Utility of PSA and Current Prostate Cancer Diagnosis & Treatment

Daniel J Lewinshtein, MD
Chief, Urologic Surgery, CH Pierre Boucher
Assistant Clinical Professor
University of Sherbrooke
November 2018

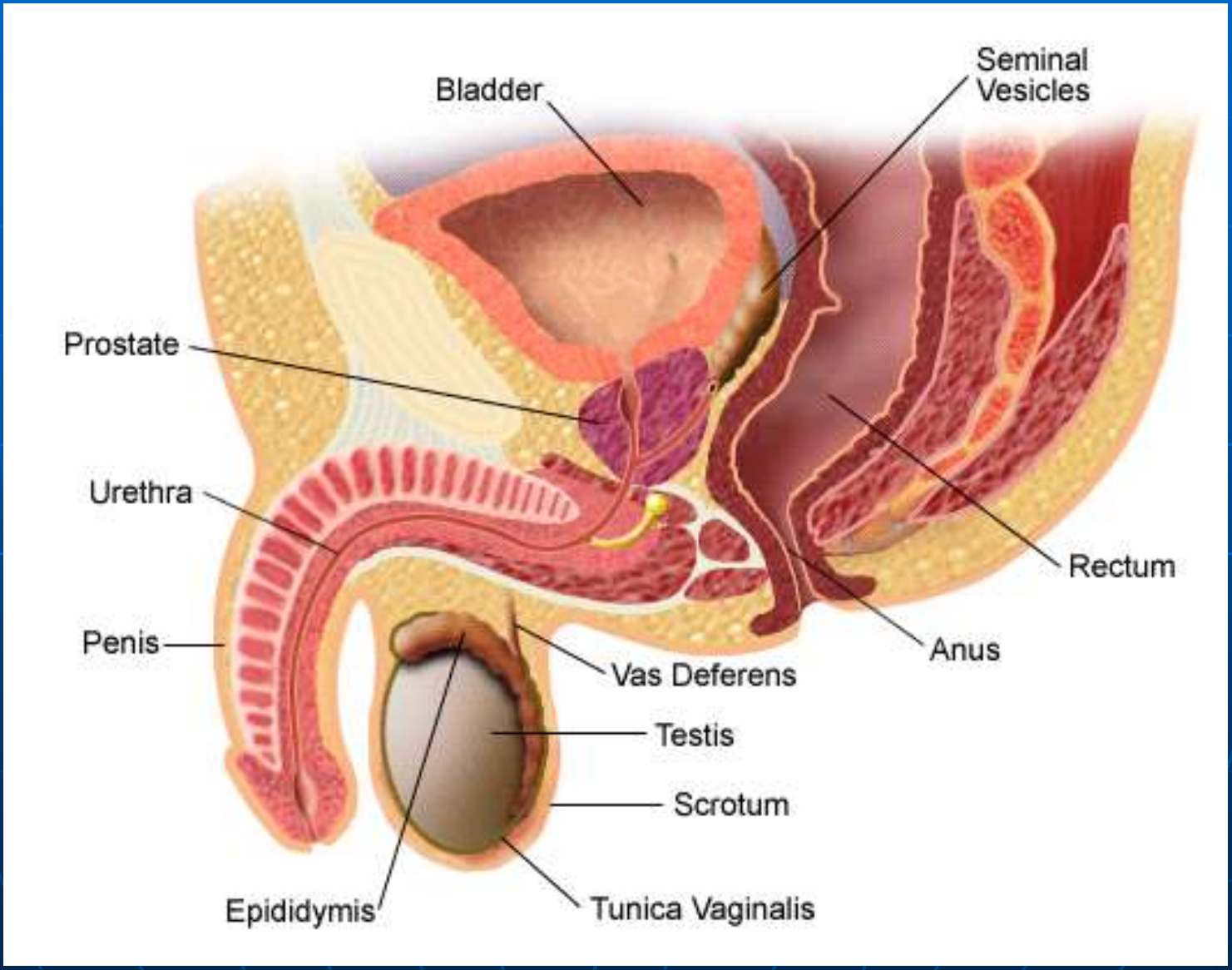
Disclosure

- Sanofi
- Astellas
- Abvie

Objectives

- Brief overview of the prostate and PSA
- When to use PSA
- MRI and other predictive tools
- TRUS And MRI-fusion Biopsy
- Active Surveillance
- Treatment of local disease
- Treatment of metastatic disease

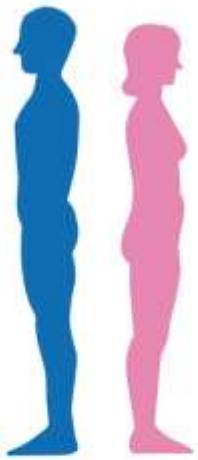
Where is it?


Bladder
Seminal Vesicles
Prostate
Urethra
Rectum
Penis
Anus
Vas Deferens
Testis
Scrotum
Epididymis
Tunica Vaginalis

Prostate Cancer: Epidemiology

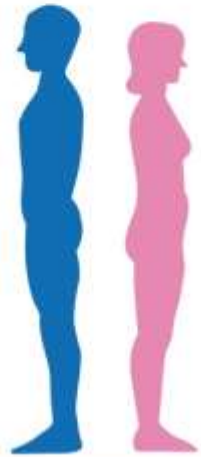
Estimated New Cases*

Males			Females		
Prostate	217,730	28%	Breast	207,090	28%
Lung & bronchus	116,750	15%	Lung & bronchus	105,770	14%
Colon & rectum	72,090	9%	Colon & rectum	70,480	10%
Urinary bladder	52,760	7%	Uterine corpus	43,470	6%
Melanoma of the skin	38,870	5%	Thyroid	33,930	5%
Non-Hodgkin lymphoma	35,380	4%	Non-Hodgkin lymphoma	30,160	4%
Kidney & renal pelvis	35,370	4%	Melanoma of the skin	29,260	4%
Oral cavity & pharynx	25,420	3%	Kidney & renal pelvis	22,870	3%
Leukemia	24,690	3%	Ovary	21,880	3%
Pancreas	21,370	3%	Pancreas	21,770	3%
All Sites	**789,620**	**100%**	**All Sites**	**739,940**	**100%**



