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Prostate Cancer

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Objectives

1. To learn the prostate cancer incidence and mortality
2. To understand the prostate anatomy
3. To learn the prostate cancer screening and detection methods
4. To understand different treatment modalities for prostate cancer
5. To understand the history of radical prostatectomy



Background

- Prostate Cancer/Adenocarcinoma of the prostate
 - The most common non-skin cancer in U.S. men*
 - The third most common cause of cancer death

- Radical Prostatectomy
 - The most frequently performed treatment modality for clinically localized prostate cancer*

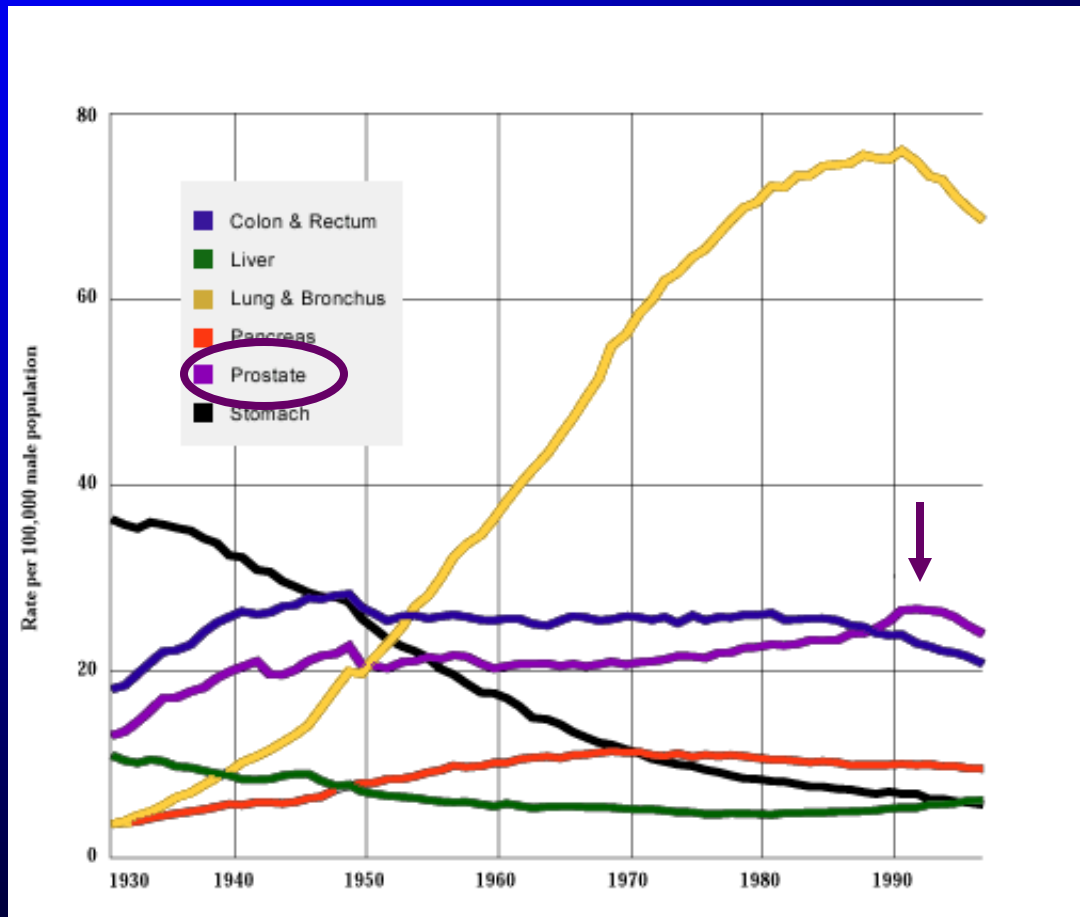
Leading Sites of New Cancer Cases & Deaths (2007 Estimates)



Estimated New Cases		Estimated Deaths	
Male	Female	Male	Female
Prostate 218,890 (29%)	Breast 178,480 (26%)	Lung & Bronchus 89,510 (31%)	Lung & Bronchus 70,880 (26%)
Lung & Bronchus 114,760 (15%)	Lung & Bronchus 98,620 (15%)	Prostate 27,050 (9%)	Breast 40,460 (15%)
Colon & Rectum 79,130 (10%)	Colon & Rectum 74,630 (11%)	Colon & Rectum 26,000 (9%)	Colon & Rectum 26,180 (10%)
Urinary bladder 50,040 (7%)	Uterine corpus 39,080 (6%)	Pancreas 16,840 (6%)	Pancreas 16,530 (6%)
Non-Hodgkin Lymphoma 34,200 (4%)	Non-Hodgkin Lymphoma 28,990 (4%)	Leukemia 12,320 (4%)	Ovary 15,280 (6%)
Melanoma of the skin 33,910 (4%)	Melanoma of the skin 26,030 (4%)	Liver/intrahepatic bile duct 11,280 (4%)	Leukemia 9,470 (4%)
Kidney & renal pelvis 31,590 (4%)	Thyroid 25,480 (4%)	Esophagus 10,900 (4%)	Non-Hodgkin Lymphoma 9,060 (3%)
Leukemia 24,800 (3%)	Ovary 22,430 (3%)	Urinary bladder 9,630 (3%)	Uterine corpus 7,400 (3%)
Oral cavity & Pharynx 224,180 (3%)	Kidney & renal pelvis 19,600 (3%)	Non-Hodgkin lymphoma 9,600 (3%)	Brain/nervous system 5,590 (2%)
Pancreas 18,830 (2%)	Leukemia 19,440 (3%)	Kidney & renal pelvis 8,080 (3%)	Liver/intrahepatic bile duct 5,500 (2%)
All sites 766,860 (100%)	All sites 678,060 (100%)	All sites 289,550 (100%)	All sites 270,100 (100%)



