

Prostate Cancer: Screening, Treatment, and Survivorship

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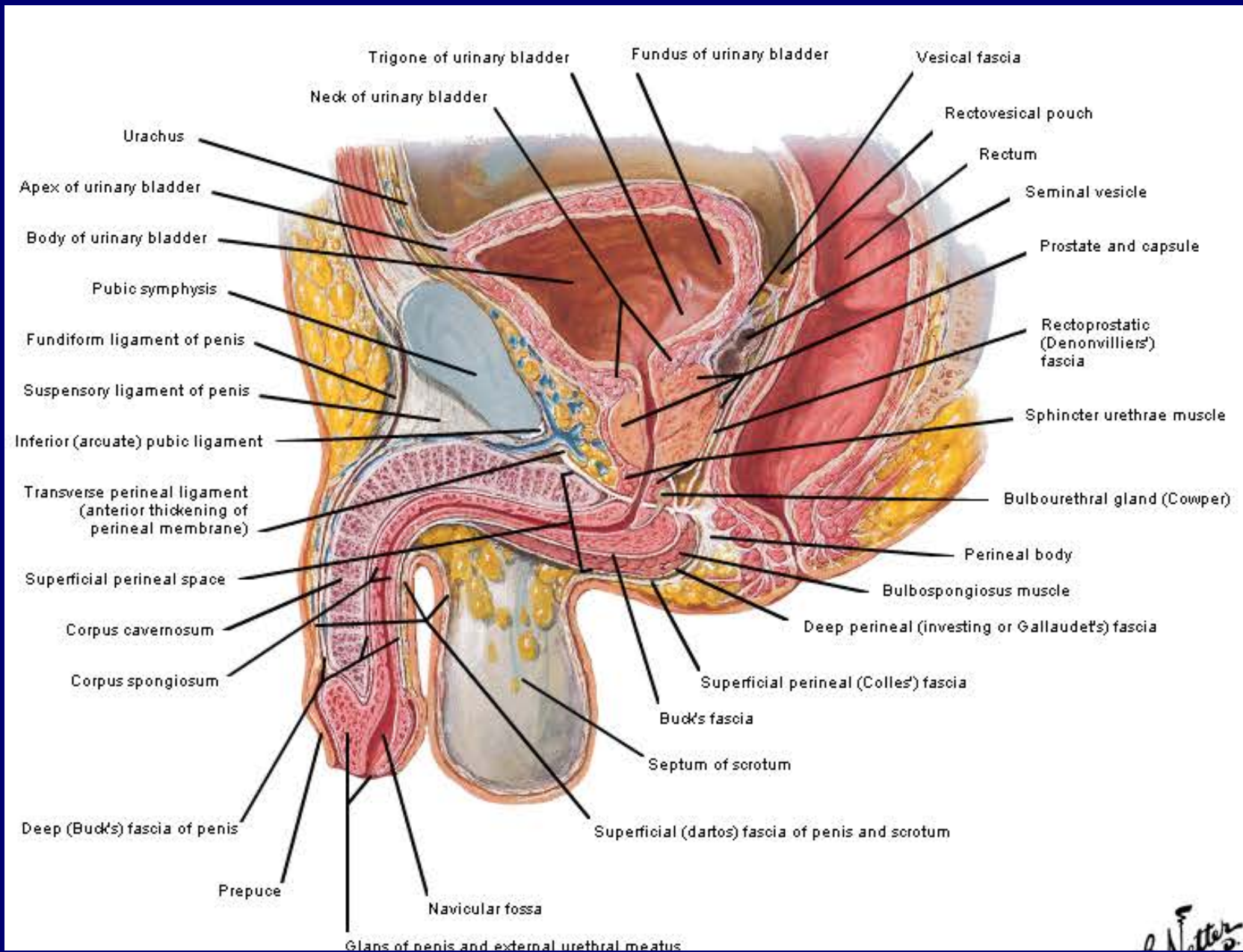
Madigan Army Medical Center



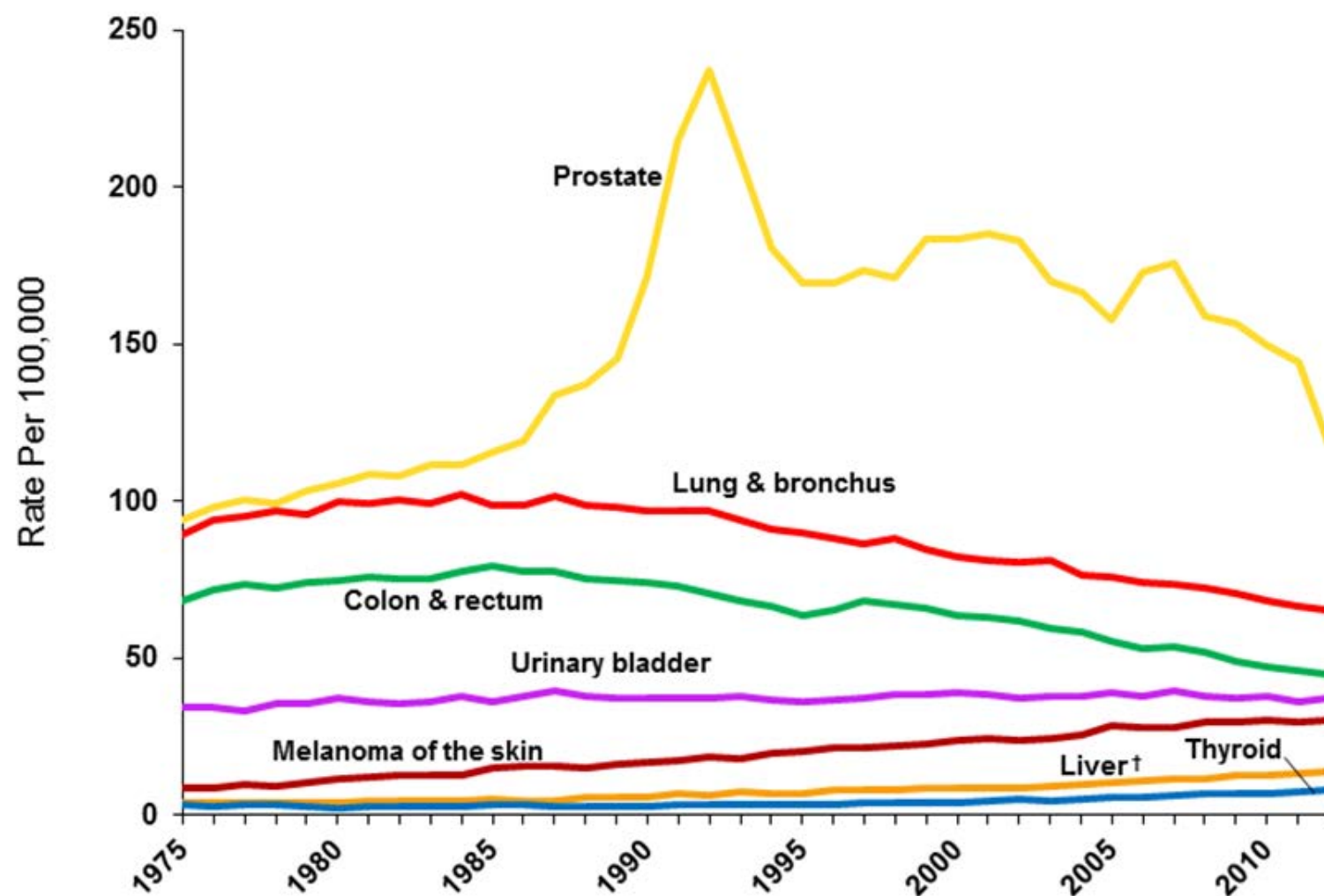
No Disclosures –
These views are
my own and not
that of the DoD.



Anatomy and Physiology



Trends in Cancer Incidence Rates* Among Males, US, 1975-2012



*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting. †Includes the intrahepatic bile duct.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2015.

THE FREQUENCY OF CARCINOMA AND INTRAEPITHELIAL NEOPLASIA OF THE PROSTATE IN YOUNG MALE PATIENTS

W. A. SAKR,* G. P. HAAS, B. F. CASSIN, J. E. PONTES AND J. D. CRISSMAN

From the Departments of Pathology and Urology, Harper Hospital, Wayne State University School of Medicine and Medical Examiner's Office, Wayne County, Detroit, Michigan