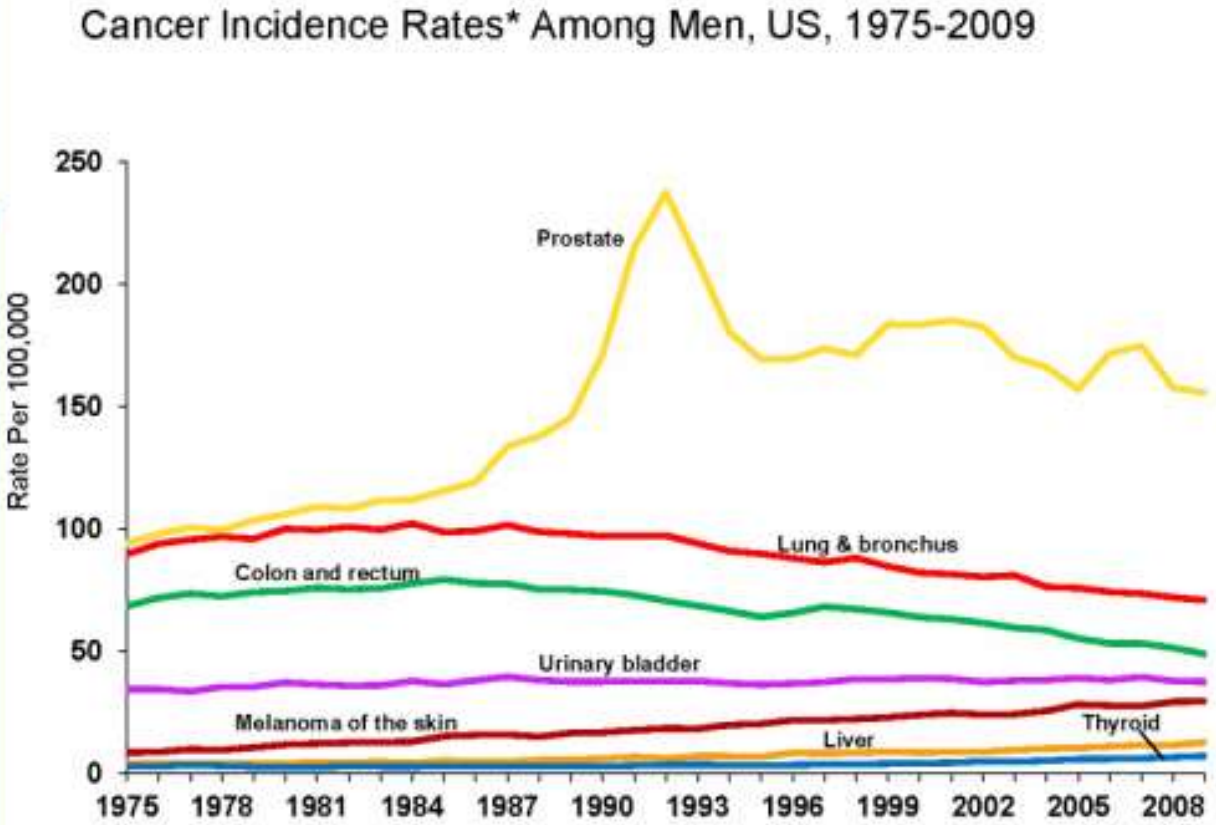
Estimated Deaths

Males			Females		
Lung & bronchus	86,220	29%	Lung & bronchus	71,080	26%
Prostate	32,050	11%	Breast	39,840	15%
Colon & rectum	26,580	9%	Colon & rectum	24,790	9%
Pancreas	18,770	6%	Pancreas	18,030	7%
Liver & intrahepatic bile duct	12,720	4%	Ovary	13,850	5%
Leukemia	12,660	4%	Non-Hodgkin lymphoma	9,500	4%
Esophagus	11,650	4%	Leukemia	9,180	3%
Non-Hodgkin lymphoma	10,710	4%	Uterine Corpus	7,950	3%
Urinary bladder	10,410	3%	Liver & intrahepatic bile duct	6,190	2%
Kidney & renal pelvis	8,210	3%	Brain & other nervous system	5,720	2%
All Sites	**299,200**	**100%**	**All Sites**	**270,290**	**100%**

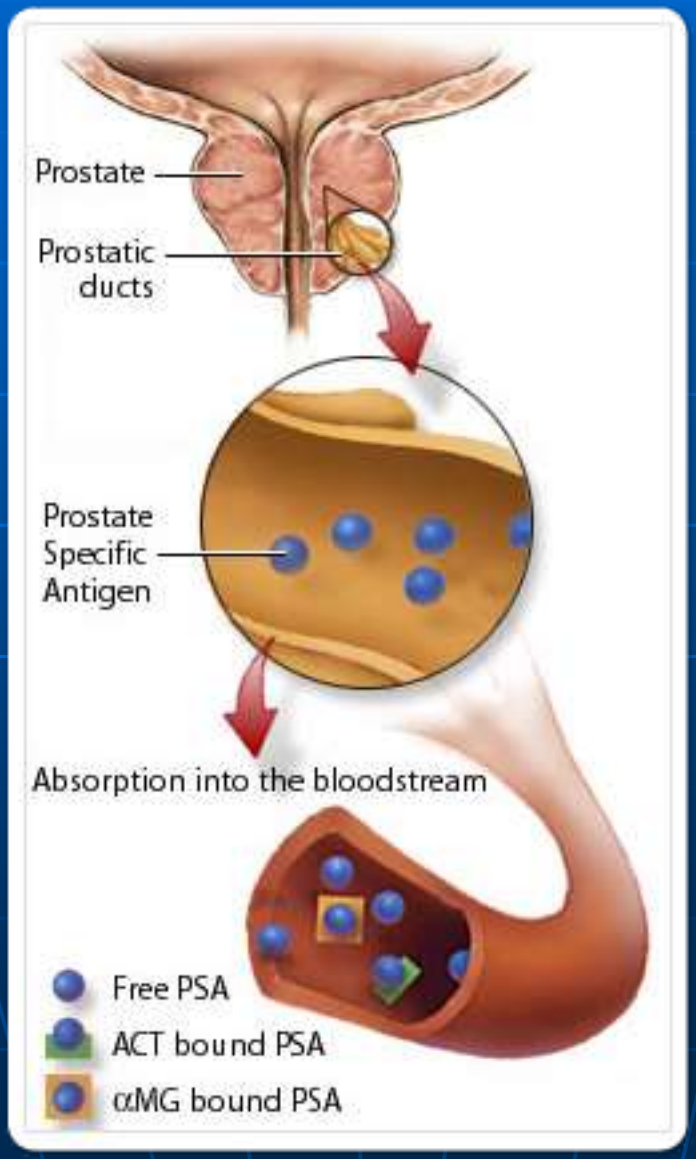


Do you Screen?

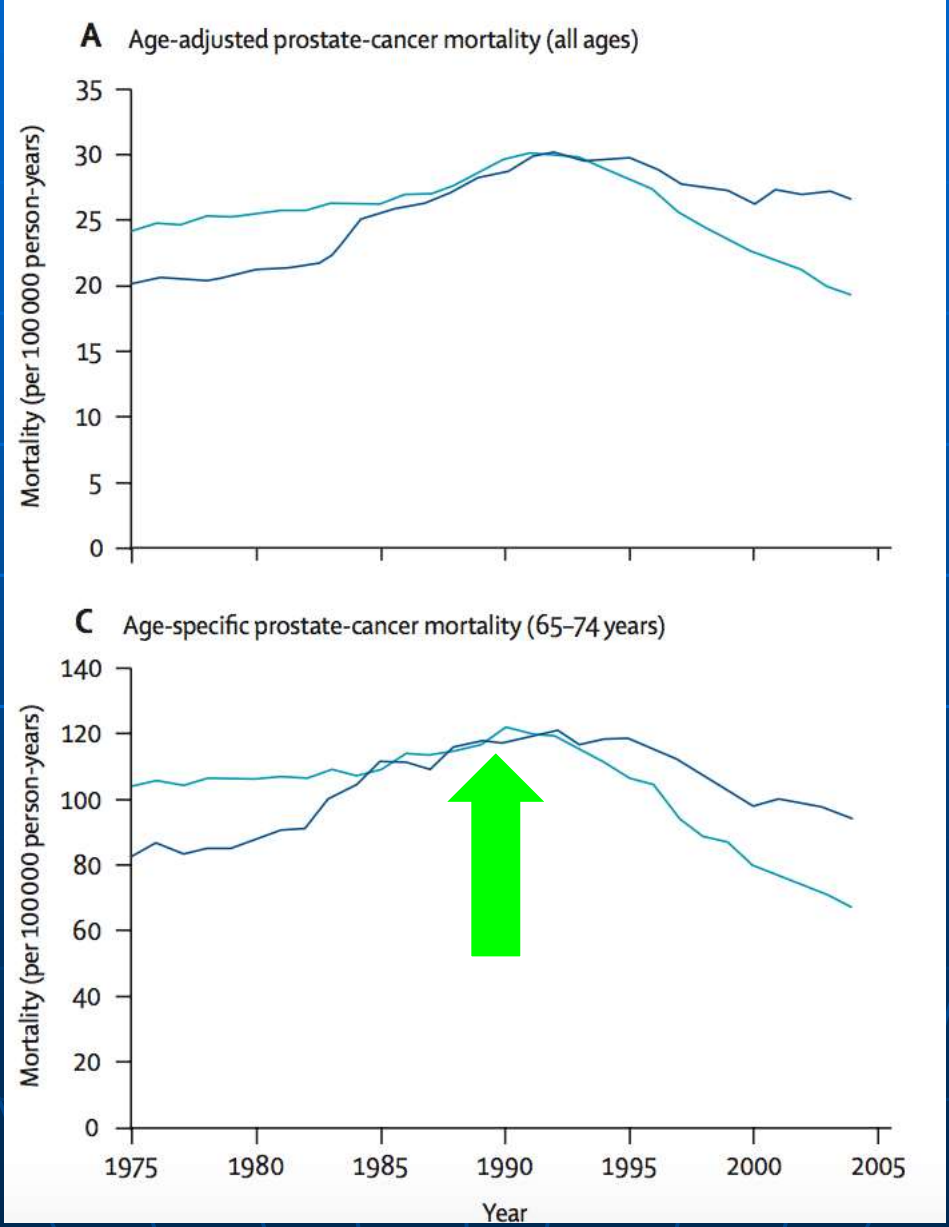
PSA: Overdiagnosis and Overtreatment



PSA: The Molecule



PSA: Decreased Mortality



Oncology lancet 9:445

USPTF: 2012

aafp NEWS NOW

Printer-friendly version

Share this on AAFP Connection

Share this page

AAFP, USPSTF Issue Final Recommendation Against Routine PSA-based Screening for Prostate Cancer