Age-Adjusted Cancer Death Rates, Males by Site, US, 1930-1996



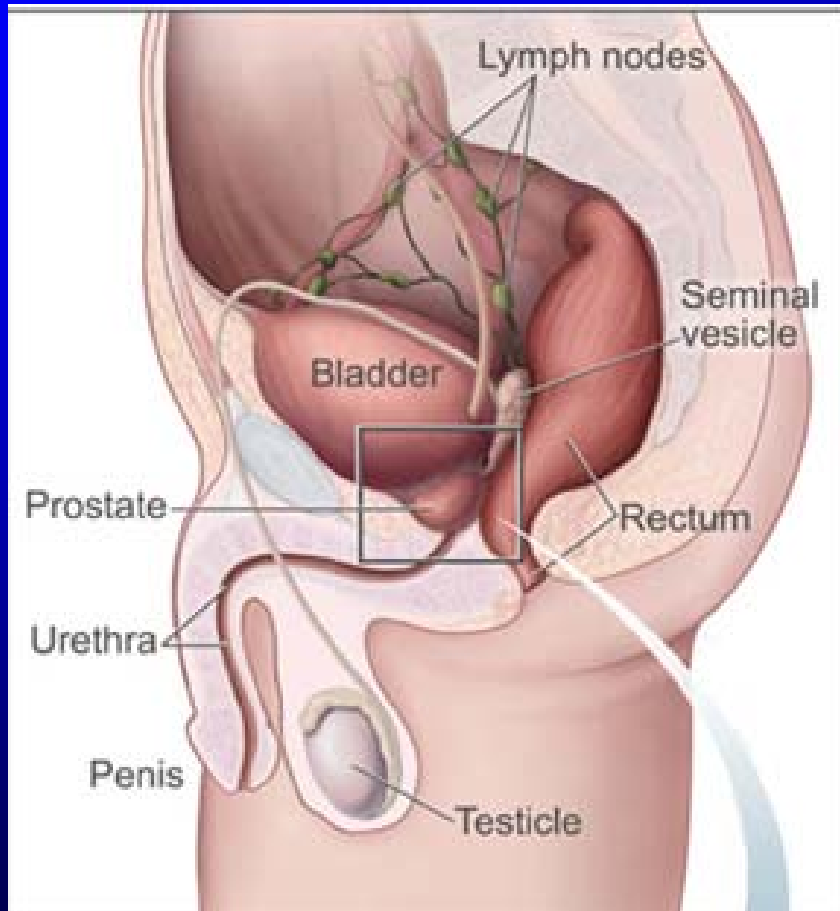
Per 100,000, age-adjusted to the 1970. US standard population US Mortality,
US Mortality Volumes 1930-1959, National Center for Health Statistics,
Centers for Disease Control and Prevention, © 1999.



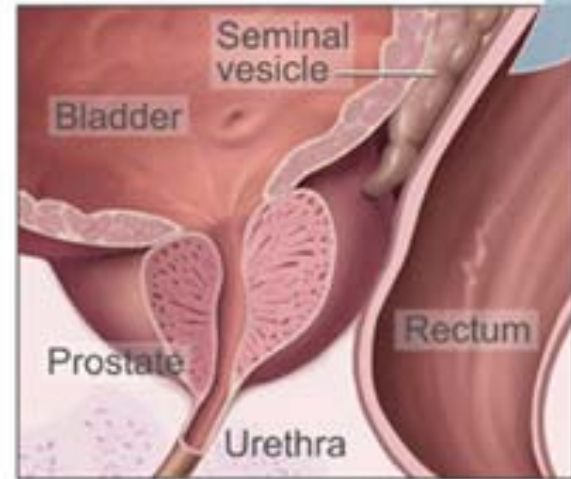
Risk Factors

- Age
- Family History
- Race or Ethnic Origin
- Diet

Anatomy

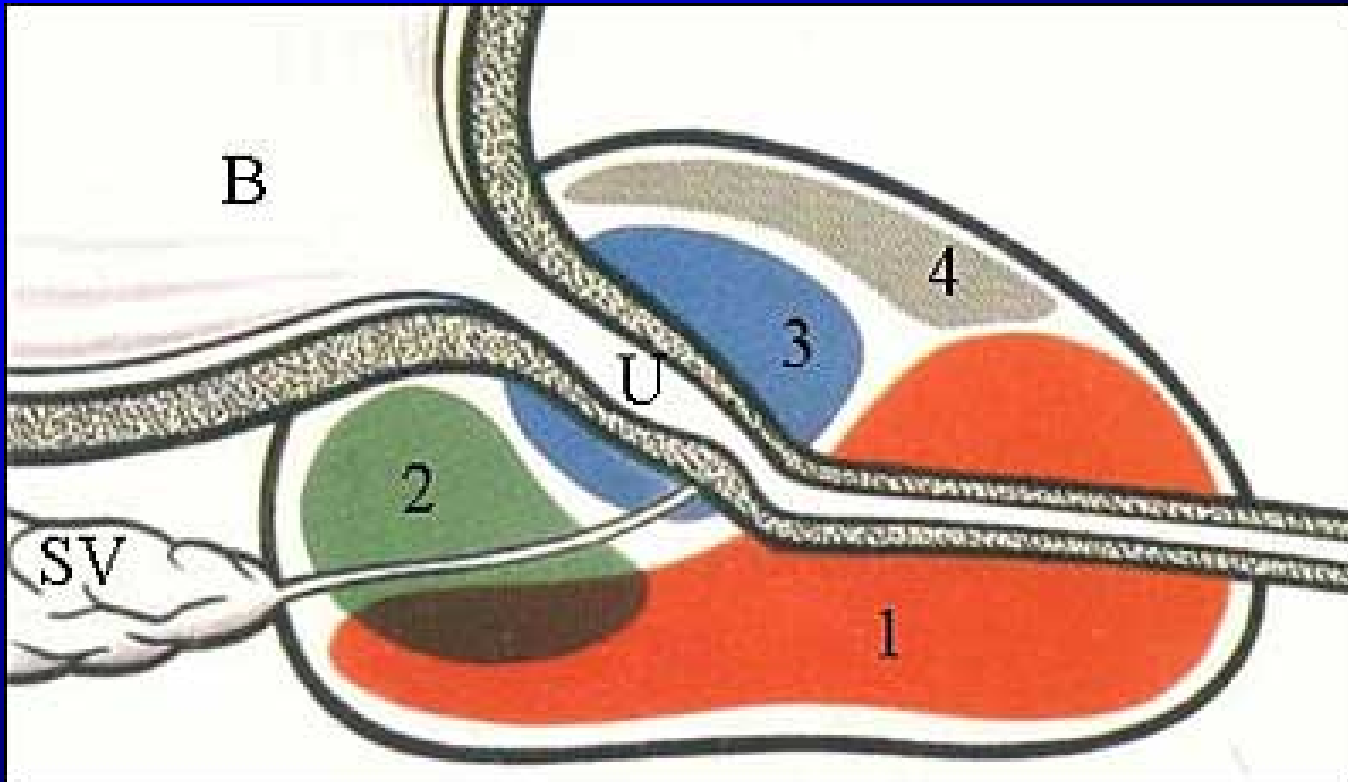


This shows the prostate and nearby organs.



This shows the inside of the prostate, urethra, rectum, and bladder.

Anatomy



1 = Peripheral Zone, 2 = Central Zone, 3 = Transitional Zone, 4 = Anterior Fibromuscular Zone. B = Bladder, U = Urethra, SV = Seminal Vesicle.