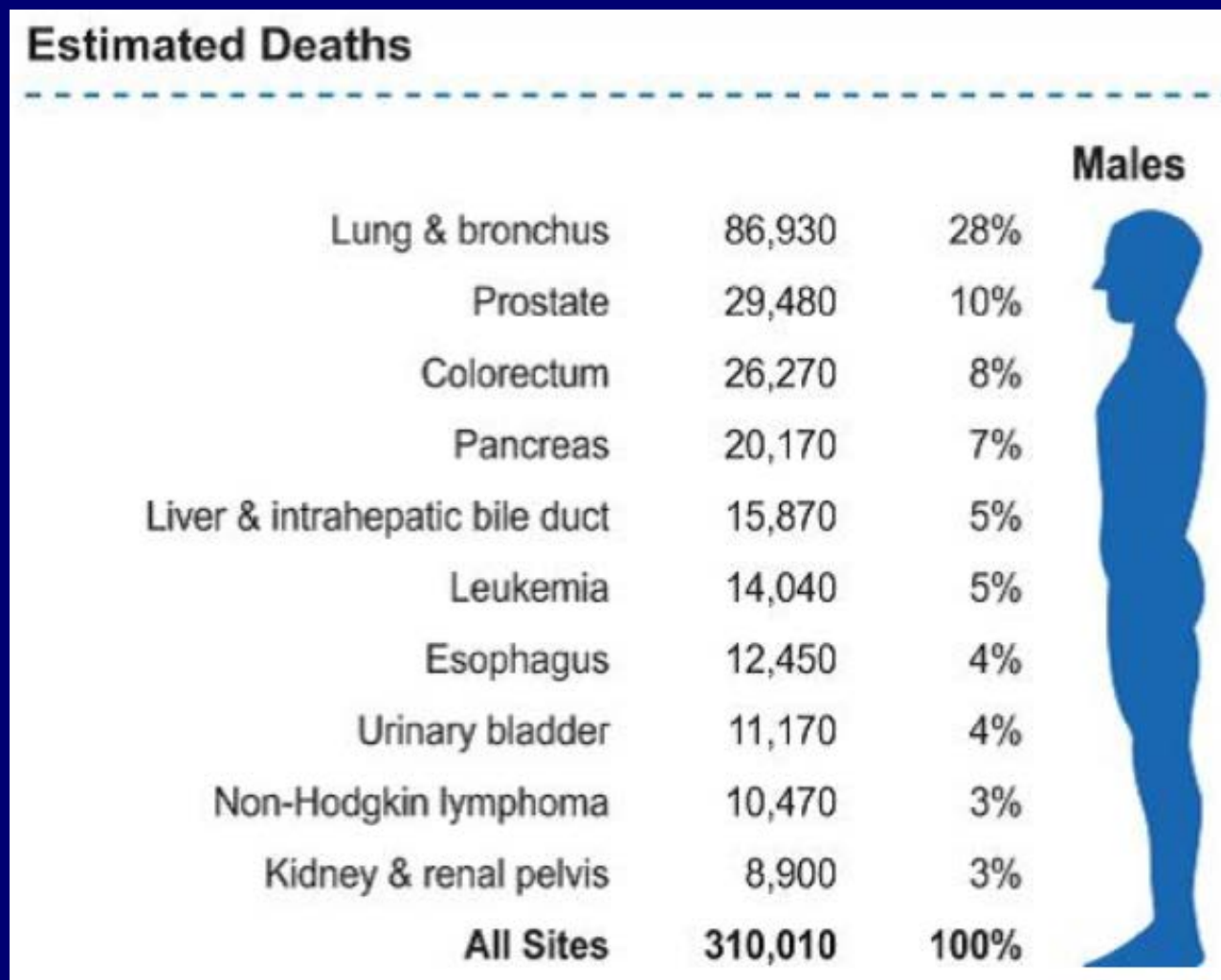
TABLE 1. *Histological findings distributed by age and race*

Histology	Pt. Age (yrs.)				Totals (%)
	10-19	20-29	30-39	40-49	
Prostatic intraepithelial neoplasia:					
Low grade:					
Black pts.	0/10 (0)	2/28 (7)	7/32 (22)	11/28 (39)	20/98 (20)
White pts.	0/2 (0)	1/7 (14)	4/23 (17)	6/22 (27)	11/54 (20)
Totals	0/12 (0)	3/35 (9)	11/55 (20)	17/50 (34)	31/152 (20)
High grade:					
Black pts.	0/10 (0)	0/28 (0)	0/32 (0)	3/28 (11)	3/98 (3)
White pts.	0/2 (0)	0/7 (0)	0/23 (0)	2/22 (9)	2/54 (4)
Totals	0/12 (0)	0/35 (0)	0/55 (0)	5/50 (10)	5/152 (3)
Histological Ca:					
Black pts.	0/10 (0)	0/28 (0)	8/32 (25)	10/28 (36)	19/98 (18)
White pts.	0/2 (0)	0/7 (0)	7/23 (30)	7/22 (32)	14/54 (26)
Totals	0/12 (0)	0/35 (0)	15/55 (27)	17/50 (34)	32/152 (21)

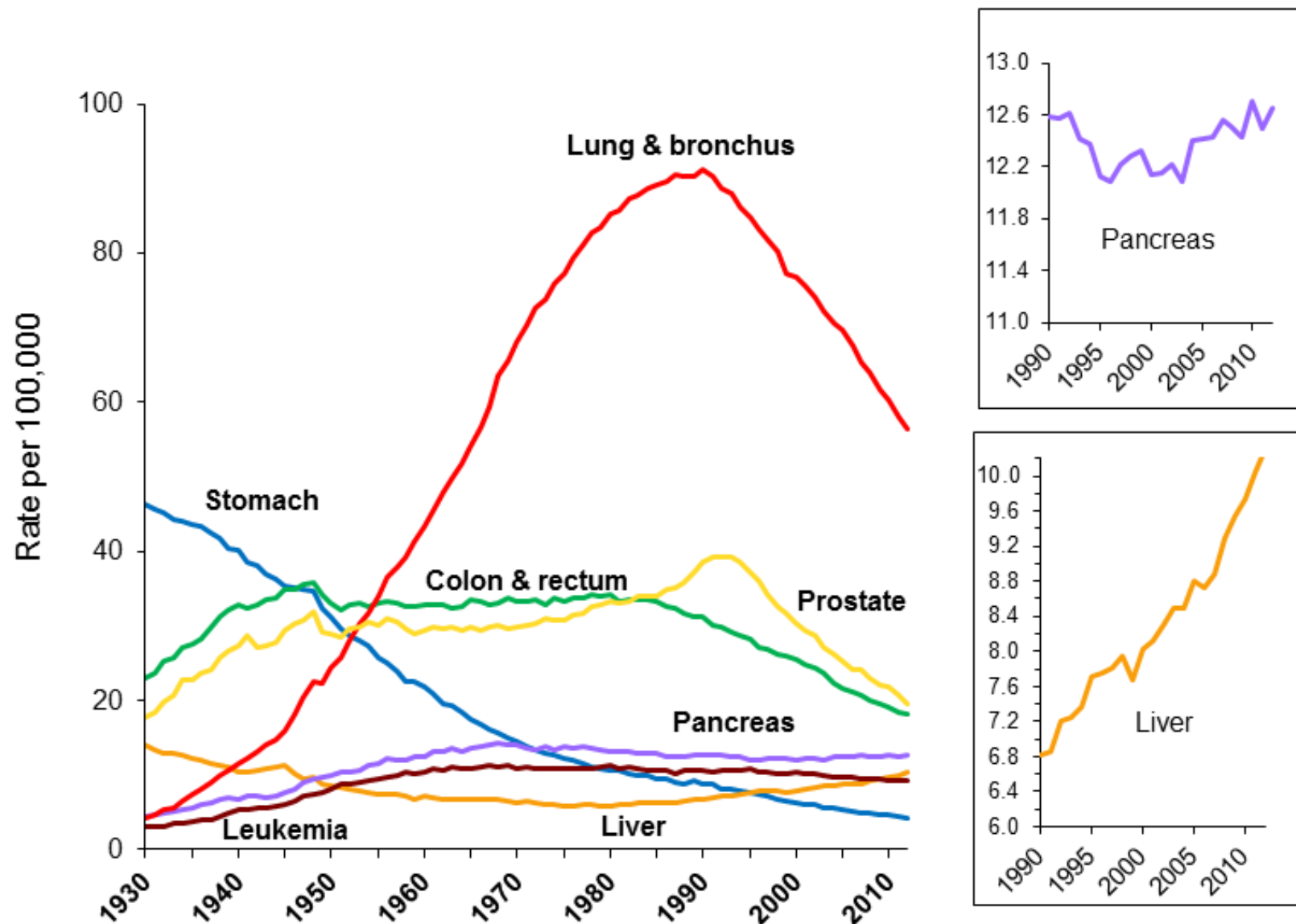
All values are reported as number of patients/total (%).

But, PCA remains a dread disease!

29,480 prostate cancer deaths in 2014



Trends in Cancer Death Rates* Among Males, US, 1930-2012



*Age-adjusted to the 2000 US standard population.

NOTE: Due to International Classification of Diseases coding changes, numerator information for colorectal and lung cancers has changed over time

Source: National Center for Health Statistics, Centers for Disease Control and Prevention, 2015.

ORIGINAL ARTICLE

Mortality Results from a Randomized Prostate-Cancer Screening Trial

Gerald L. Andriole, M.D., Robert L. Grubb III, M.D., Sandra S. Buys, M.D.,

N ENGL J MED 360;13 NEJM.ORG MARCH 26, 2009

PLCO Trial Design

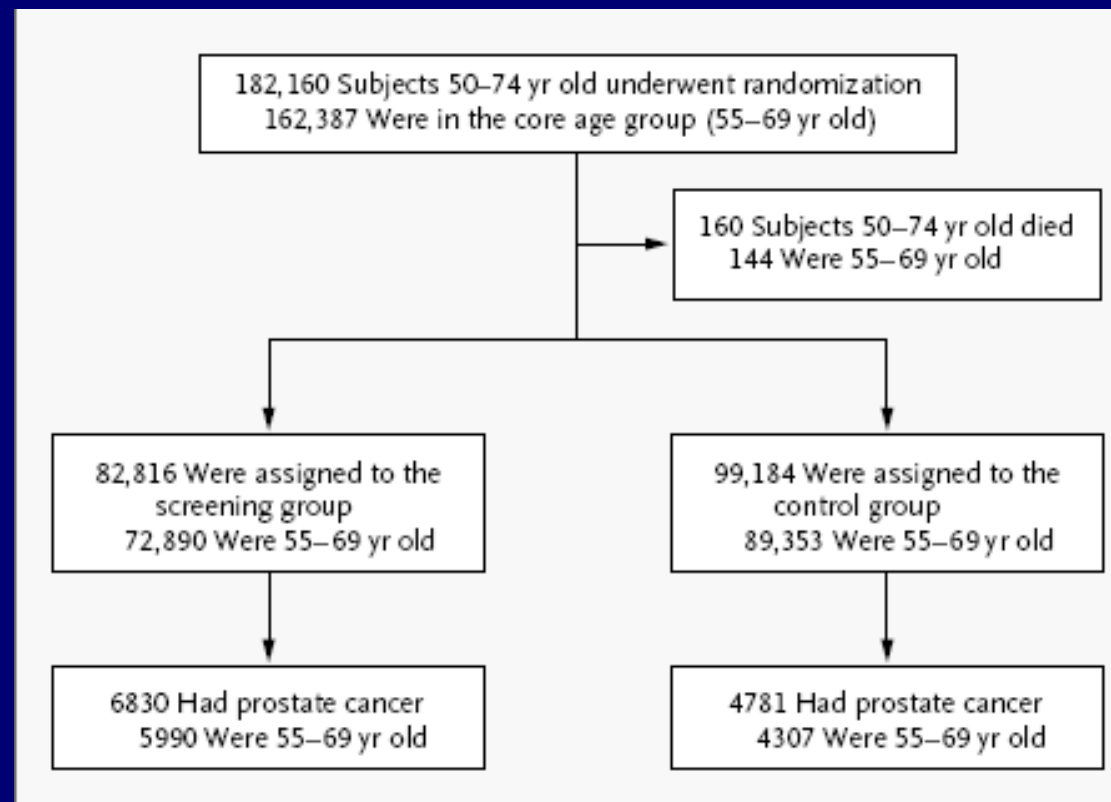
- 1993-2001 randomized 76,693 men to annual PSA testing for 6 years, annual DRE for 4 years. PSA > 4 – ‘positive’ or usual community care.
- At study entry, 44% of men had undergone one or more PSA tests.
 - Cumulative death rate from PCA 25% lower in those who underwent ≥ 2 PSA tests at baseline.