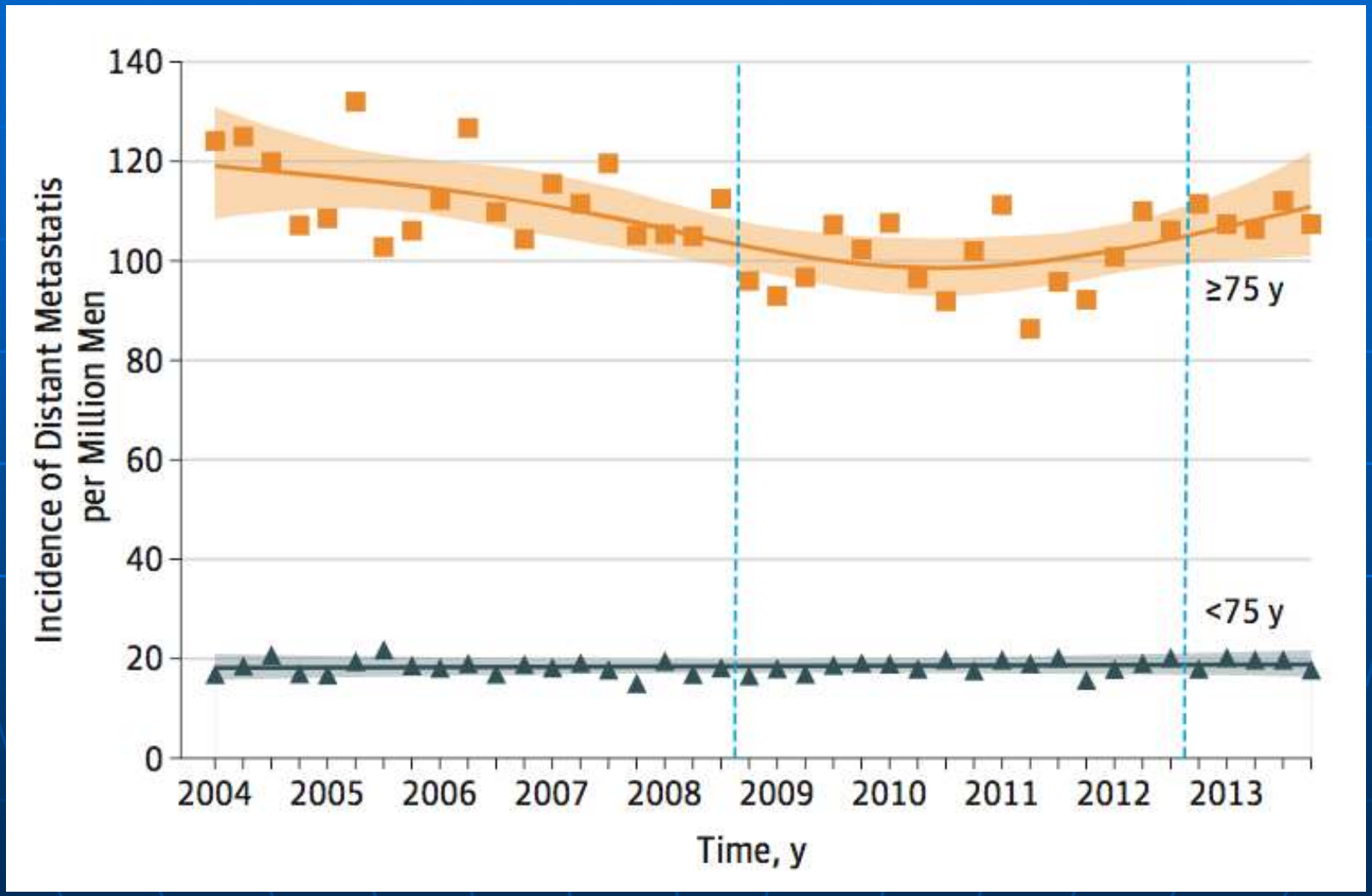
Evidence Simply Does Not Support Test's Benefit, Says Task Force Co-chair

By Matt Brown

Posted: 5/22/2012, 4:00 p.m. -- The AAFP is recommending against performing prostate-specific antigen (PSA)-based screening for prostate cancer in asymptomatic men, a position that is in line with a final recommendation from the U.S. Preventive Services Task Force (USPSTF) that was published May 22 in the *Annals of Internal Medicine*.

Dan Lewinshtein 2014

Since USPTF: Metastatic disease



JAMA Oncology 3:705

Since USPTF: BX and RRP

Figure 1. Temporal Trend in Prostate Biopsy Volume of Certifying Urologists

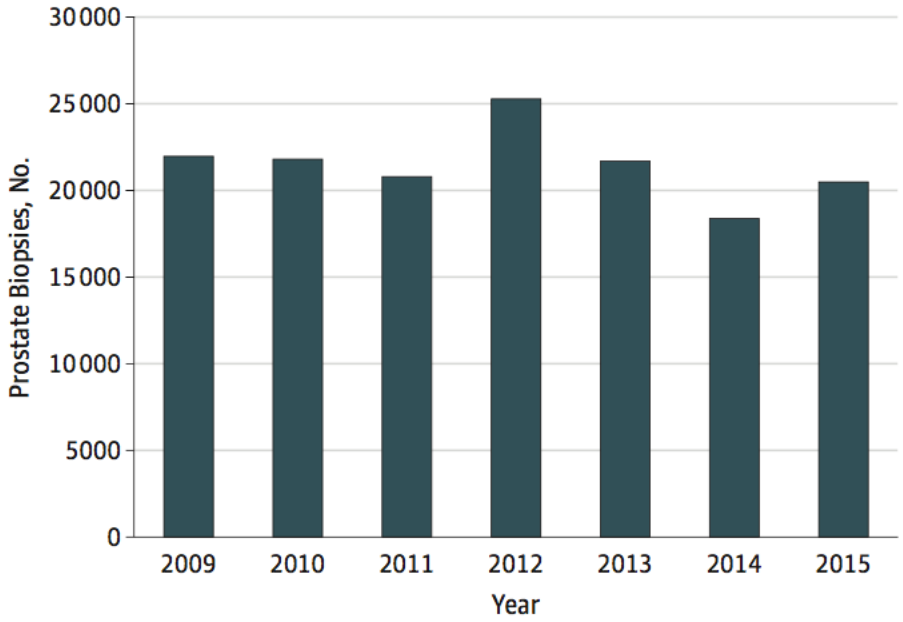
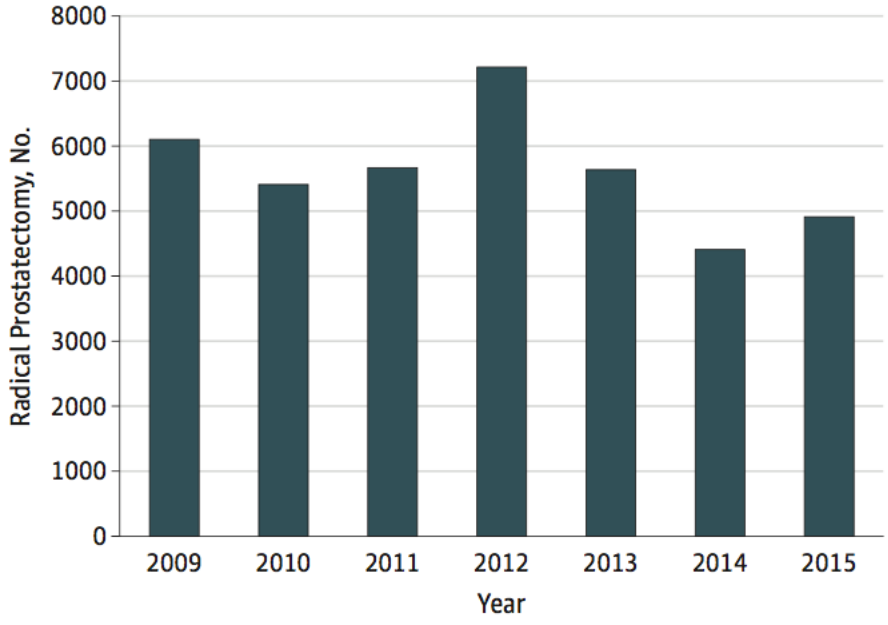


Figure 2. Temporal Trend in Radical Prostatectomy Volume of Certifying Urologists