Figure 2 from Frydenberg M, Lawrentschuk N. Benign Prostate Disorders. In: McLachlan R, ed. Endocrinology of Male Reproduction. Available at: www.endotext.org. Used with permission from



Screening/Detection

- The combination of DRE (digital rectal examination) and serum PSA (prostate specific antigen) is the most useful first-line test for assessing the risk of prostate cancer being present in an individual*
- DRE can identify nodule or induration on the prostate
- Transrectal ultrasound guided prostate biopsy is recommended for men with elevated serum PSA level and abnormal DRE*

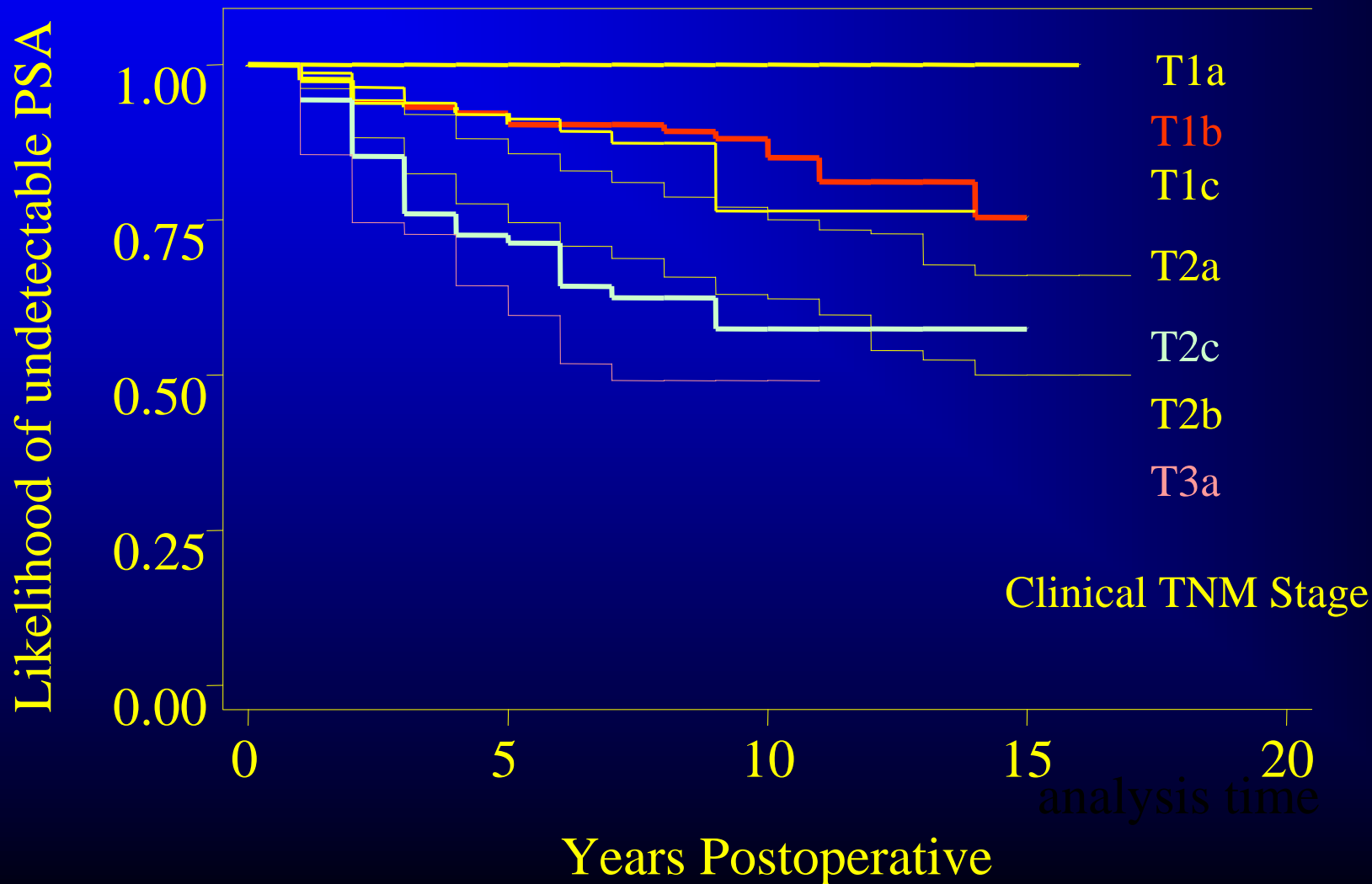


Prostate Cancer Staging System

Stage	Definition
T0	No evidence of primary tumor
T1	Non-palpable tumor not evident by imaging
T2	Palpable tumor confined to the prostate
T3	Palpable tumor beyond the prostate
T4	Tumor is fixed or invades adjacent structures (except SV)



Kaplan-Meier actuarial likelihood of PSA recurrence following radical prostatectomy by clinical stage (2002 AJCC)





PSA (prostate specific antigen)

- Single chain 237 AA glycoprotein
- Serine protease, functions to liquify human semen
- Human Kallikrein family member
- Androgen sensitive
- Produced by both malignant and benign prostate epithelium*
- The most important prostate cancer serum marker



PSA (prostate specific antigen)

- Serum PSA level can be elevated with
 - Prostatitis
 - Prostate cancer
 - BPH (benign prostatic hyperplasia)
 - Lab error
 - Biopsy
 - Manipulation (DRE, ejaculation)
- Serum PSA level can be decreased with a long term intake of finasteride (5-alpha reductase inhibitor)



History of PSA

- Catalona et al (1991)
 - A large community-based screening study
 - PSA could be used as a first-line screening test for prostate cancer
 - PSA was more accurate in this regard than the digital rectal examination



History of PSA

- Gann et al (1995)
 - Retrospective study of archived serum samples
 - A study cohort that was not screened for prostate cancer
 - PSA levels in the stored plasma samples are associated with the subsequent risk of developing prostate cancer
 - Estimated mean lead time = 5.5 years



Improving the Accuracy of PSA

- PSA > 10 ng/ml : 67% with prostate cancer
- PSA of 4 ~ 10 ng/ml: 22% with prostate cancer
- PSA lacks a specificity (requiring many negative transrectal ultrasound guided prostate biopsies with elevated PSA)
 - PSA > 10 ng/ml: 33% without prostate cancer
 - PSA of 4 ~ 10 ng/ml: 78% without prostate cancer



Improving the Accuracy of PSA

- Methods to optimize PSA screening include:
 - PSA density
 - Age-specific PSA reference ranges
 - Percent free PSA
 - PSA isoforms
 - PSA velocity
- What is the ideal PSA cutoff (prompt) to recommend a prostate biopsy?



