year

#### **Tumors 2009**

Why is the death rate lower?
prostate specific antigen
screening [PSA + DRE]
radical prostatectomy\*
conformal radiotherapy\*
TRUS guided brachytherapy\*
\* all technical exercises

# **Prostate Biopsy**

indications 80% PSA 20% abnormal digital rectal exam

#### **Prostate Biopsy**

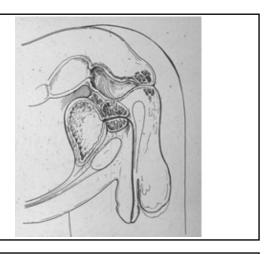
indications 181 patients

PSA 87 48.9% nodule 13 7.3% asymmetry 6 3.3% hardness 3 1.7%

#### **Prostate Biopsy**

indications 181 patients

PSA + nodule 27 14.1% PSA + asymmetry 22 12.2% PSA + hardness 23 12.7%



#### **Rectal Exam**

examiner comfort biopsy indications asymmetry nodule [s] hardness [diagram]

#### **Tumors 2009**

234,460 new patients diagnosed
213,358 confined
radical prostatectomy
30% plus; insignificant cancer
Patient is at low risk to develop
life threatening disease
Gleason 6 or less, p T2,

#### **Tumors 2009**

screening is leading to
unnecessary, expensive treatments,
radical \$ 24,000; IMRT \$ 56,000
anxiety,
side effects,
need for follow-up,
quality of life issues, potency,
urine continence,

ERSPC and PLCO studies no significant benefit to screening in lessening mortality

Schroeder NEJM 360: 1320, 2009 Andriole NEJM 360: 1310, 2009

## Screening 2009

**ERSPC** 

182,160 men screened,
PSA q 4 years, [2.5 to 4.0]
3 ng/ml
+/-DRE
+/-TRUS
+/-free PSA

#### Screening 2009

**ERSPC** 

162,243 men between 55 and 69
9 years
mortality 20% lower in screened,
no biopsies in control group,
1410 men screened; 1 cancer death
screened 8.2%; control 4.8%
48 diagnosed; 1 cancer death

#### Screening 2009

**ERSPC** 

large number screened,
less contamination,
20% fall in mortality,
better impact,
better patient control,
1068 screened, 48 Rx – 1 death,
27 Rx - 1 patient with mets

**PLCO** 

76,693 men 50 to 74
annual PSA 6 yrs and DRE 4 yrs
85% PSA; 86% DRE
bx; PSA > 4, abnormal DRE
40 to 52% control PSA 1 and 6 years
50s vs 44c deaths
cancer diagnosis 2820s vs 2322c

## **Screening 2009**

**PLCO** 

large number pre-screened, culls out cancers, heavily contaminated, 40 to 52%, control group PSA testing

#### Screening 2009

**PLCO** 

control group; 31% T1C @ RP 25% screened; no curative therapy insufficient time for follow-up, 7 ys BIAS

aggressive Rx, screened adjudicating committee, less CA as cause of death

# Screening 2009

**Klotz** 

300 patients
diagnosis established
active surveillance for
< 65, PSA < 10, TiC, T2A
>65, PSA < 15, T2B

1	4	1	١

Klotz q 3 month PSA and DRE, at one year, repeat biosy, serial PSAs and DREs but repeat biopsy at 3 years

## Screening 2009

Klotz 33% withdrew 12% PSA 3% DRE 4% grade change 13% anxiety

#### Screening 2009

SEER data – less advanced disease
Tyrol – three-fold decrease mortality
Olmstead – mortality declined 22%
USA and UK – early peak of ageadjusted mortality; USA declined
faster because of PSA screening
BUT Wales and England, mortality
declined by 1.7%

#### Screening 2009

BUT Wales and England, mortality declined by 1.7% Seattle vs Ct; no difference in mortality [heavy PSA]

**BIAS** 

deaths are incorrectly attributable to prostate cancer; deaths caused by another disease

1	4	1	R

American College of Physicians
Ca of the Prostate – important
Mortality benefits of screening and
Rx are limited
DRE and PSA false positive,negative
Testing leads to invasive evaluation

#### **Screening 2009**

American College of Physicians
Aggressive therapy is necessary to
benefit; death risk low,
significant risk for chronic disease,
Early detection can save lives
Early Dx and Rx may avert
cancer-related illnesses

## Screening 2009

initial visit; PSA and DRE
results visit; need for biopsy,
benefits and risks,
individual patient's co-morbidities
biopsy visit,
biopsy results,
treatment discussions,

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initial visit; PSA and DRE
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1	4	1	(

#### **Guidelines 2009**

start at 40 years of age treat young, observe older PSA q 4 months vs

repeat biopsy at 12- 24 months Active surveillance

#### **Guidelines 2009**

Active surveillance
well done biopsy necessary
careful follow-up
PSA > 1.2 in 40s, increased risk
No BPH affect on PSA?
no decision on one PSA
15-50% variability in PSA result
antibiotics have no effect

#### **Guidelines 2009**

Active surveillance
Primary Care MDs; mortality
elevated blood pressure
diabetes mellitus
controlled
mortality falls in Ca P.
Ca P is a chronic disease

#### **Treatments**

radical prostatectomy
external beam conformal RT
TRUS guided brachytherapy
watchful waiting
active surveillance
PSA and DRE serially
repeat biopsy

#### **Treatments**

diagnosis
does
not
mean
[local]
therapy!

# **Whole Mount Grading**

580 patients
44% upgraded;
22% 2 or more;
29% same grade;
28% down graded;
12% 2 or more;

Crawford and Donohue 2002

#### Gleason 3+3

580 patients
3+3 173 patients, 3 cores
3+3 whole mount 47 patients
< 6 " 67 patients
7 " 49 patients
8-10 " 10 patinets

#### Gleason 7

undergrading

580 patients
G 7 173 patients, 3 cores
4+3 35 patients; 18 4+3 Gleason
9 < G7; 8 > G 7
3+4 66 patients; 36 3+4 Gleason
22 < G7; 8 > G 7
undergrading; overgrading

1	4	2	1	

## **Undergrading**

repeat biopsy now,
4 studies; 20% variation
repeat before entering active
surveillance, Epstein
saturation, mapping, 3D biopsy

#### **Screening**

mortality rate has fallen from 40,000 to 27,000 to 29,000 men PSA is one factor, abnormality on PE, on biopsy, on pathology does not equate to therapy!!!

## **Screening**

European study is flawed!
PLCO study is flawed!
We must continue to
individualize each patient and
include age, race, co-morbidities
DRE, life span and other
malignancies in deliberations

#### **Screening**

One shoe does not fit all !!!

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#### **Active Surveillance**

39 men
Age 72.3 yrs; PSA 7.27; Gleason 6.08
biopsy 5.8% tumor; 23.3 months
PSA + DRE q 3m; biopsy 1 year
39 – at least one PSA
13 – repeat biopsy
6 Gleason 6; 5 Gleason 7; 2 neg;
7AS, 2 RP,XRT, 1 B, ! ????