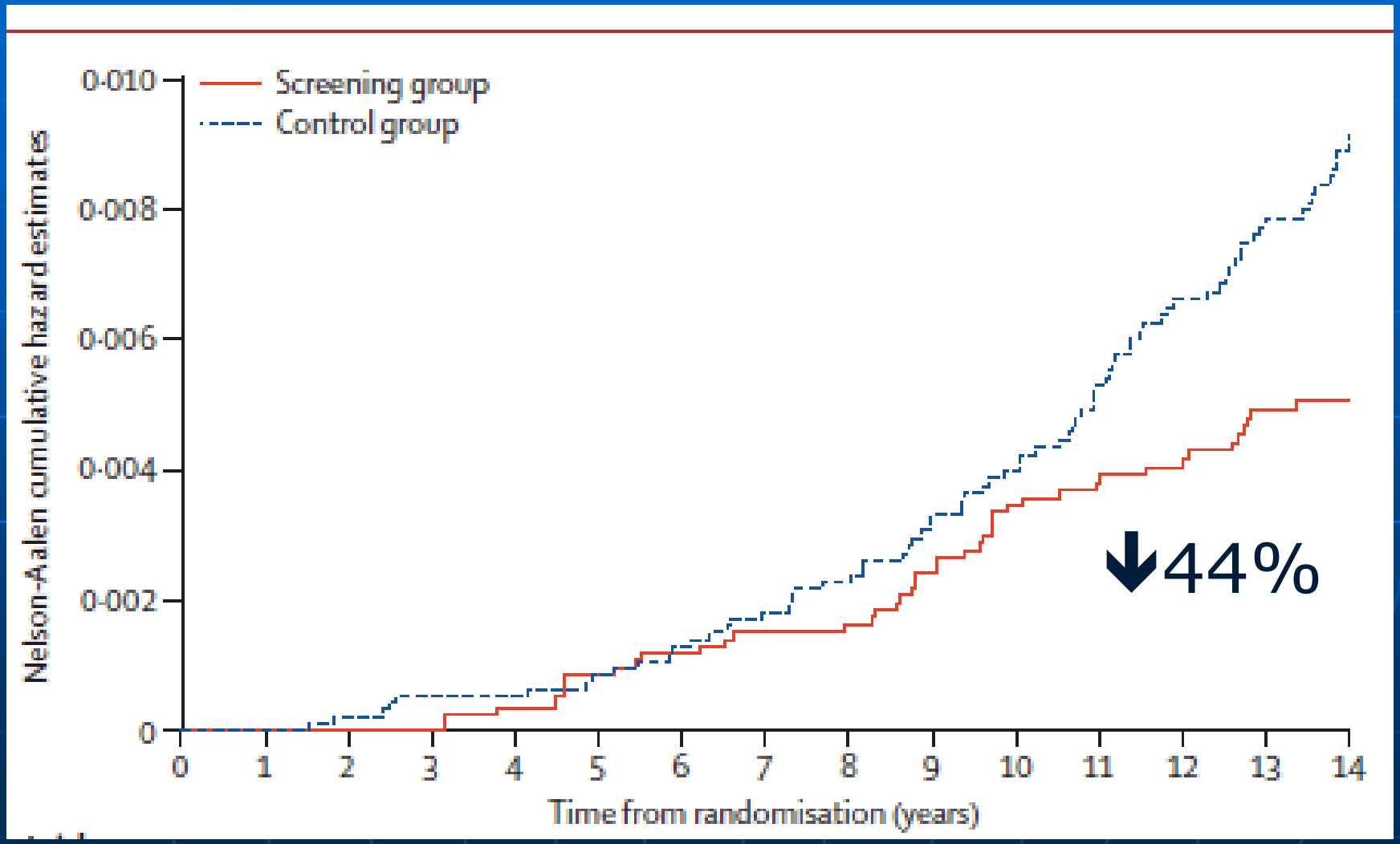
JAMA Surgery 152:192

Mortality results from the Göteborg randomised population-based prostate-cancer screening trial

- N=20 000[1]
- 3% contamination
- 14 yrs FU
- Bx if PSA> 3.5
- NNT=12 (NNT for Breast CA=20)

1:Lancet Oncol 11:725 (2010)
2:NEMJ 363:1203 (2010)

Goteborg: Mortality



Dan Lewinshtein 2014

PLCO: USA

- N=76 000
- 52% contamination
- 9 yrs FU
- BX if PSA> 4.0
- No difference overall
  - <65 ans: ↓44% PC mortalité et NNT 5

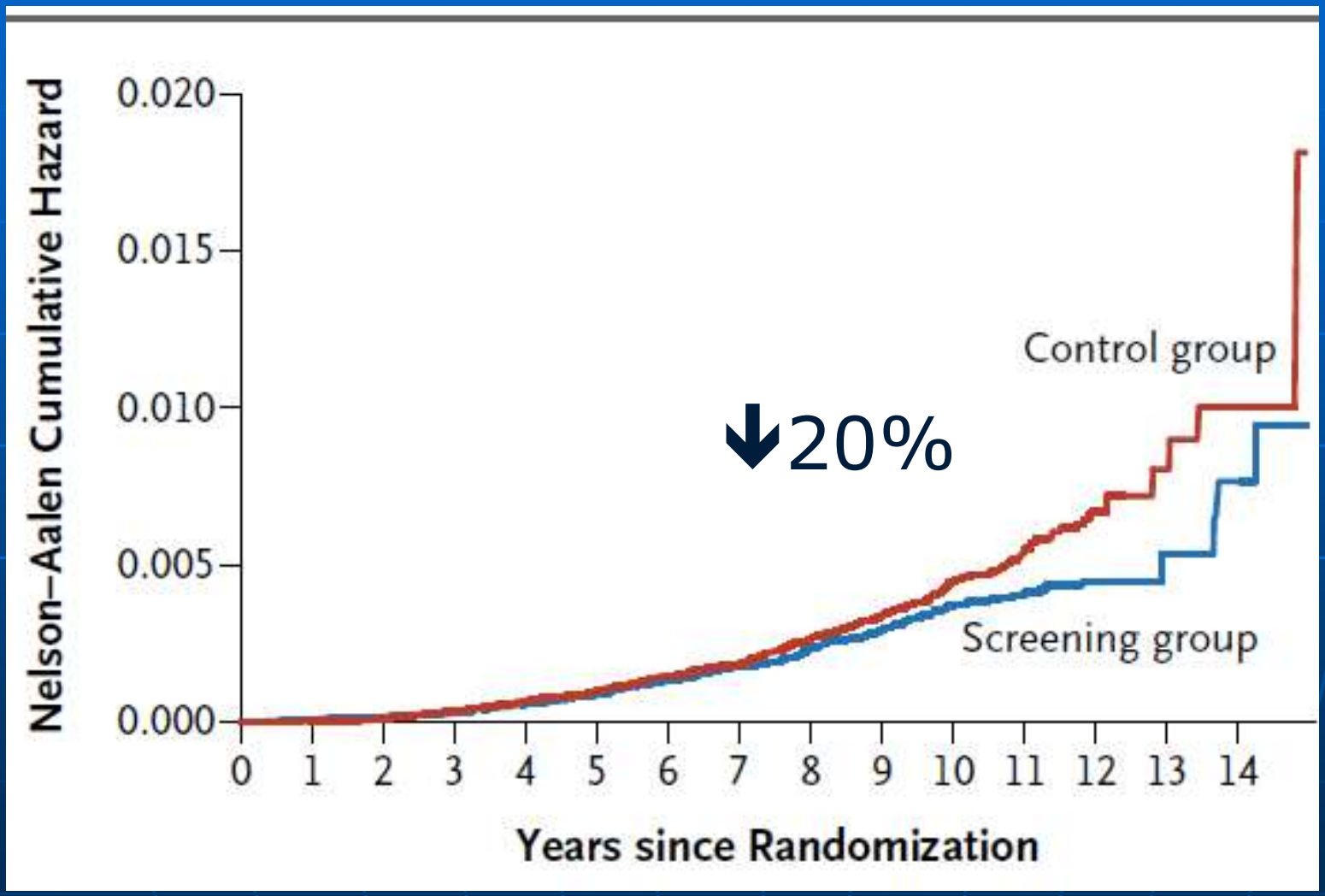
1:NEMJ 360:1320

ERSPC: Europe

- N=162 000[1]
- 15% contamination
- 14 yr FU
- Bx if PSA>3.0
- NNT=48
- ↓40% M+

1:NEMJ 360:1320

ERSPC: Mortality



Dan Lewinshtein 2014

USPTF 2017 : longer follow-up of ERSPC = Improved PSA utility

Table 1 | **Efficacy of serum PSA screening at different follow-up durations**[7,8]

Years of monitoring	Number needed to screen to avoid		Number needed to diagnose to avoid	
	1 cancer-specific death	1 incidence of metastatic disease	1 cancer-specific death	1 incidence of metastatic disease
9	1,410	736	48	25
11	979	393	35	14
13	781	333*	27	14*

*At a median follow-up duration of 12 years at four ERSPC centers[8]

Van der Kwast, T. H. & Roobol, M. J. (2017) Draft USPSTF 2017 recommendation on PSA testing — a sea-change? *Nat. Rev. Urol.* doi:10.1038/nrurol.2017.89

2017 PSA Recommendations

- CUA
  - PSA to those with >10yr
  - 50-70 yr
  - 45yr if Black, Family Hx
- USPTF: grade C for 55-69 (2017)
- CTFPHC: no

Life Expectancy: Pt dependant

Statistics Canada

Canada

Information for... | Browse by subject | Browse by key resource | Help

Home > CANSIM

Table 102-0122 [1, 2, 3, 4, 5]

Health-adjusted life expectancy, at birth and at age 65, by sex and income, Canada and provinces

occasional (years)

Data table | Add/Remove data | Manipulate | Download | Related information | Help

The data below is a part of CANSIM table 102-0122. Use the Add/Remove data tab to customize your table.