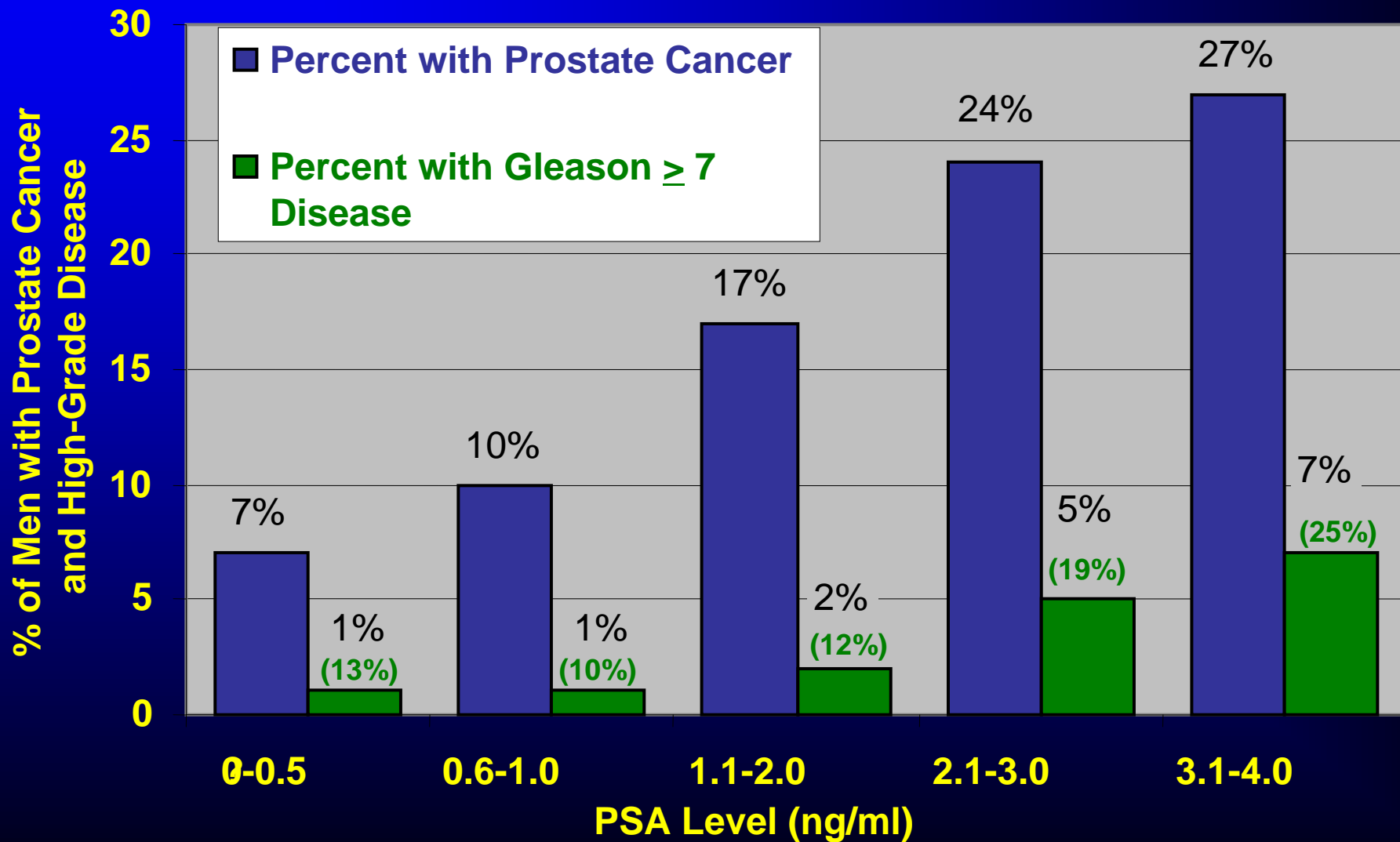
Risk of Prostate Cancer in Low PSA

Prostate Cancer Detection with PSA < 4 ng/ml

- 2,950 men in the Prostate Cancer Prevention Trial (PCPT) on placebo with PSA < 4 ng/ml and normal digital rectal examination for 7 years had end-of-study biopsy



Risk of Prostate Cancer in Low PSA





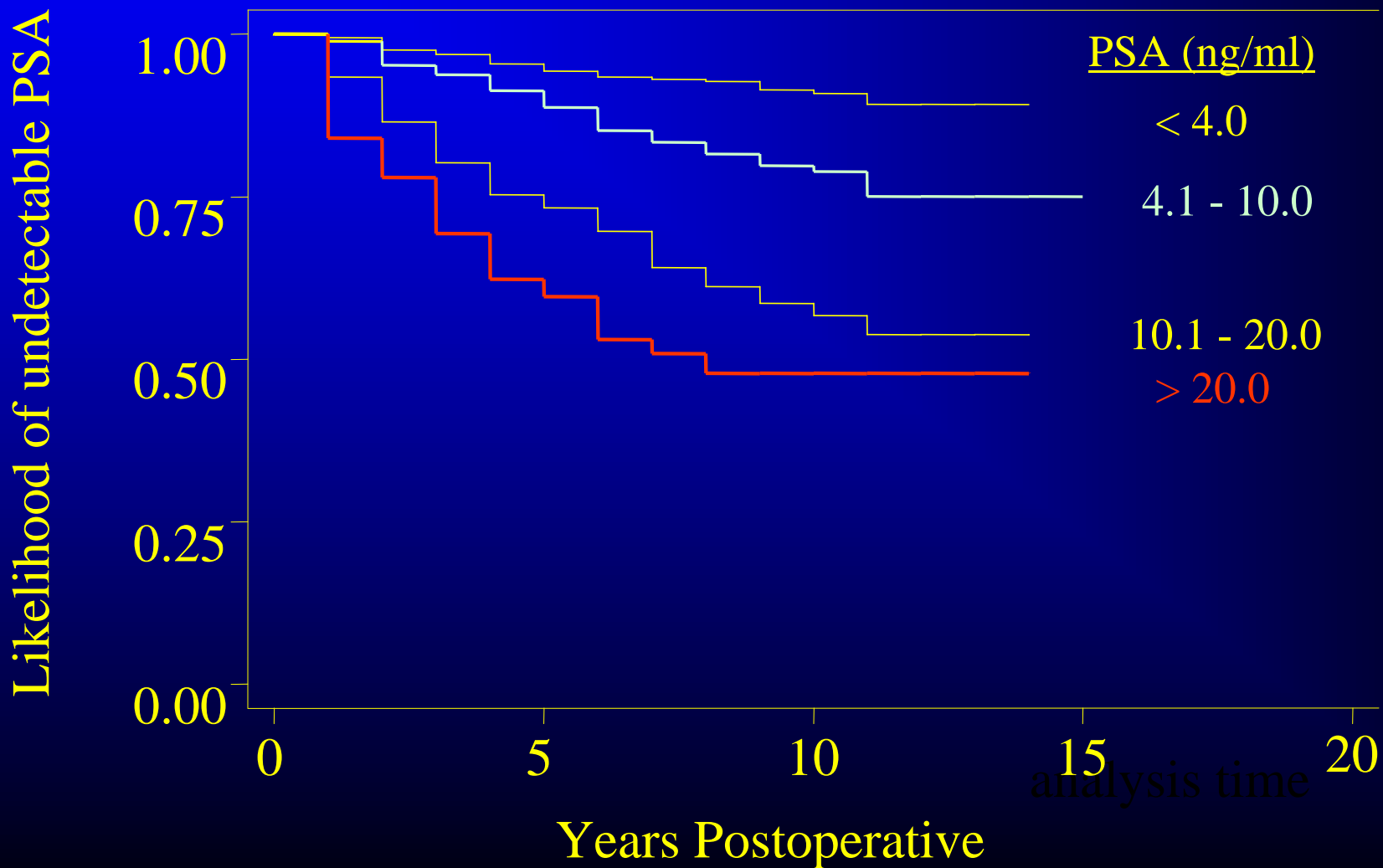
PSA Level and Prostate Cancer Risk

PSA (ng/ml)	Prostate Cancer Risk (%)	
	1991	2007
Bx Core (#)	4 – 6	8 – 14
0 - 1.0	N/A	8
1.1 - 2.0	N/A	17
2.1 - 3.0	N/A	24
3.1 - 4.0	N/A	27
4.1 – 10.0	22	35-45
> 10.0	>50	>50