PSA and Prostate Cancer Screening Controversial

- On October 6, the U.S. Preventive Services Task Force (USPSTF) issued draft recommendations that downgraded the prostate-specific antigen (PSA) test to a “D” status. May it was finalized.
- Other organizations (American Cancer Society, American Urological Association, and others) continue to endorse prostate cancer screening after discussion with the individual

Screening and Prostate-Cancer Mortality in a Randomized European Study

Fritz H. Schröder, M.D., Jonas Hugosson, M.D., Monique J. Roobol, Ph.D.,



Study design

- Collection of designs.
 - Recruitment and randomization differed.
 - Age range varied (50-54, 55-74, 55-69...)
 - Randomization varied (1:1, 1:1.5...)
 - PSA cutoff varied (2.5, 3.0, 4.0, 10!)
 - Varying use of DRE
 - Varying biopsy (6, 10, 12)
 - Screening interval 94 years, 2 years, 7 years)
 - No central pathology review
 - Treatment not standardized. Differed for control and screening groups at some sites.


Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement

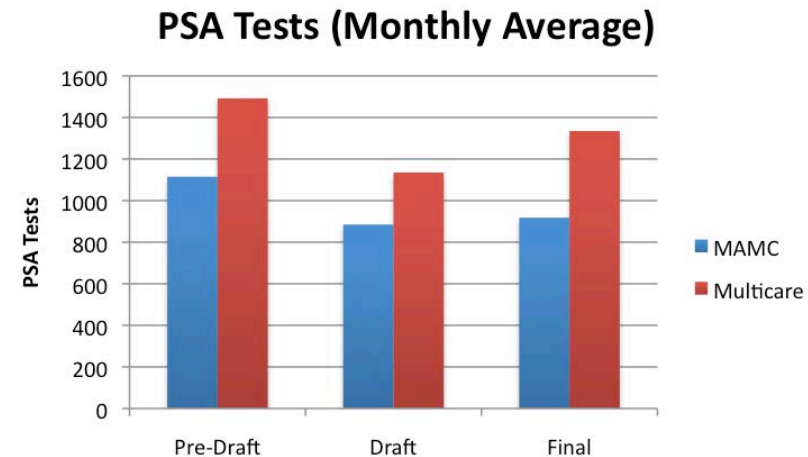
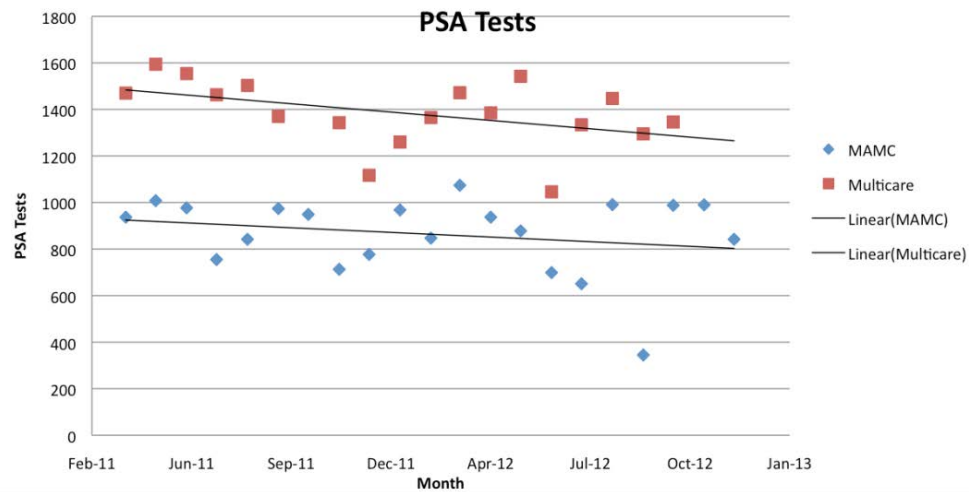
Virginia A. Moyer, MD, PhD, on behalf of the U.S. Preventive Services Task Force*

- ***Grade D designation***
- **On October 6, 2011 draft recommendations. May, 2012 it was finalized.**
- **Other organizations (American Cancer Society, American Urological Association, and others) continue to endorse prostate cancer screening after discussion with the individual**

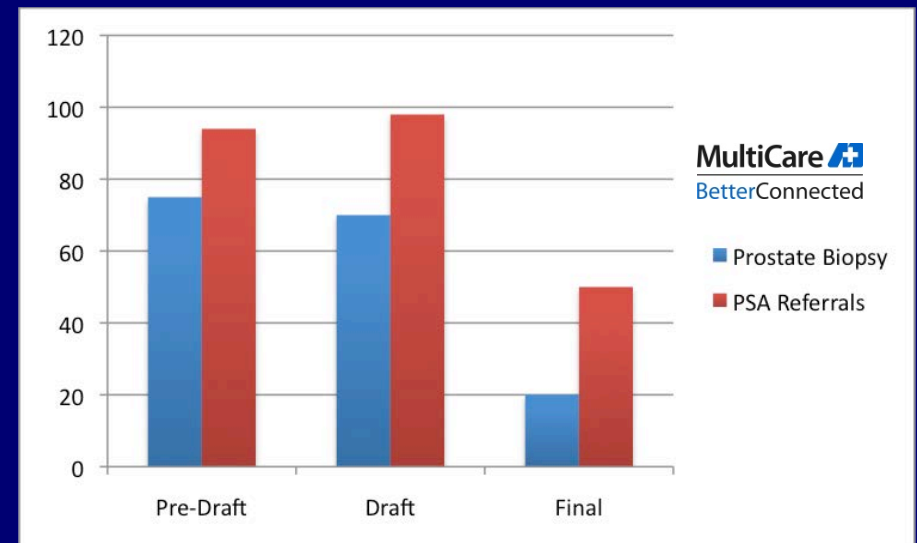
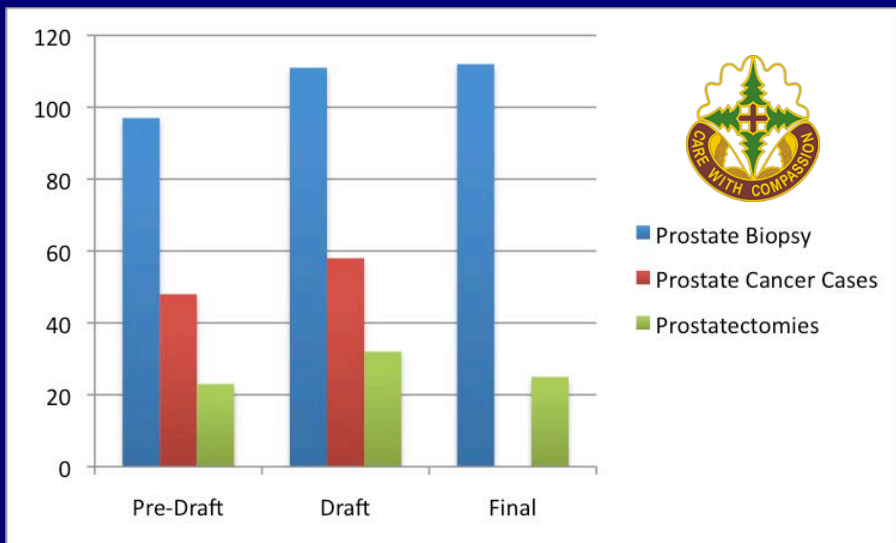


	Pre-Draft Apr 2011 – Nov 2011	Draft Dec 2011 – Apr 2012	Final May 2012 – Oct 2012
Total PSA Tests	6692 (1115)	6195 (885)	5506 (918)
Prostate Biopsy	97 (16)	111 (16)	112 (19)
Prostate Cancer Cases	48 (8)	58 (8)	24 (6)
Prostatectomies	23 (4)	32 (5)	25 (4)

MultiCare  BetterConnected	Pre-Draft Apr 2011 – Nov 2011	Draft Dec 2011 – Apr 2012	Final May 2012 – Dec 2012
PSA Tests	8954 (1492)	7942 (1135)	8010 (1135)
Prostate Biopsy	75 (13)	70 (10)	25 (4)
PSA Referrals	94 (16)	98 (14)	50 (8)



	Draft	Final	Total Change (Pre-Draft to Final)
MAMC PSA	- 20%	+ 0.04%	- 18% (P=0.2)
Multicare PSA	- 24%	+ 18%	- 11% (P=0.4)



	Pre-Draft	Draft	Final
MAMC Biopsy	16	16	19
MAMC Prostate Cancer Cases	8	8	6
MAMC Prostatectomies	4	5	4