Selected items [Add/Remove data]

Sex = Males
Income group [6, 7] = All income groups
Characteristics [2, 3, 4, 8, 9, 10] = Life expectancy

Geography	Age group	2000-2002	2005-2007
Newfoundland and Labrador	At birth	75.3	75.8
	At age 65	15.4	16.2
Quebec	At birth	76.4	78.2
	At age 65	16.5	18.0
British Columbia	At birth	78.0	78.9
	At age 65	18.0	18.9


Sun Life Financial
Find an advisor
Get a quote
Customer support
CANADA | EN
INSURANCE
INVESTMENTS
LEARN & PLAN
Home > Learn & Plan > Tools & Calculators > Life expectancy calculator
Share this:
Life expectancy calculator
Print
Save
87
Based on what you told us, your life expectancy is 87, which you'll reach in the year 2034.
Did you know that many Canadians are now outliving common life expectancies?
With at least 17 years of retirement to look forward to, you need to plan for your money to last. To get help, review your results with an advisor.

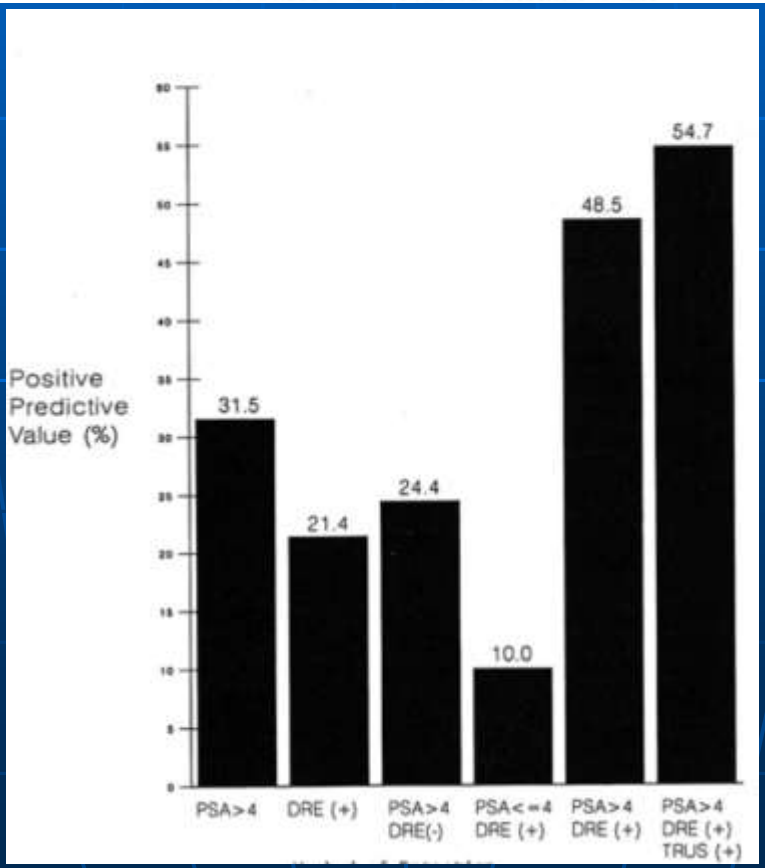
When not to order PSA!

- Retention
- UTI

When to Send to URO?

COMPARISON OF DIGITAL RECTAL EXAMINATION AND SERUM PROSTATE SPECIFIC ANTIGEN IN THE EARLY DETECTION OF PROSTATE CANCER: RESULTS OF A MULTICENTER CLINICAL TRIAL OF 6,630 MEN

WILLIAM J. CATALONA,* JEROME P. RICHIE, FREDERICK R. AHMANN, M'LISS A. HUDSON, PETER T. SCARDINO, ROBERT C. FLANIGAN, JEAN B. DEKERNION, TIMOTHY L. RATLIFF, LOUIS R. KAVOUSSI, BRUCE L. DALKIN, W. BEDFORD WATERS, MICHAEL T. MACFARLANE AND PAULA C. SOUTHWICK



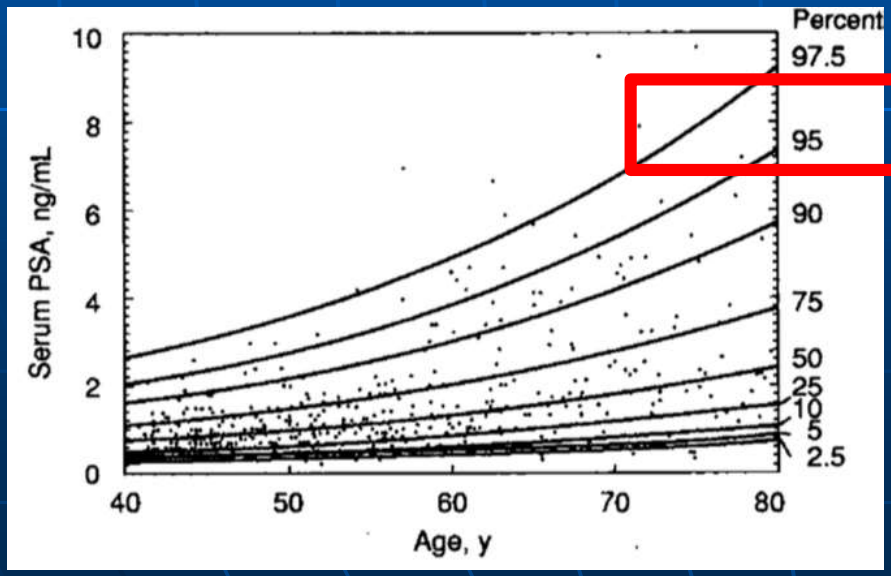
Serum Prostate-Specific Antigen in a Community-Based Population of Healthy Men