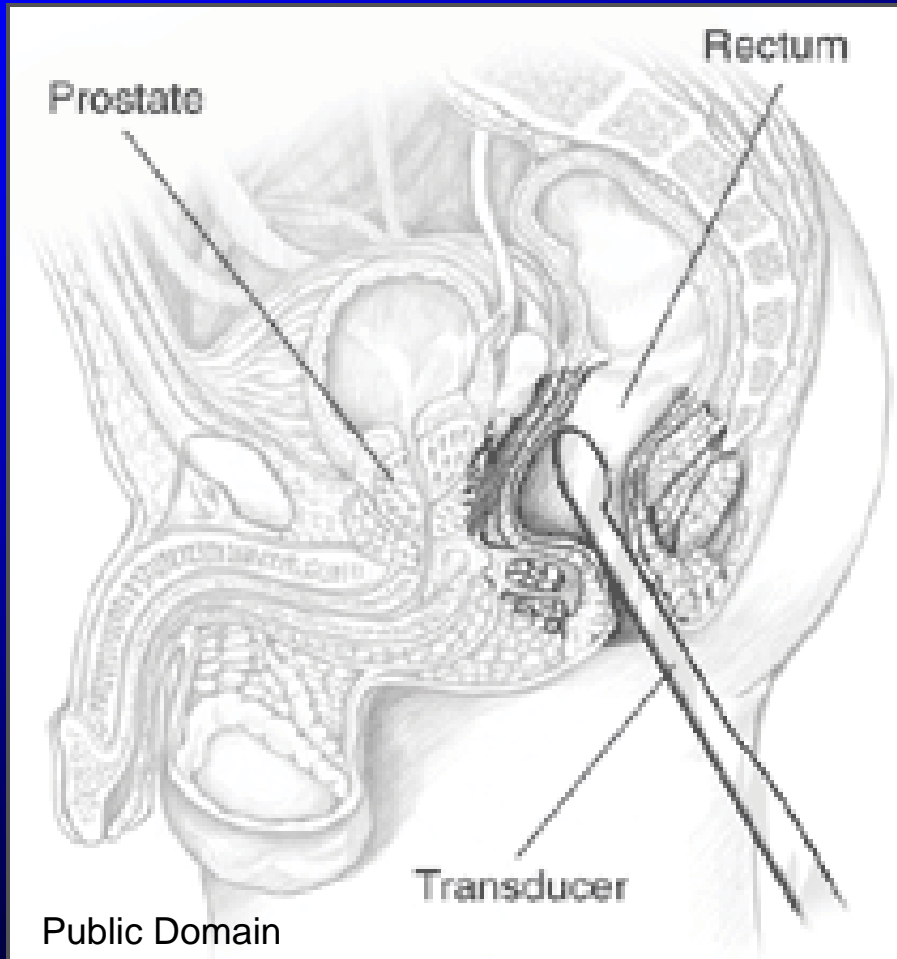
- No perfect PSA cutoff for screening/biopsy
- The importance of PSA velocity



Kaplan-Meier actuarial likelihood of PSA recurrence following radical prostatectomy by preoperative serum PSA levels

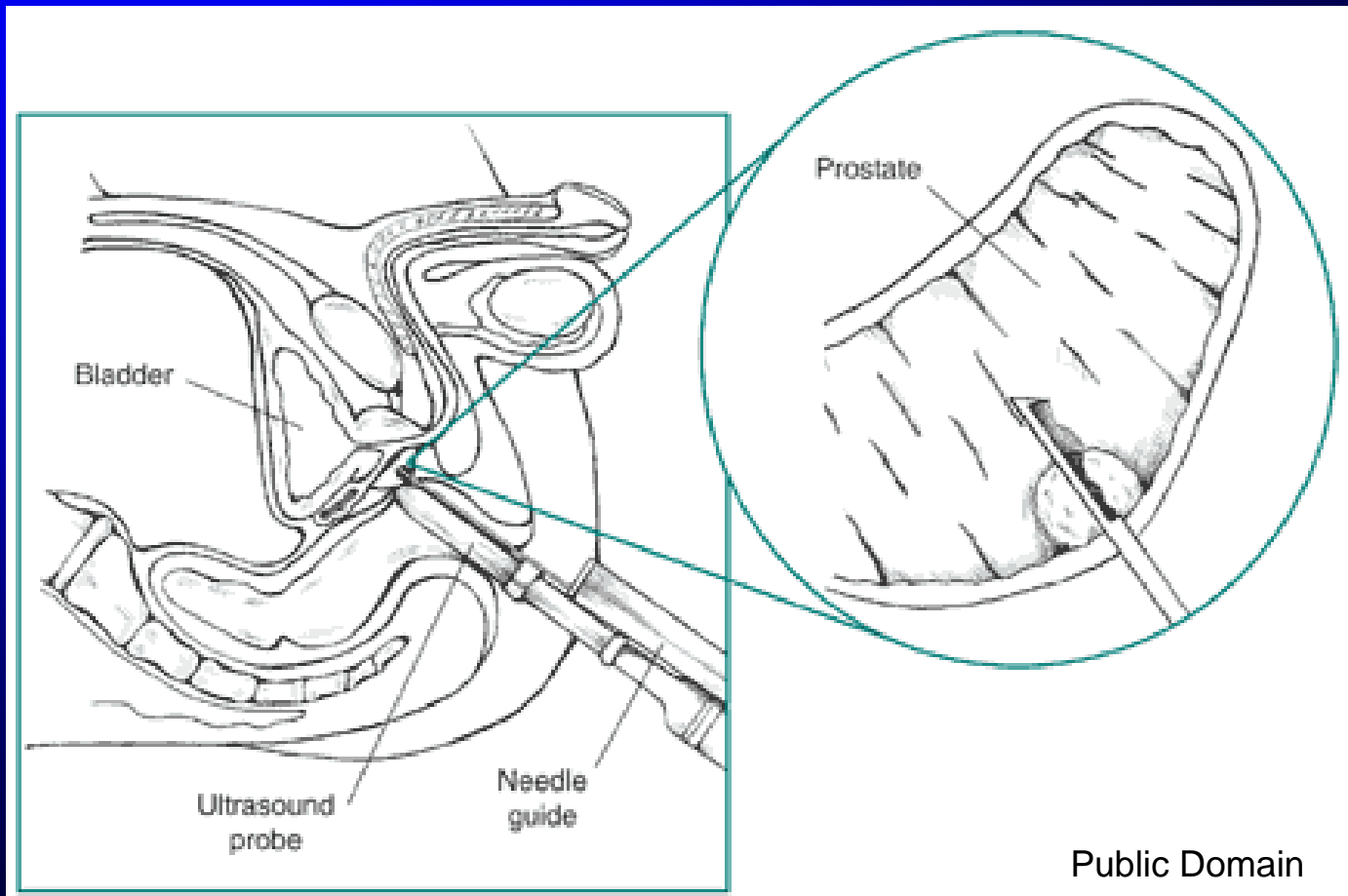


Transrectal ultrasound of prostate





Transrectal ultrasound guided prostate biopsy



Grading of prostate cancer (Gleason system)