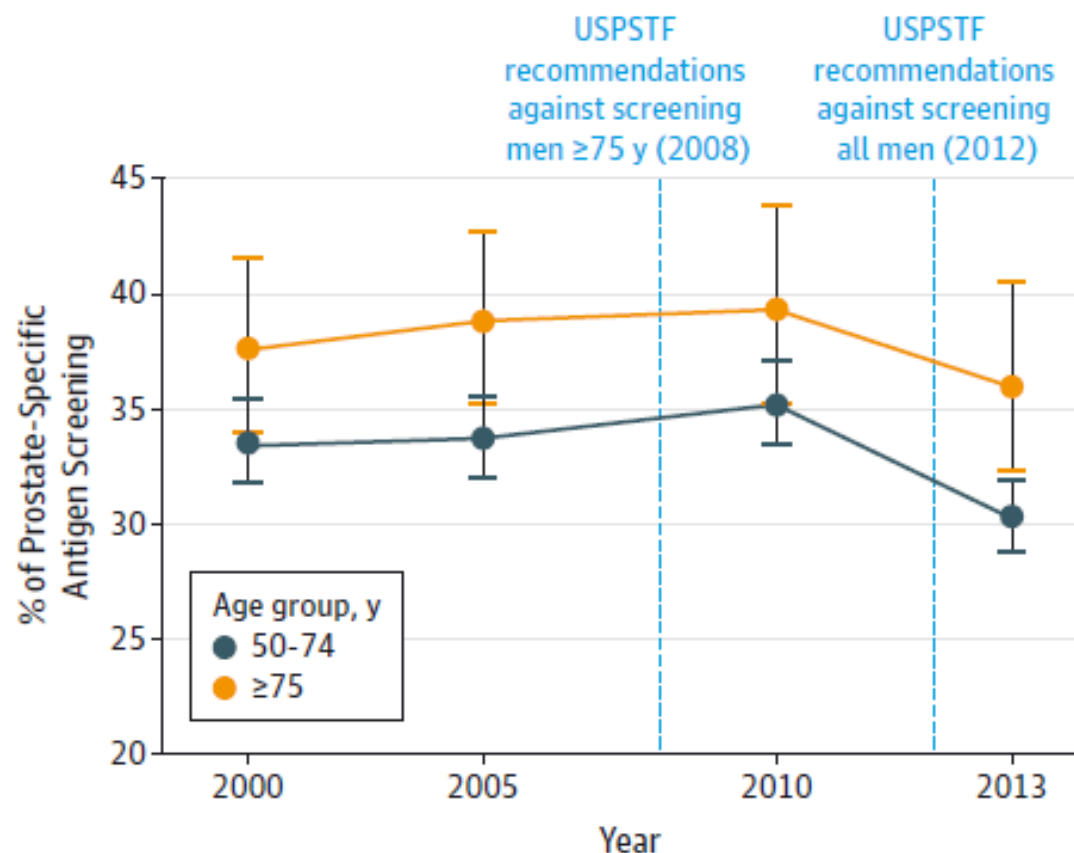
	Pre-Draft	Draft	Final
Multicare Biopsy	13	10	4
Multicare PSA Referrals	16	14	8

Methods | We examined PSA screening data from the 2000, 2005, 2010, and 2013 National Health Interview Survey (NHIS)

Sammon, et al.

JAMA November 17, 2015 Volume 314, Number 19

Figure. Prevalence of Prostate-Specific Antigen Screening From National Health Interview Survey (2000, 2005, 2010, and 2013)



No. surveyed

With age ≥ 75 y	761	834	707	984
With age 50-74 y	3937	4277	3891	5366

Error bars indicate 95% confidence intervals.

Jemal, et al.

JAMA November 17, 2015 Volume 314, Number 19

DESIGN AND SETTINGS Ecologic study of age-standardized prostate cancer incidence (newly diagnosed cases/100 000 men aged ≥ 50 years) by stage from 2005 through 2012 using data from 18 population-based Surveillance, Epidemiology, and End Results (SEER) registries and PSA screening rate in the past year among men 50 years and older without a history of prostate cancer who responded to the 2005 (n = 4580), 2008 (n = 3476), 2010 (n = 4157), and 2013 (n = 6172) National Health Interview Survey (NHIS).

Figure 1. Delay-Adjusted Prostate Cancer Incidence (per 100 000 Men) and

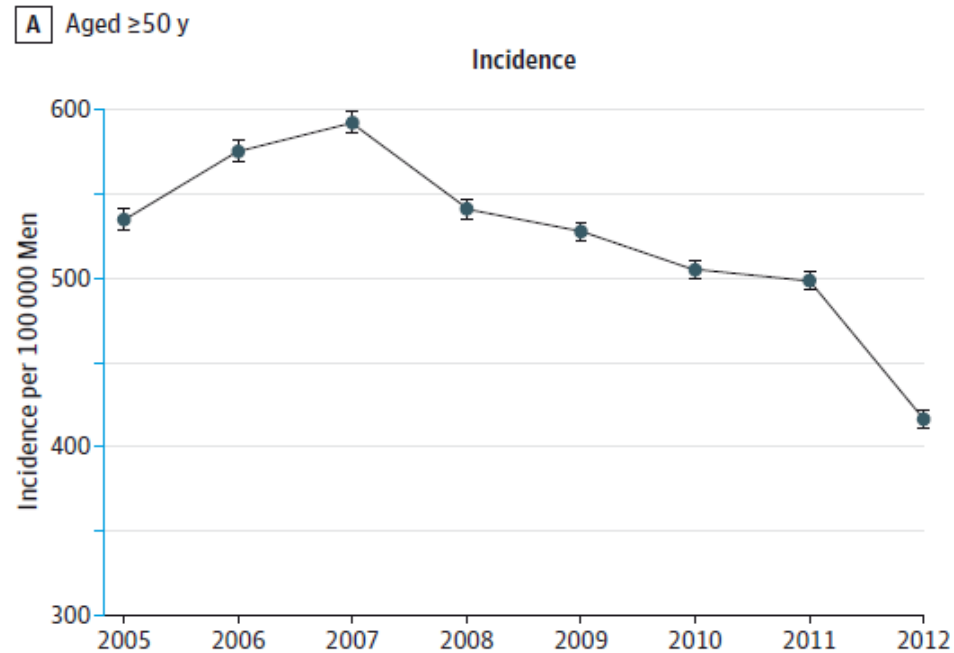
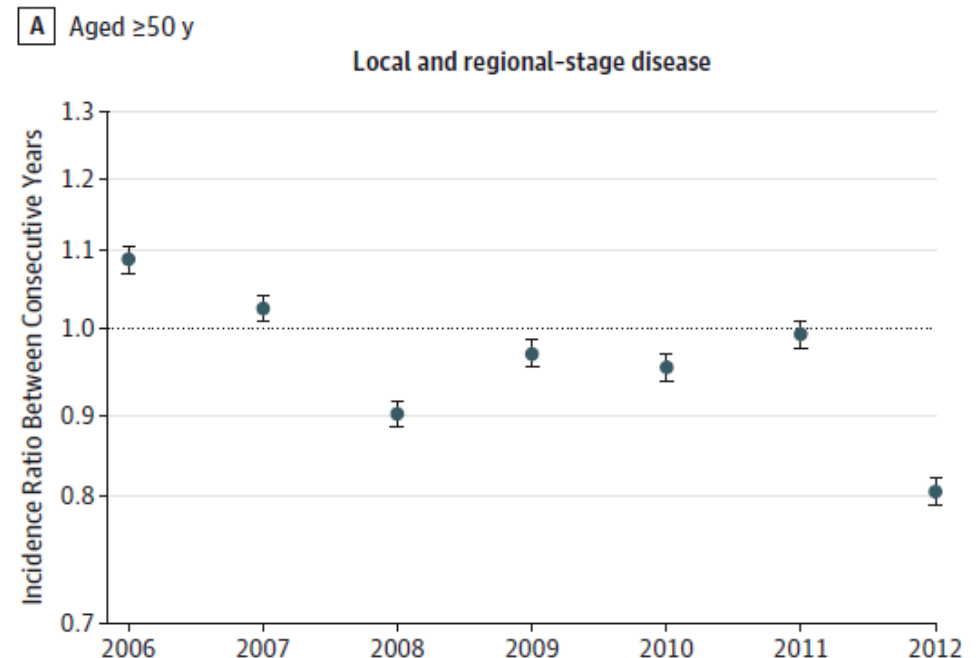


Figure 2. Prostate Cancer Incidence Ratio by Age Group and Summary Stage,

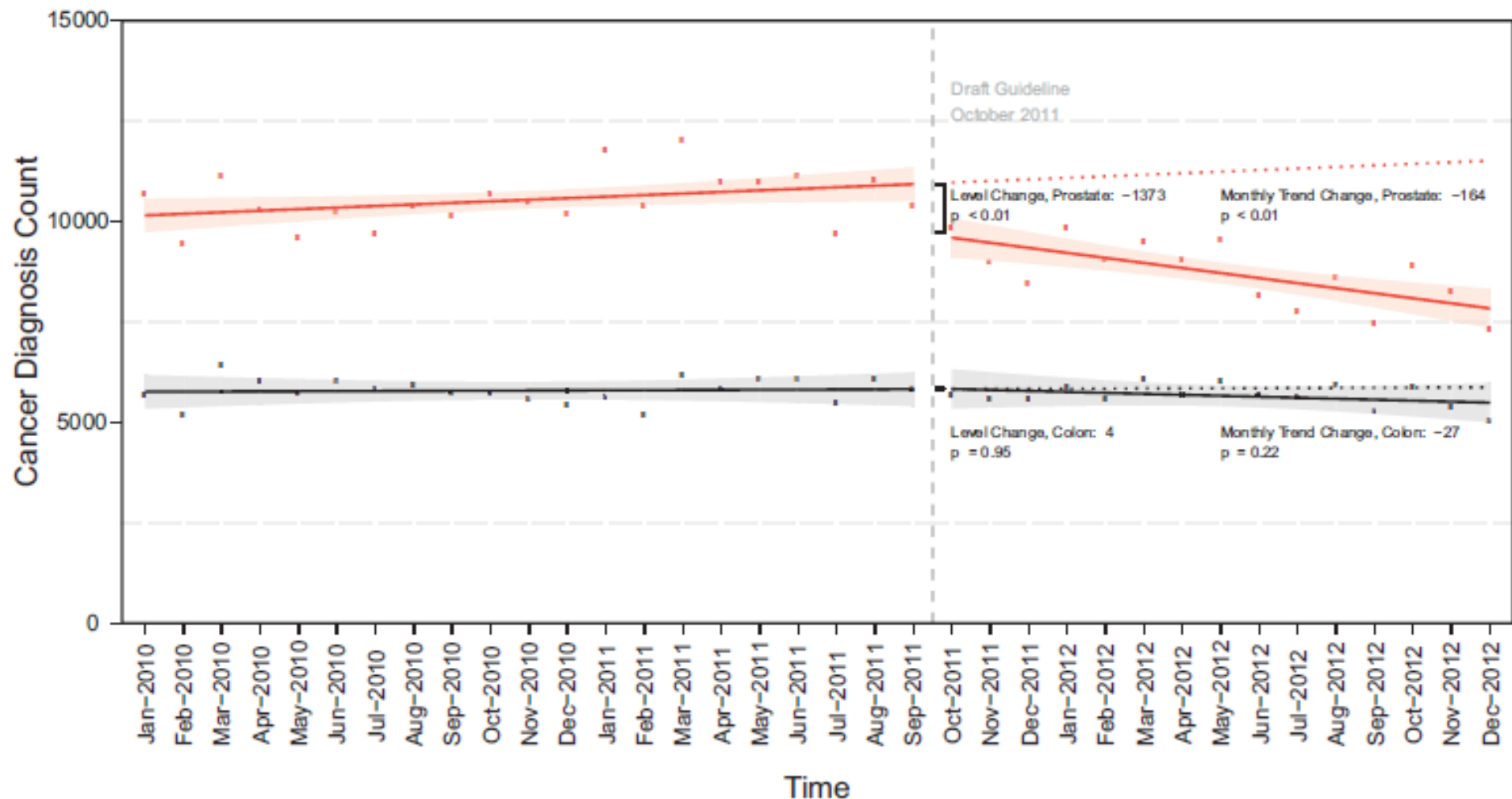


Barocas, et al

THE JOURNAL OF UROLOGY®

Vol. 194, 1587-1593, December 2015

Materials and Methods: We identified incident cancers diagnosed between January 2010 and December 2012 in NCDB (National Cancer Database). We



The *national experiment* in PSA screening. How did we get a cutoff value of 4.0?