Establishment of Age-Specific Reference Ranges

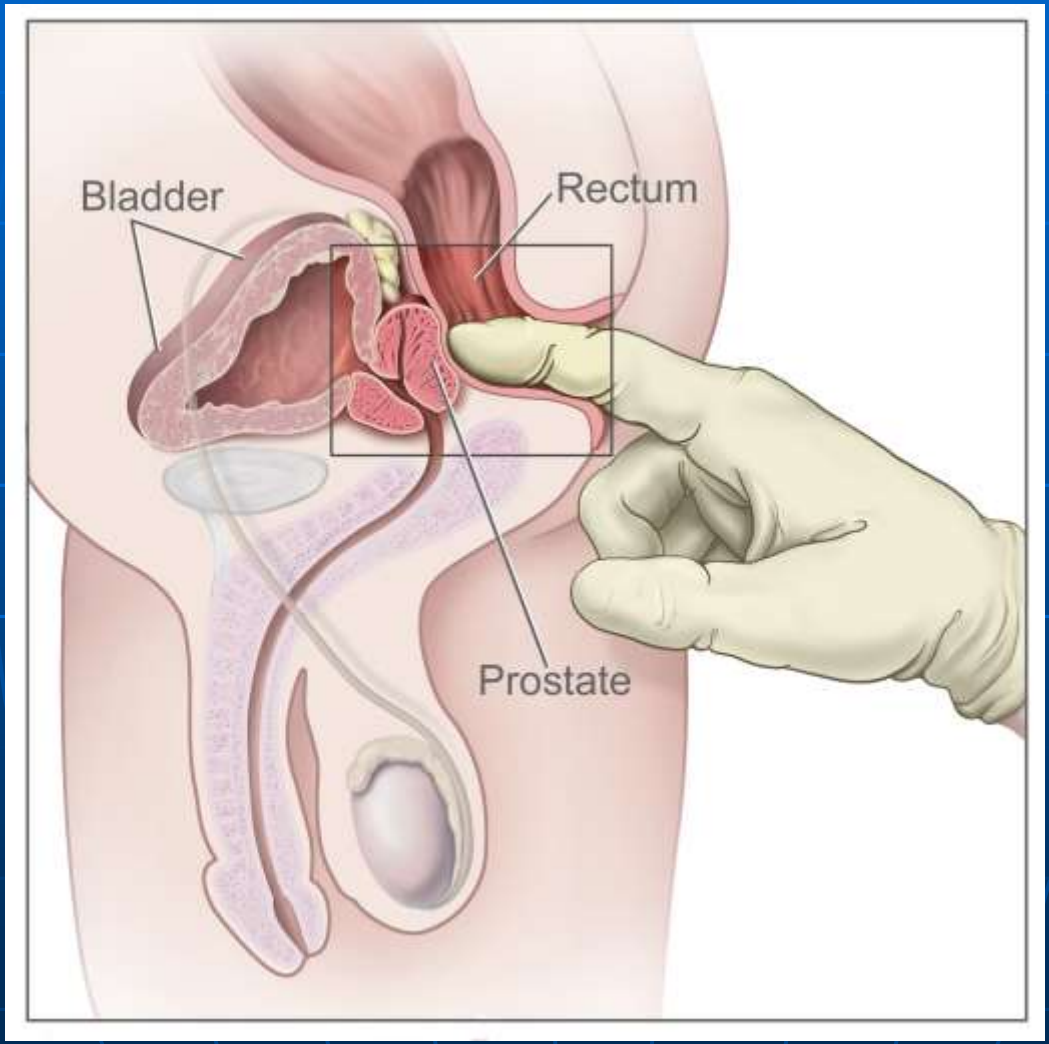
Joseph E. Oesterling, MD; Steven J. Jacobsen, MD, PhD; Christopher G. Chute, MD, DrPH; Harry A. Guess, MD, PhD; Cynthia J. Girman, MS; Laurel A. Panser, MA, MS; Michael M. Lieber, MD

Table 2.—Age-Specific Reference Ranges* for Serum PSA Concentration, Prostatic Volume, and PSA Density

	Age Group, y			
Parameter	**40-49**	**50-59**	**60-69**	**70-79**
Serum PSA concentration, ng/mL	0.0-2.5	0.0-3.5	0.0-4.5	0.0-6.5



Detection: DRE



PCPT

Characteristics

Race

Caucasian

Age

60

PSA [ng/ml]

5

Family History of Prostate Cancer

No

Digital rectal examination

Normal

Prior biopsy

Never had a prior biopsy

☐ Percent free PSA available?

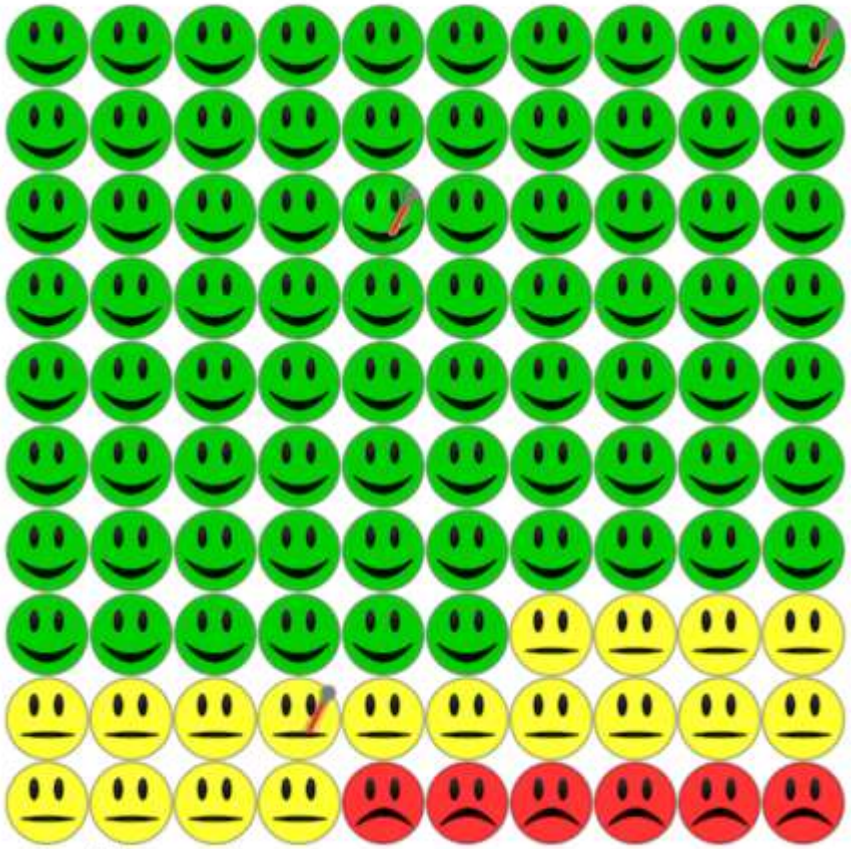
Calculate Risk

Risk of prostate cancer if biopsy were to be performed

Based on the provided risk factors a prostate biopsy performed would have a:

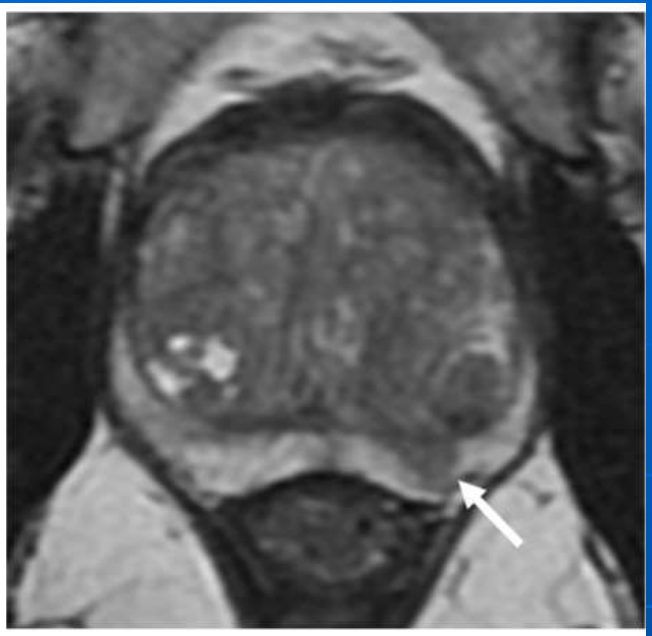
- 6% chance of high-grade prostate cancer,
- 18% chance of low-grade cancer,
- 76% chance that the biopsy is negative for cancer.
- About 2 to 4% of men undergoing biopsy will have an infection that may require hospitalization.

Please consult your physician concerning these results.

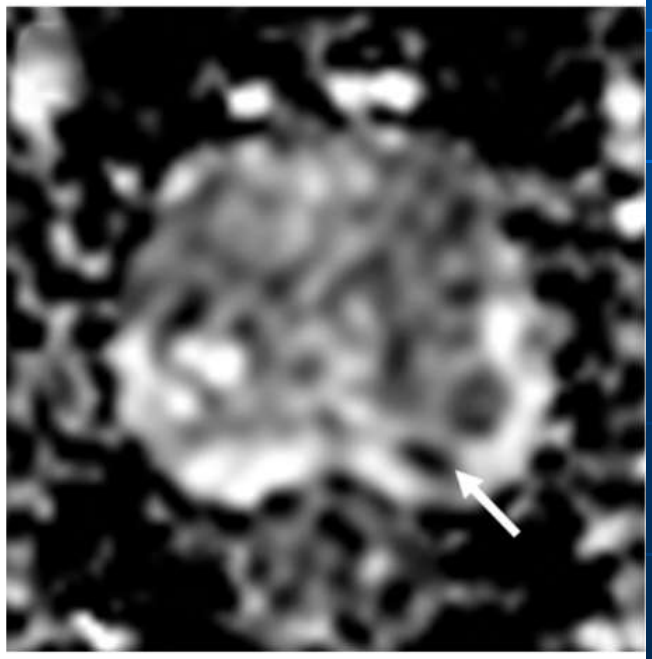


Click here to watch a video overview of these results.