Gleason's Pattern



1. Small, uniform glands

2. More stroma between glands

3. Distinctly infiltrative margins

4. Irregular masses of neoplastic glands

5. Only occasional gland formation

Well differentiated



Moderately differentiated



Poorly diff./
Anaplastic



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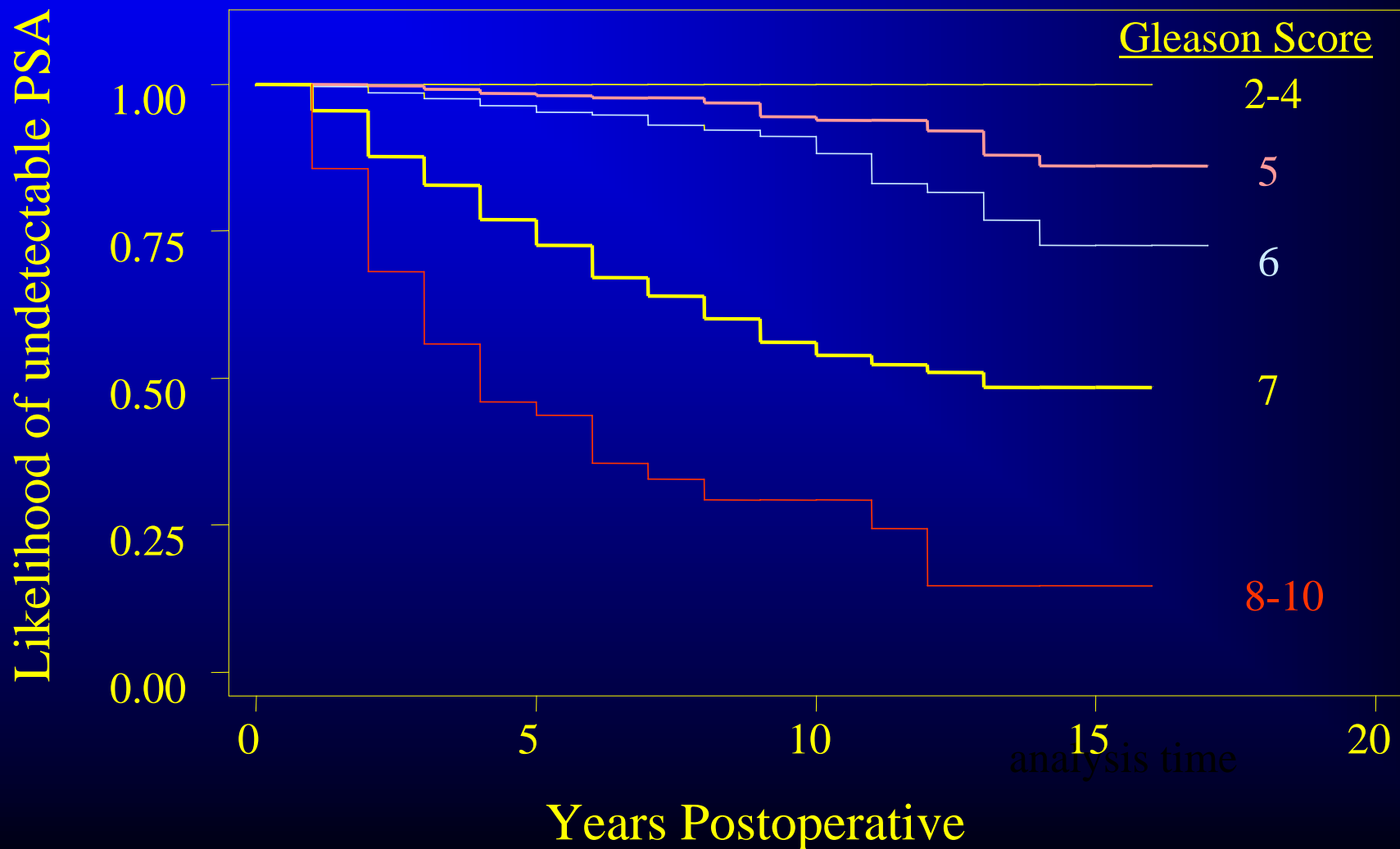


Gleason Score for Prostate Cancer

- Well differentiated : Gleason 2-5
- Moderately differentiated: Gleason 6-7
- Poorly differentiated : Gleason 8-10



Kaplan-Meier actuarial likelihood of PSA recurrence following radical prostatectomy by Gleason score





Radiographic imaging for prostate cancer

- Nuclear bone scan/scintigraphy – to detect bony metastases
- CT, MRI scans
- Plain radiographs
- U/S