Lifetime risk of prostate cancer in 1985 – 8%

About 8% of screened men had PSA > 4.0

PSA > 4.0 ng/ml – 25% PPV.

Felt to be an acceptable PPV.

Screening series conducted

Lo and behold: if you biopsy older men, you find prostate cancer.

Screening proliferated

Assessing Prostate Cancer Risk: Results from the Prostate Cancer Prevention Trial

Ian M. Thompson, Donna Pauler Ankerst, Chen Chi, Phyllis J. Goodman, Catherine M. Tangen, M. Scott Lucia, Ziding Feng, Howard L. Parnes, Charles A. Coltman, Jr.

5519 men

All had prostate biopsy and

- PSA and DRE at time of biopsy
- At least 2 prior PSA values

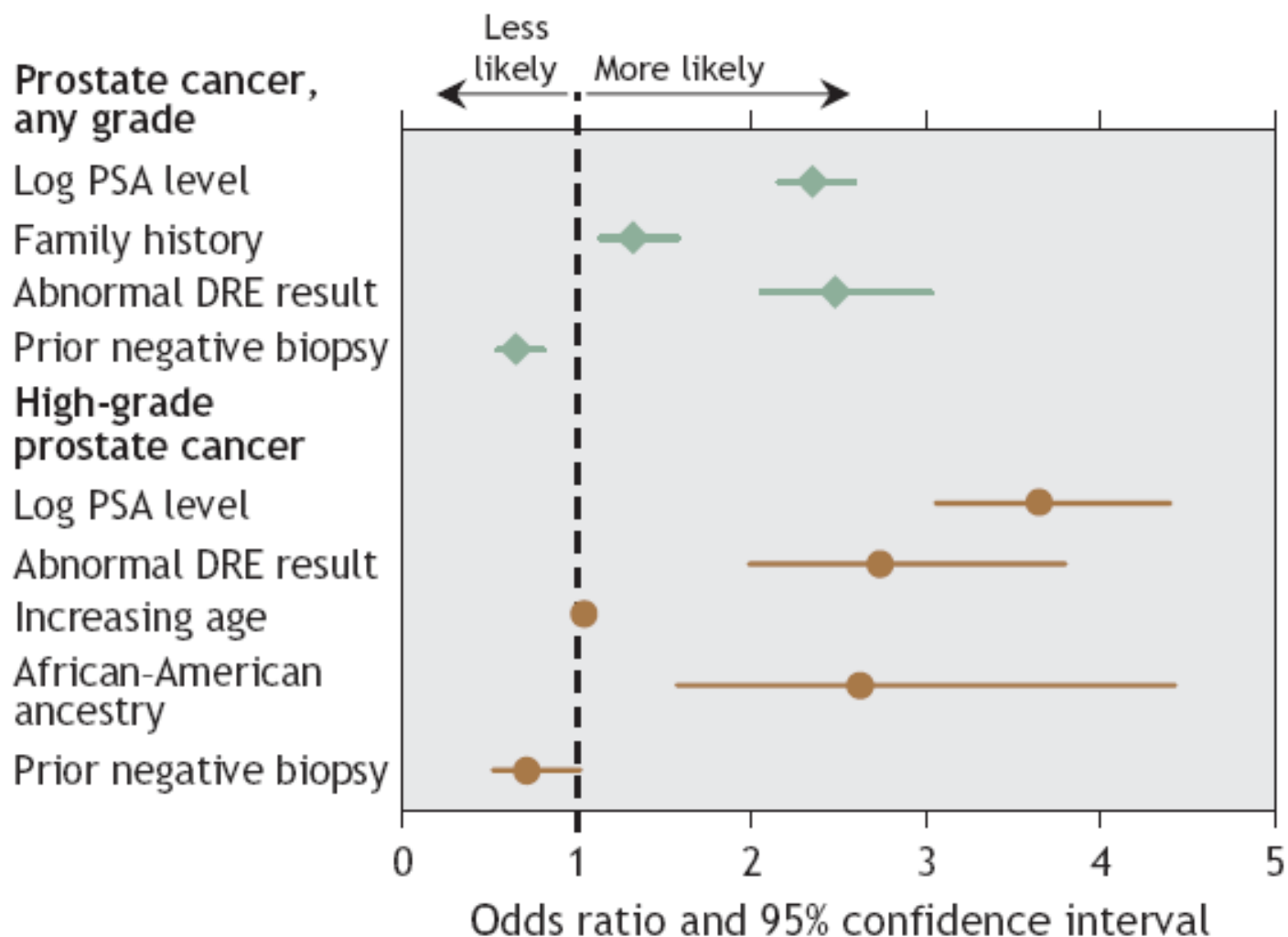


Fig. 3: Forest plot of risk factors for prostate cancer and for high-grade prostate cancer (Gleason score ≥ 7) if a prostate biopsy is performed. PSA = prostate-specific antigen, DRE = digital rectal examination.

How to find the risk calculator

1. Google 'prostate cancer risk calculator'
2. Click on top 'hit'

Web [Images](#) [Maps](#) [News](#) [Video](#) [Gmail](#) [more](#) ▼



[Sign in](#)

prostate cancer risk calculator

Search

[Advanced Search](#)

[Preferences](#)



Web

Results 1 - 10 of about 108,000 for [prostate cancer risk calculator](#). (0.27 seconds)

1. [Risk of Biopsy-Detectable Prostate Cancer](#)

The **Cancer Risk Calculator for Prostate Cancer** was developed based upon 5519 men in the placebo group of the **Prostate Cancer Prevention Trial**. ...

[deb.uthscsa.edu/URORiskCalc/Pages/uroriskcalc.jsp](#) - 6k - [Cached](#) - [Similar pages](#)

2. [The Sunnybrook prostate cancer risk calculator](#) « THE "NEW ...

The Sunnybrook **prostate cancer risk calculator**. Posted on May 28, 2008 by E. Michael D. ("Mike") Scott. A new online **calculator**, developed by a Canadian ...

[prostatecancerinfolink.net/2008/05/28/the-sunnybrook-prostate-cancer-risk-calculator/](#) - 23k

- [Cached](#) - [Similar pages](#)

3. [The Sunnybrook prostate cancer risk calculator](#) « THE "NEW ...

The Sunnybrook **prostate cancer risk calculator** is the second online **prostate cancer risk assessment tool**

Risk of Biopsy-Detectable Prostate Cancer

Fields marked with
asterisks (*) are
required.

Enter Your Information	
* Race	<input type="text"/>
* Age	<input type="text"/>
* PSA Level ?	<input type="text"/> ng/ml
* Family History of Prostate Cancer ?	<input type="text"/>
* Digital Rectal Examination ?	<input type="text"/>
* Prior Prostate Biopsy ?	<input type="text"/>
* Is the patient taking finasteride?	<input type="text"/>

Calculate Cancer Risk

Prostate Biopsy



Prostate Cancer

Staging

- Stage T1
 - Nonpalpable prostate cancer
 - Detected only on pathologic examination
 - Incidentally noted after
 - Transurethral resection for benign hypertrophy (T1a and T1b) or
 - On biopsy obtained because of an elevated PSA (T1c-the most common clinical stage at diagnosis)
- Stage T2
 - Palpable tumor
 - Appears to be confined to the prostatic gland (T2a if one lobe, T2b if two lobes)
- Stage T3
 - Tumor with extension through the prostatic capsule (T2a if focal, T2b if seminal vesicles are involved)
- Stage T4
 - Invasion of adjacent structures
 - Bladder neck
 - External urinary sphincter
 - The rectum
 - The levator muscles
 - The pelvic sidewall
- Nodal metastases
 - Can be microscopic and can be detected only by biopsy or lymphadenectomy, or they can be visible on imaging studies
- Distant metastases
 - Predominantly to bone
 - Occasional visceral metastases occur.