MRI: Pre BX utility -T2W and DWI



(a)

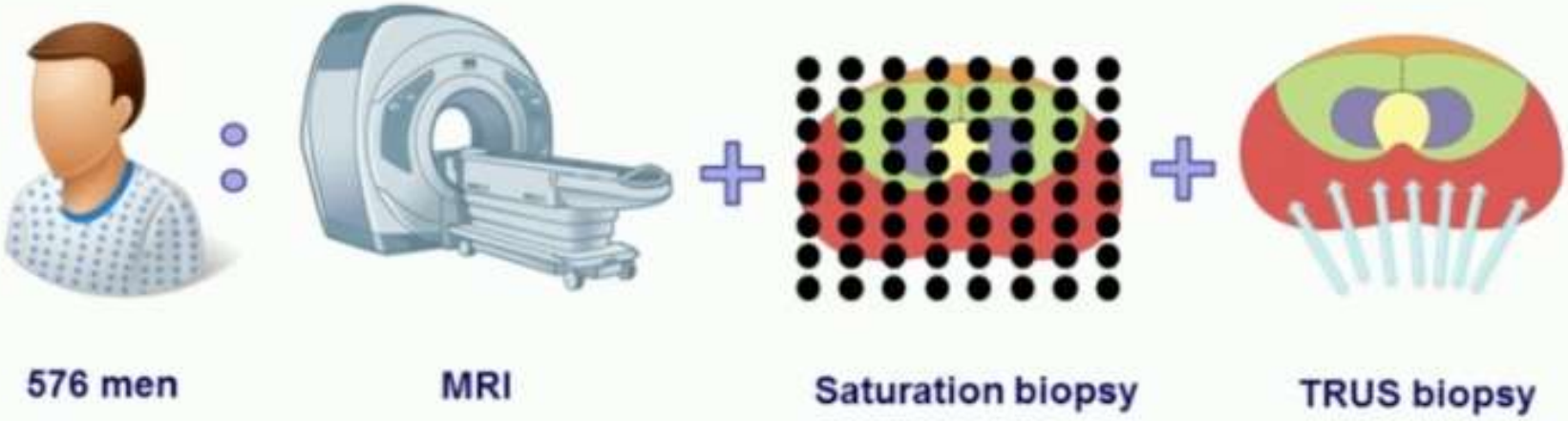


(b)

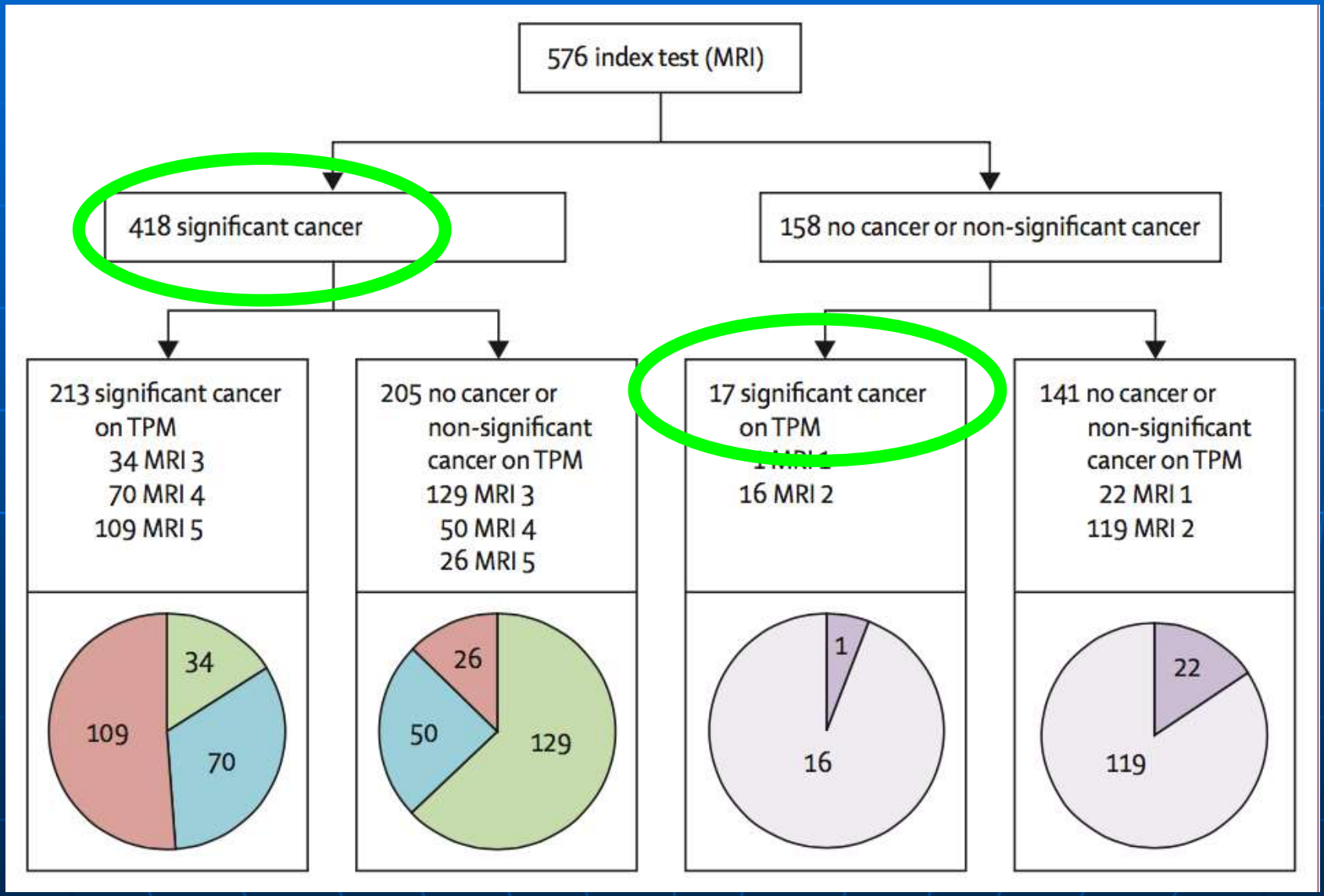
Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study

Hashim U Ahmed, Ahmed El-Shater Bosaily*, Louise C Brown*, Rhian Gabe, Richard Kaplan, Mahesh K Parmar, Yolanda Collaco-Moraes, Katie Ward, Richard G Hindley, Alex Freeman, Alex P Kirkham, Robert Oldroyd, Chris Parker, Mark Emberton, and the PROMIS study group†*

PROMIS Trial



MRI


576 index test (MRI)
418 significant cancer
158 no cancer or non-significant cancer
213 significant cancer on TPM
34 MRI 3
70 MRI 4
109 MRI 5
205 no cancer or non-significant cancer on TPM
129 MRI 3
50 MRI 4
26 MRI 5
17 significant cancer on TPM
16 MRI 2
141 no cancer or non-significant cancer on TPM
22 MRI 1
119 MRI 2
34
109
70
26
50
129
1
16
22
119