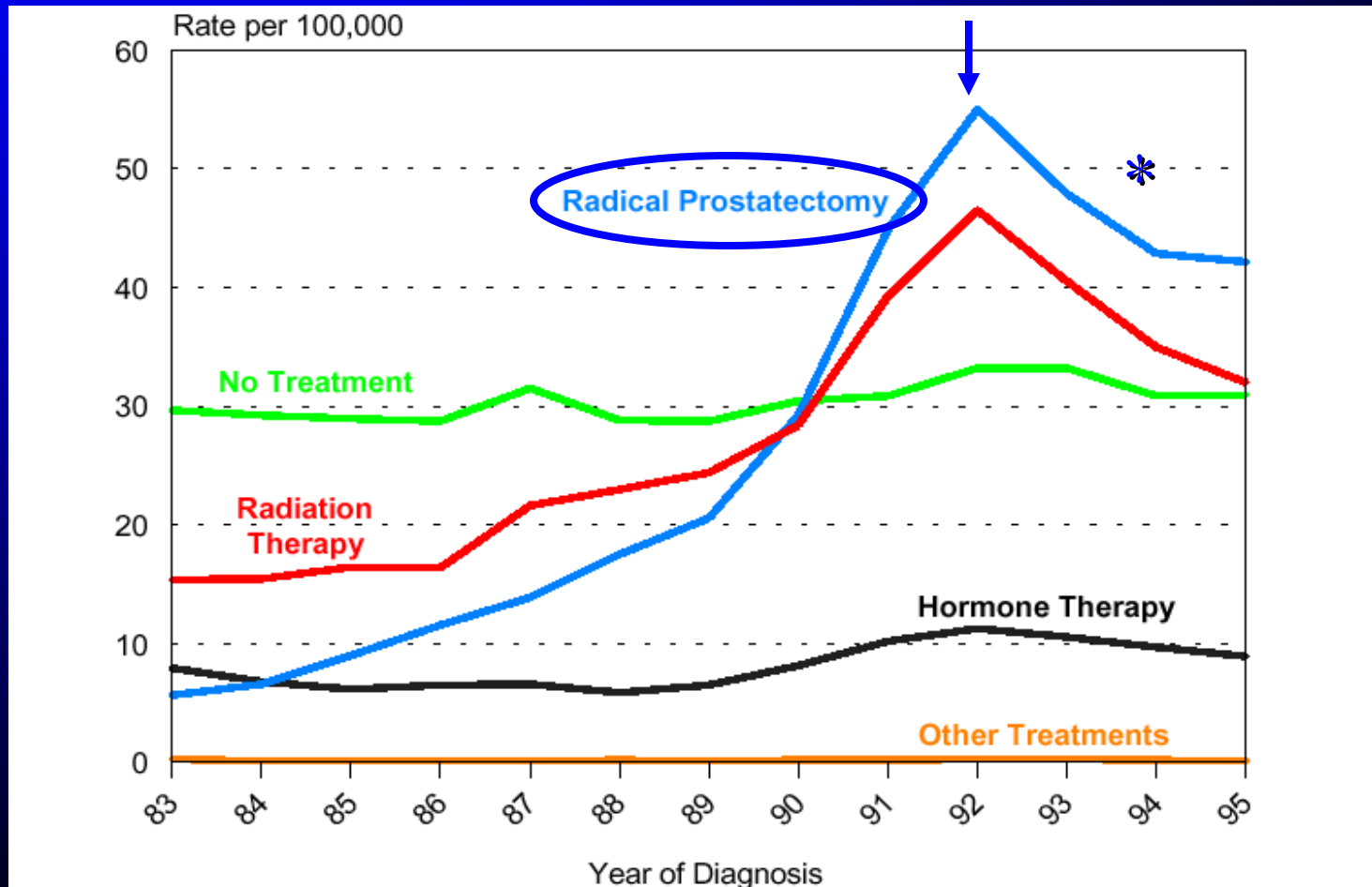
Potential Treatments : should be tailored to individual patient

- Watchful waiting/no treatment
- Surgery – radical prostatectomy (if cancer is localized and 10-15 year life expectancy*)
- Radiation therapy – external beam radiation and/or brachytherapy (radioactive seed implant)
- Hormonal manipulation (a.k.a. androgen deprivation therapy, usually in palliation therapy for advanced disease*)
- Combination therapy (hormonal therapy and radiation)



Prostate Cancer SEER Incidence by Treatment, 1983-1995 (Localized and Regional Stages)

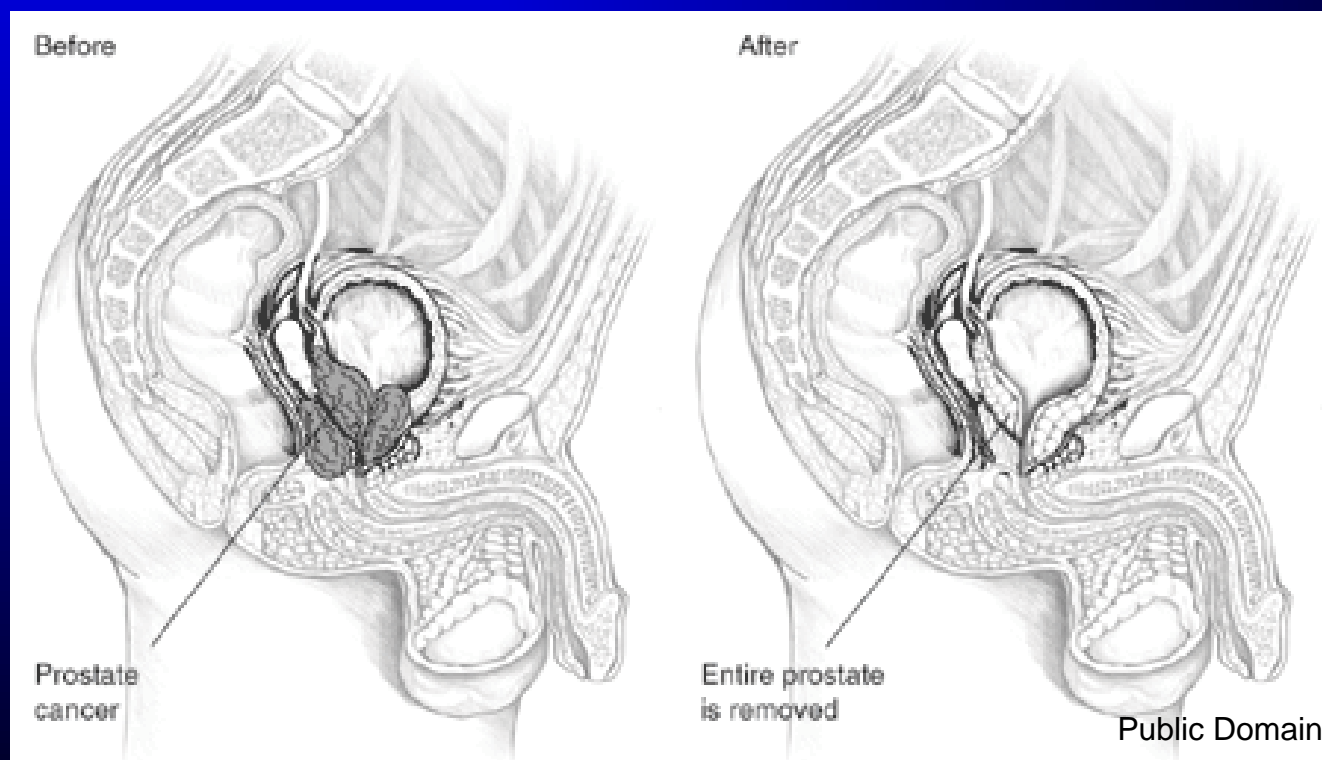
Incidence rate





History of radical prostatectomy

- 1904 : A first radical perineal prostatectomy for prostate cancer by Dr. Hugh Hampton Young at Johns Hopkins Hospital
- 1940's : A first radical retropubic prostatectomy





“As a study of the literature revealed that no such radical operation had ever been attempted, I made careful sketches of what I thought would be necessary and showed them to my chief, Dr. Halsted.... He appeared greatly impressed, strongly advised me to carry out the operation.”