Prostate Cancer

Staging

- Stage T1
 - Nonpalpable prostate cancer
 - Detected only on pathologic examination
- Stage T2
 - Palpable tumor
 - Appears to be confined to the prostatic gland (T2a if one lobe, T2b if two lobes)
- Stage T3
 - Tumor with extension through the prostatic capsule (T2a if focal, T2b if seminal vesicles are involved)
- Stage T4
 - Invasion of adjacent structures

Prostate Cancer

Treatment

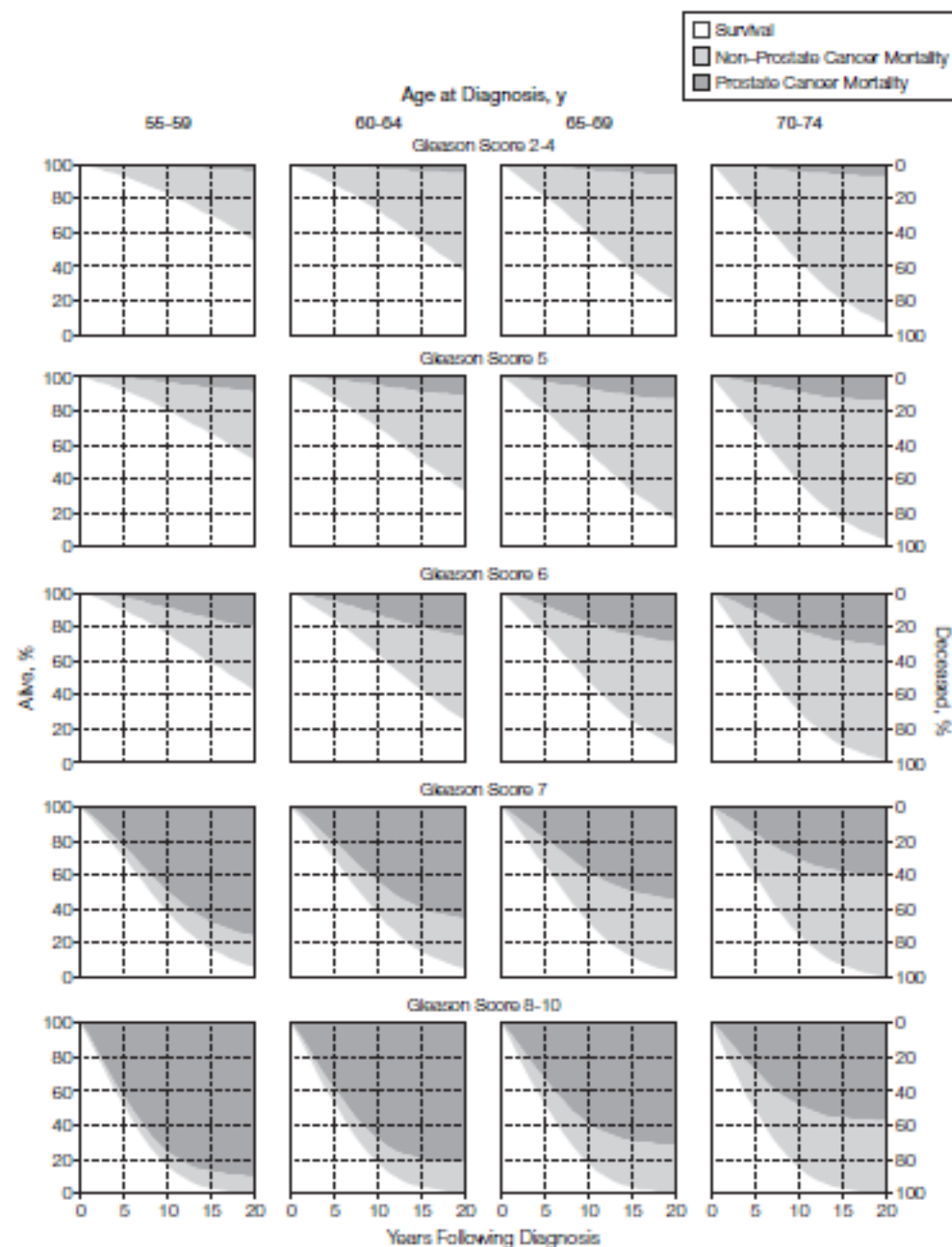
- Localized
 - Surgery
 - Traditional
 - Robotic
 - Radiation
 - Brachytherapy
 - External beam
 - Cryotherapy
 - Watchful waiting
- Advanced
 - Androgen Deprivation
 - Castrate Refractory



Albertsen's Competing Risks

JAMA, May 4, 2005—Vol 293, No. 17

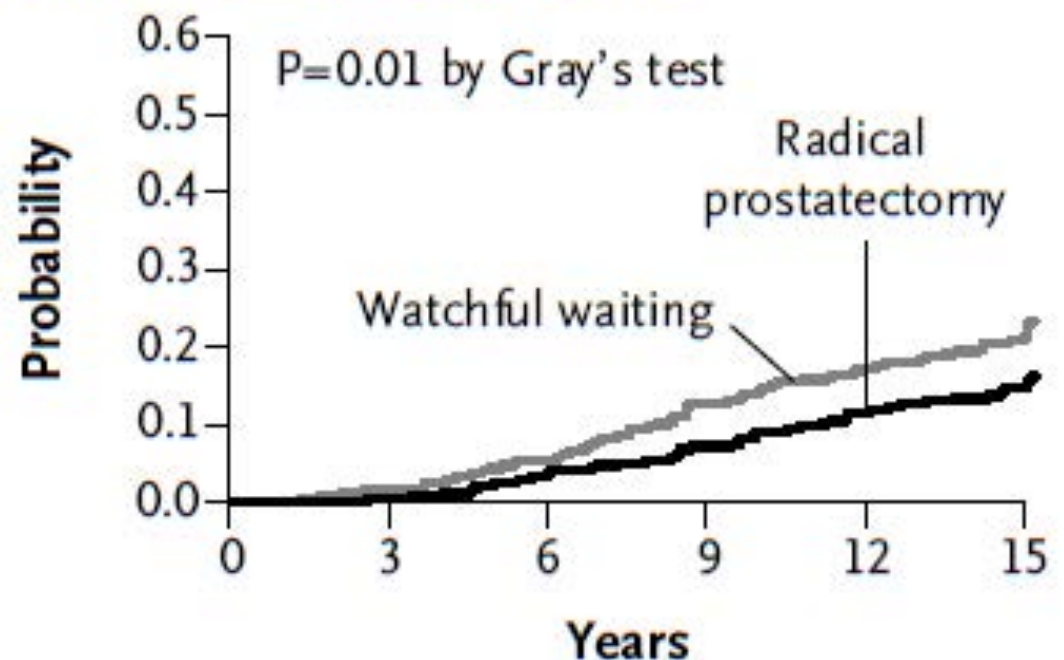
Figure. Survival and Cumulative Mortality From Prostate Cancer and Other Causes Up to 20 Years After Diagnosis, Stratified by Age at Diagnosis and Gleason Score



Bill-Axelsson's Active Surveillance vs. Prostatectomy

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

B Death from Prostate Cancer, Total Cohort



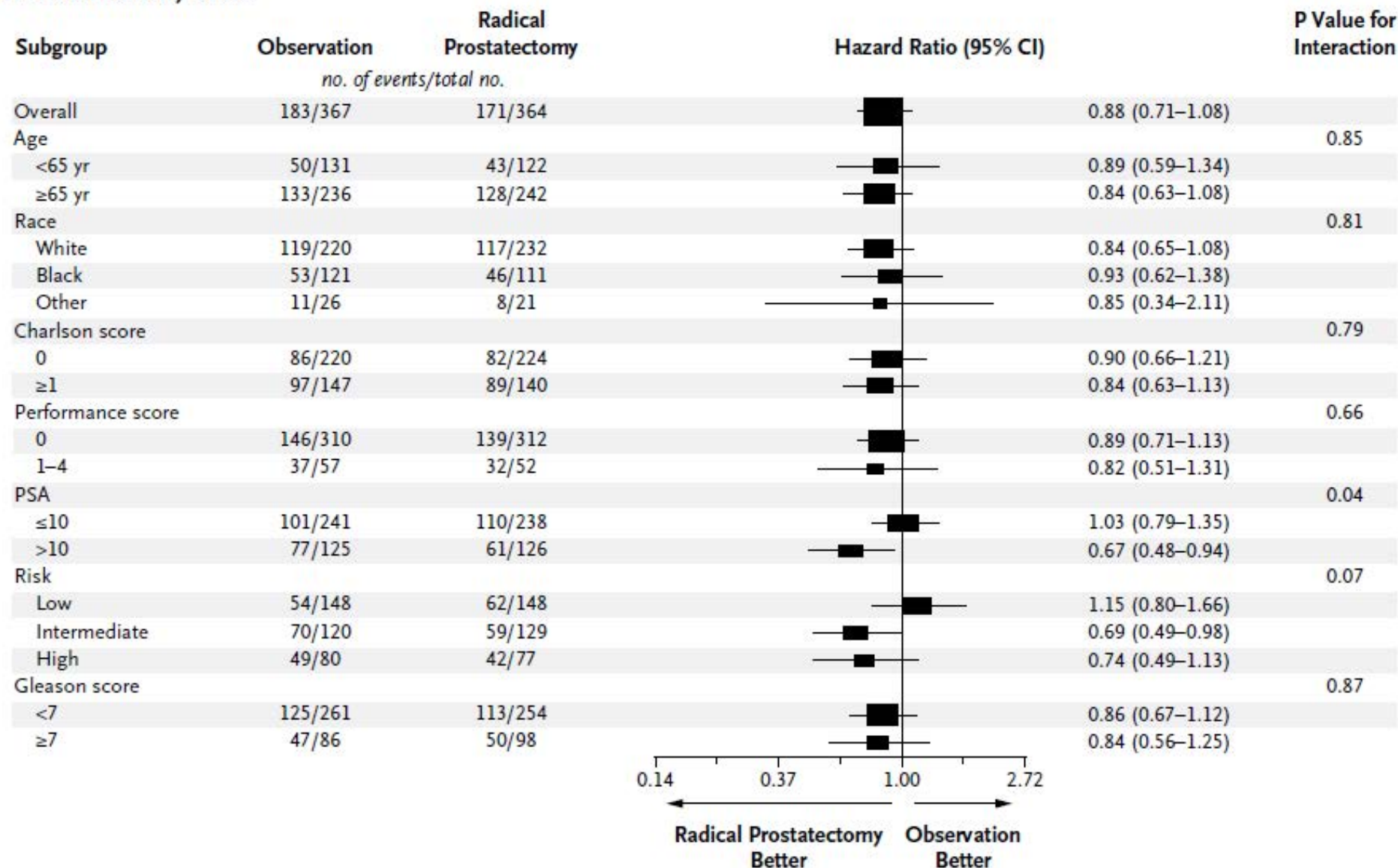
No. at Risk

Radical prostatectomy	347	339	311	271	214	109
Watchful waiting	348	334	306	251	192	96

PIVOT Trial

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

A Death from Any Cause



SWOG 8890

SCHEMA

REGISTRATION*

Randomize Prior to Pelvic Lymph Node Dissection (PLND)
PLND within 8 weeks of Registration

(+)
Off-Study

(-)
Proceed with Treatment
Assigned

ARM I SURGERY

Radical Prostatectomy (retropubic or
perineal)

FOLLOW

Death

Progression

ARM II RADIOTHERAPY

External Radiation
6800 cGy/34 fractions
TDF 200 cGy fractions
M-F (7-10 weeks)

FOLLOW

Progression

Death

Off-Study

SWOG 8890

Study accrual: 6 patients over 21 months.

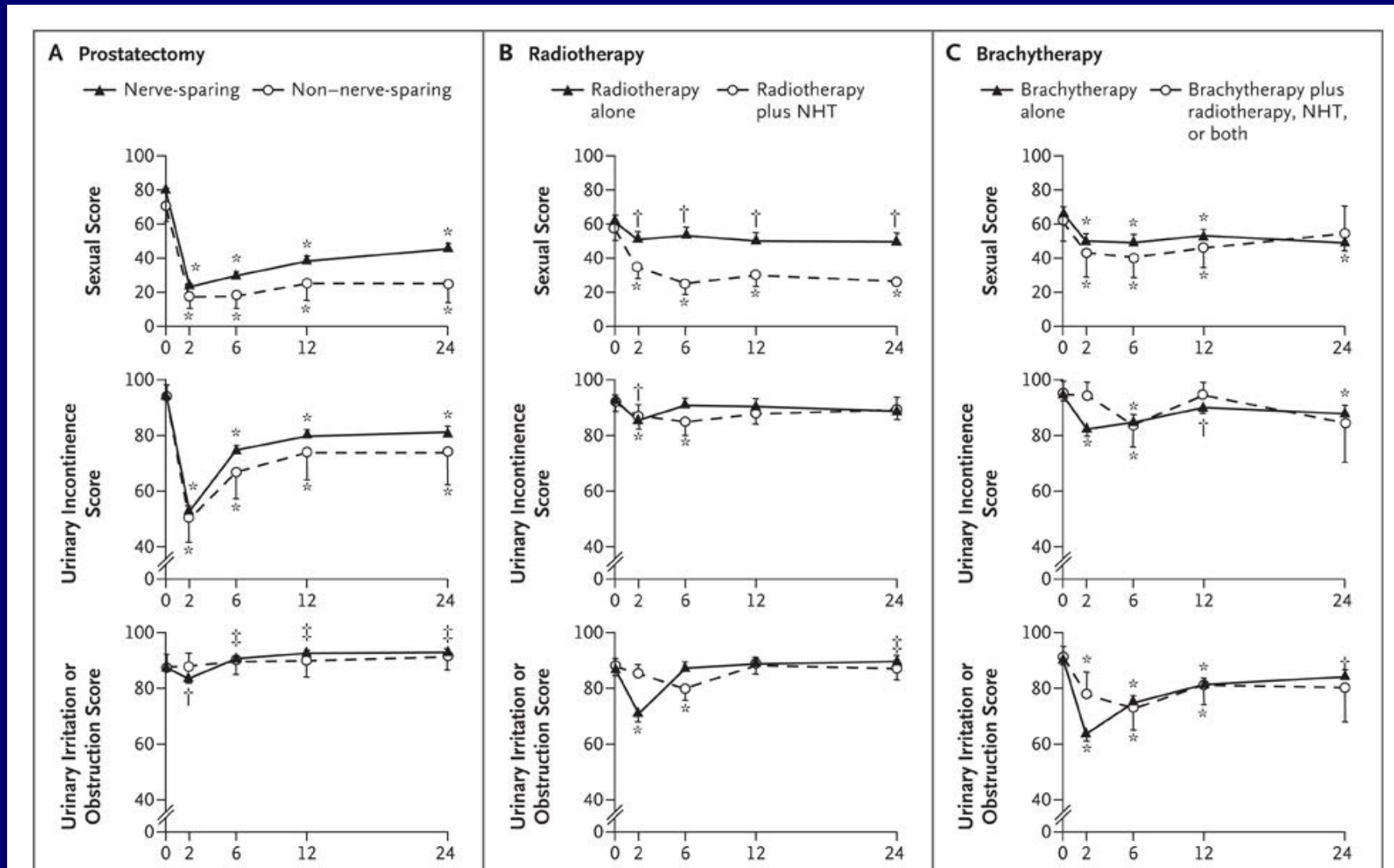
Closed to accrual

Prostate Cancer

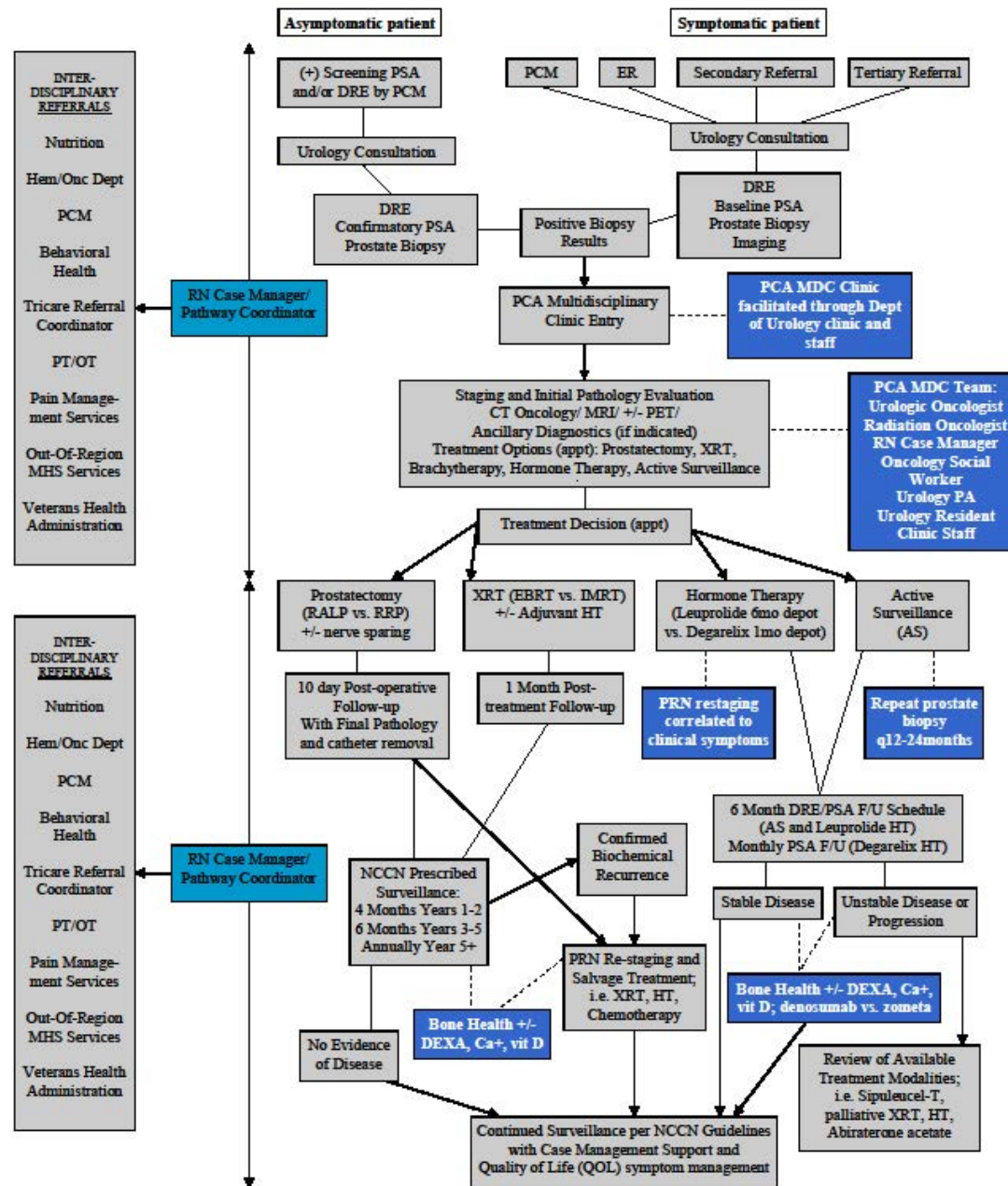
Treatment

- Require individualization
 - Must take into account
 - Patient's comorbidity
 - Life expectancy
 - Likelihood of cure
 - Personal preferences
 - Based on an understanding of potential morbidity associated with each treatment
 - A multidisciplinary approach (recommended)
 - Integrate
 - » Surgery
 - » Radiation therapy
 - » Androgen deprivation
 - » Behavioral therapy

Changes in Quality of Life after Primary Treatment for Prostate Cancer.



Prostate Cancer Multi-Disciplinary Pathway, Madigan Healthcare System



Patient-Specific Meta-Analysis of Multiple Studies to Predict Pathologic Outcomes in Clinically Localized Prostate Cancer Using a 17-Gene Genomic Prostate Score

Brand T,¹ Cooperberg M,² Sesterhenn I,³ Simko J,² Zhang N,⁴
Crager M,⁴ Maddala T,⁴ Lawrence HJ,⁴ Febbo P,⁴ Chan J,²
Carroll P,² Srivastava S,⁵ and Cullen J⁵

¹Madigan Army Medical Center, Tacoma, WA; ²University of California, San Francisco, San Francisco, CA; ³Joint Pathology Center, Silver Spring, MD;
⁴Genomic Health, Inc., Redwood City, CA; ⁵Center for Prostate Disease Research, Rockville, MD