Hugh Hampton Young on establishing the first radical perineal prostatectomy for prostate cancer on April 7, 1904



History of radical prostatectomy

- Devastating side effects of previous radical prostatectomy:
 - Life-threatening bleeding with radical retropubic prostatectomy
 - Urinary incontinence in 25%
 - Impotence in almost 100%



Anatomical radical retropubic prostatectomy

1982: Anatomical “nerve-sparing” Radical Retropubic Prostatectomy (RRP) developed



Patrick C. Walsh, MD

David Hall McConnell Professor & Director (1974-2004)

Johns Hopkins Medical Institutions

Chairman

Brady Urological Institute

Anatomical radical retropubic prostatectomy

A complete description of the nerve sparing radical retropubic prostatectomy with still images is available at the following site:

[Johns Hopkins Brady Urological Institute](#)



Goals of radical prostatectomy

1. Cancer Control
2. Preservation of Urinary Continence
3. Preservation of Potency



Actuarial 15 year status following RRP

- Local recurrence 6%
- Distant metastasis 18%
- All recurrences (PSA elevation) 34%

Surgery → PSA elevation → Metastasis → Death

- PSA elevation-free survival 66%
- Metastasis-free survival 82%
- Cancer specific survival 91%



Preservation of Urinary Continence

- Urinary incontinence following RRP: usually secondary to intrinsic sphincter deficiency
- Older men: thinner striated urinary sphincter
- Injury to the urinary striated sphincter can occur during ligation and division of the dorsal vein complex
- Bladder detrusor hypertrophy and decreased bladder compliance from preexisting bladder outlet obstruction (eg. BPH)



Robot-Assisted Laparoscopic Radical Prostatectomy

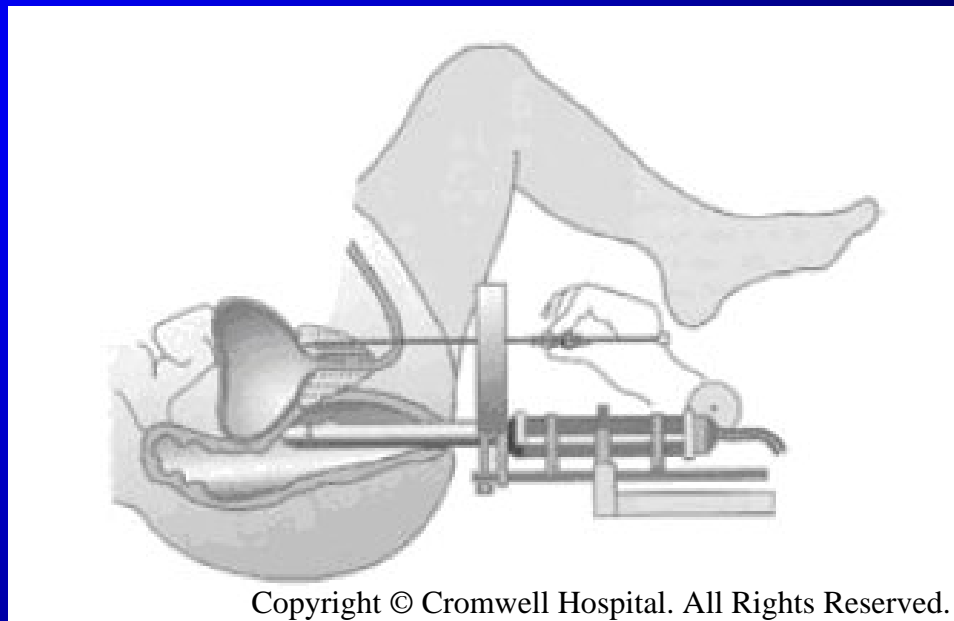


External Beam Radiation Therapy

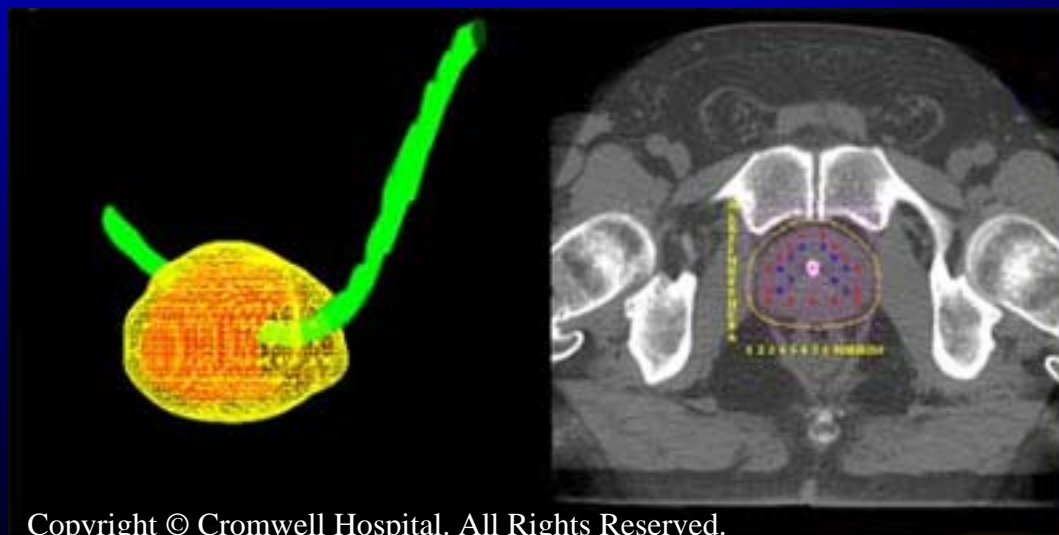
- Erectile dysfunction
- Urge incontinence
- Rectal injury
- Dysuria



Brachytherapy (radioactive seed implant)



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Hormonal therapy (Androgen Deprivation Therapy)

- Not curative*
- Goal: deprivation of androgen (testosterone)*
- PSA *temporarily* decreases and a *temporary* symptomatic relief in the majority of men with metastatic diseases

Eventual development of hormone-refractory prostate cancer with a median survival of 6-12 months after relapse

- Bilateral orchiectomy
- Estrogen therapy
- Gonadotropin-releasing hormone agonists (LHRH agonists)
- Nonsteroidal antiandrogens
- Steroidal antiandrogens
- Combined androgen blockade

- Intermittent Hormonal Therapy



Hormonal therapy (Androgen Deprivation Therapy)

Side effects

- Osteoporosis
- Unfavorable body composition
- Sexual dysfunction
- Reduced QOL



Conclusions

- Prostate cancer is the most common non-skin cancer in the US men
- Radical prostatectomy is the most commonly preformed treatment modality for localized prostate cancer
- Detection/screening by combined DRE and PSA
- Ultrasound guided prostate biopsy for diagnosis
- Staging (TNM) and grade (Gleason score) of prostate cancer



Conclusions

- Curative treatment modalities exist for clinically localized disease
- Excellent oncological and clinical outcome can be achieved with a careful surgery using nerve sparing technique
- Wide spread early detection programs for prostate cancer resulted in a downward stage migration