17-Gene Oncotype DX® Genomic Prostate Score

Genes Associated with Worse Outcome

Stromal Response

BGN
COL1A1
SFRP4

Proliferation

TPX2

Genes Associated with Better Outcome

Androgen Signaling

AZGP1
FAM13C
KLK2
SRD5A2

Cellular Organization

FLNC
GSN
GSTM2
TPM2

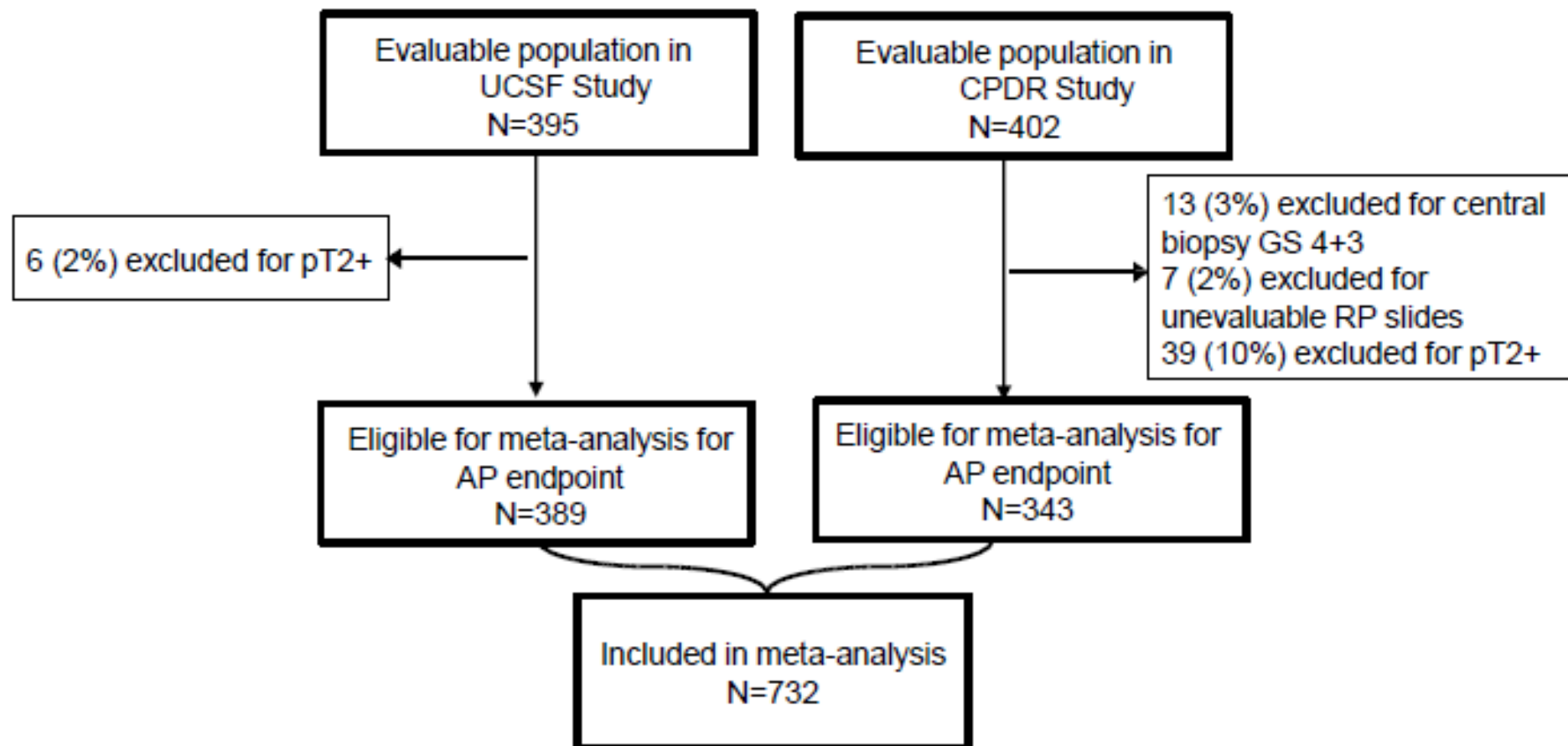
Reference Genes

ARF1 *GPS1*
ATP5E *PGK1*
CLTC

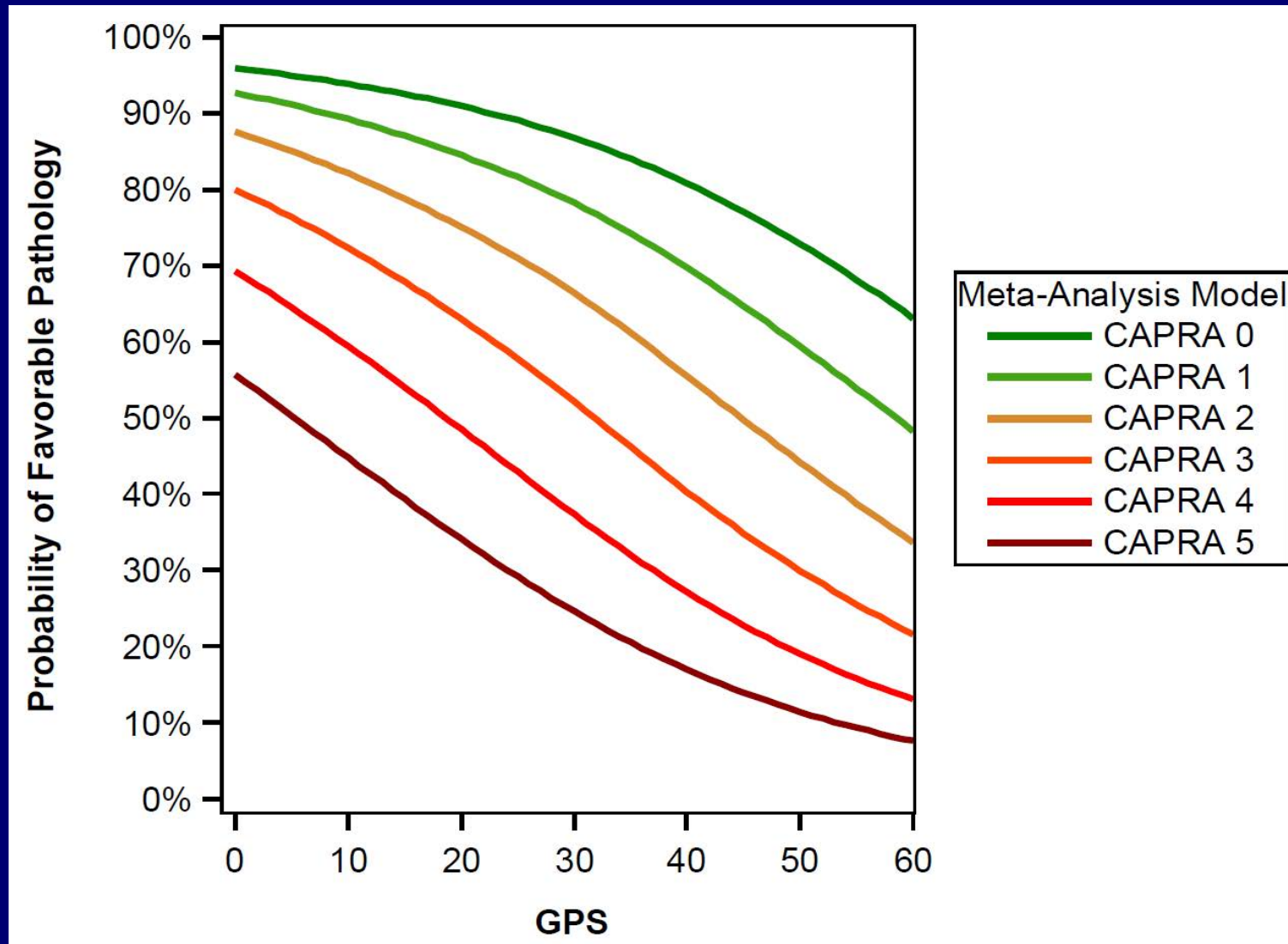
GPS (scaled 0-100) =

{Stromal Response Group}
- {Androgen Signaling Group}
- {Cellular Organization Group}
+ {Proliferation}

Each gene is individually weighted in the final algorithm

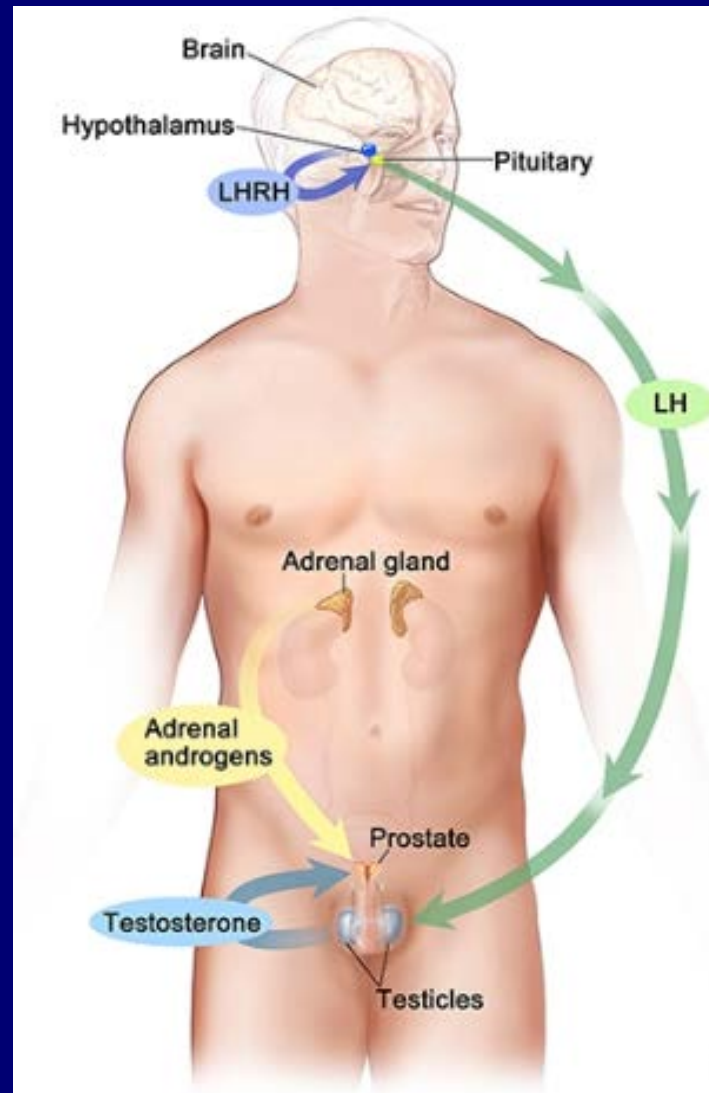


Risk Profiles for GPS and CAPRA Score



Treatment for Systemic Disease

Hormone Therapy



Treatment after Hormone Therapy

- Enzalutamide
- Abiraterone
- Sipulicel-T
- Xofigo
- Xgeva, Zometa
- Docetaxel
- Clinical Trial