MRI Accuracy

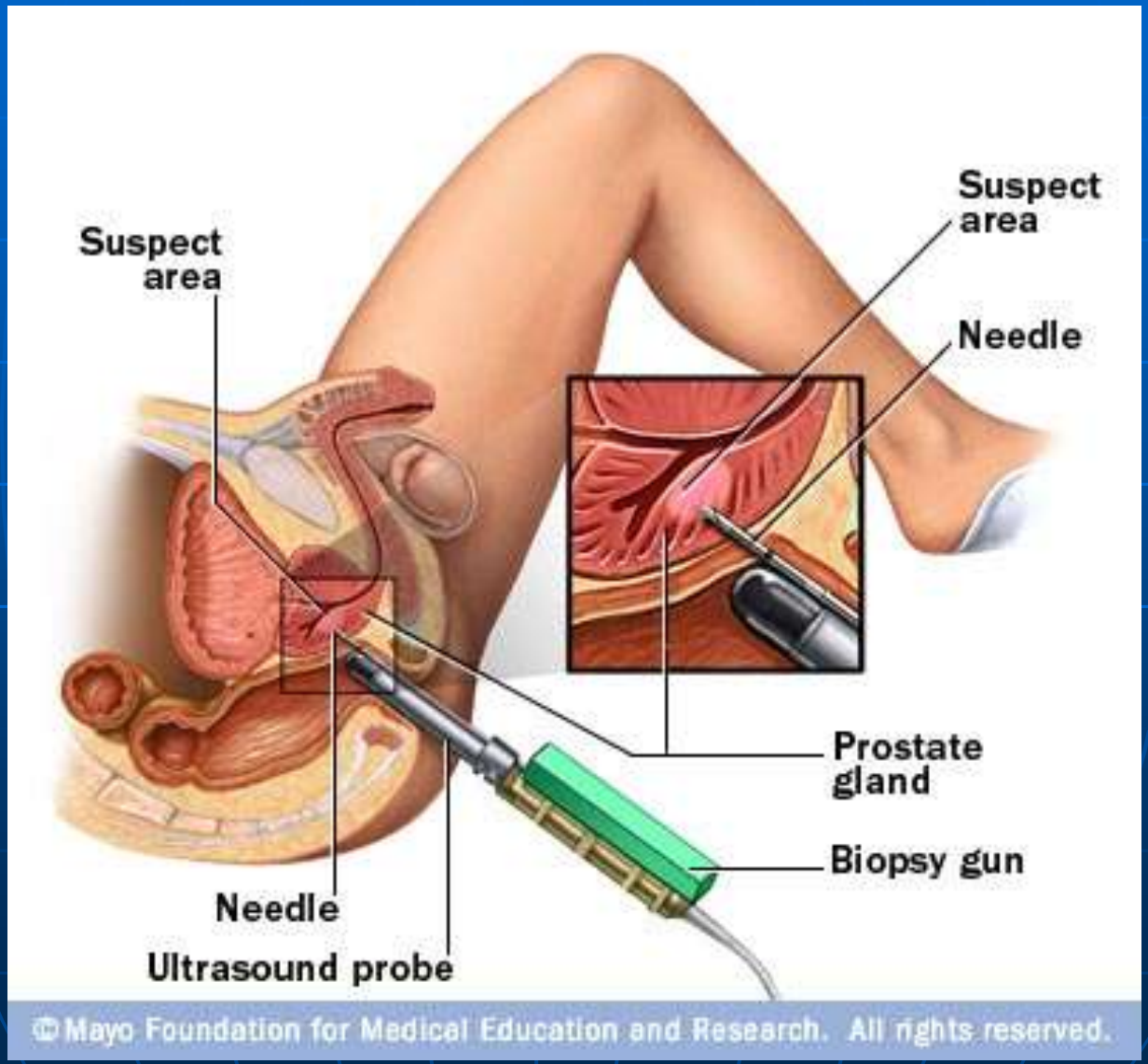
	MP-MRI, % (95% CI)	TRUS-biopsy, % [95% CI]	Test ratio* [95% CI]	p value
Primary definition (Gleason score ≥4+3 or cancer core length ≥6 mm), prevalence of clinically significant cancer 230 (40% 36–44%)				
Sensitivity test	93 (88–96)	48 (42–55)	0·52 (0·45–0·60)	p<0·0001
Specificity test	41 (36–46)	96 (94–98)	2·34 (2·08–2·68)	p<0·0001
PPV	51 (46–56)	90 (83–94)	8·2 (4·7–14·3)	p<0·0001
NPV	89 (83–94)	74 (69–78)	0·34 (0·21–0·55)	p<0·0001

Prostate Magnetic Resonance Imaging and Magnetic Resonance Imaging Targeted Biopsy in Patients with a Prior Negative Biopsy: A Consensus Statement by AUA and SAR

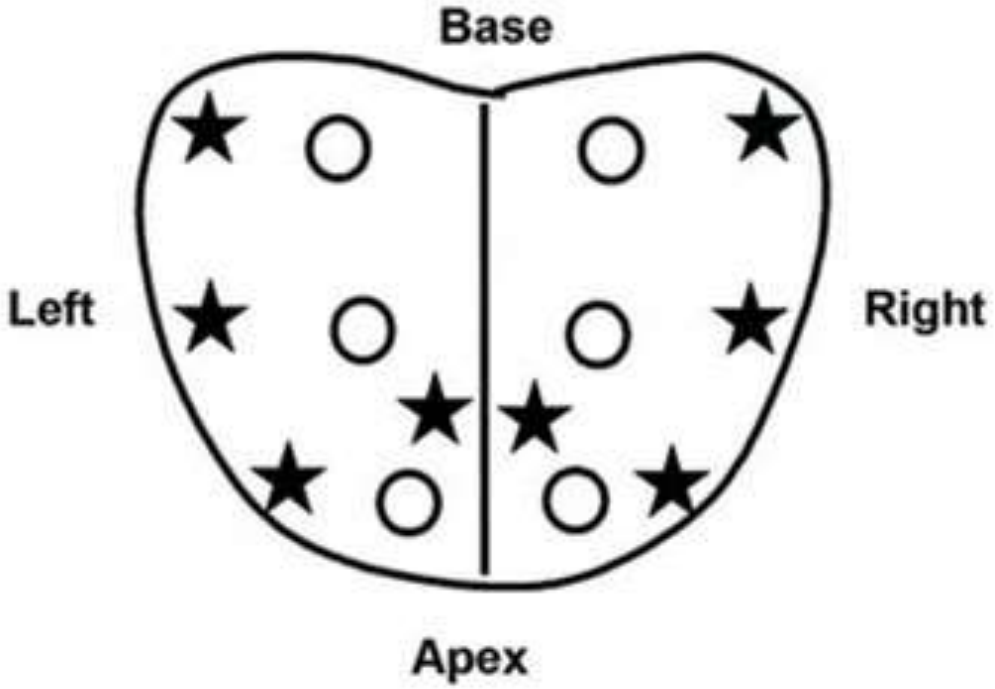
Andrew B. Rosenkrantz,*,† Sadhna Verma, Peter Choyke, Steven C. Eberhardt, Scott E. Eggener,‡ Krishnanath Gaitonde, Masoom A. Haider, Daniel J. Margolis, Leonard S. Marks, Peter Pinto, Geoffrey A. Sonn and Samir S. Taneja§

- MRI if suspicion for PC after first BX
- Wait 8 weeks!
- Targeted BX if PIRADS 3-5

Trans-Rectal Biopsy



Biopsy Strategy



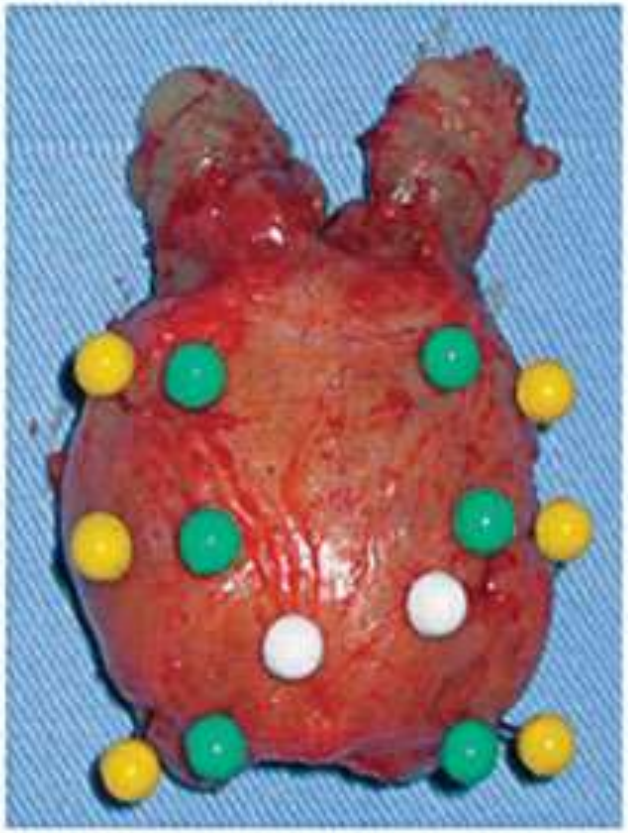
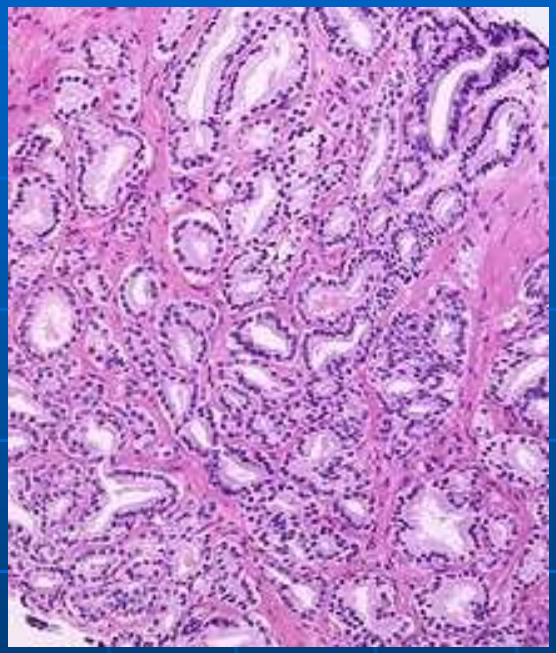
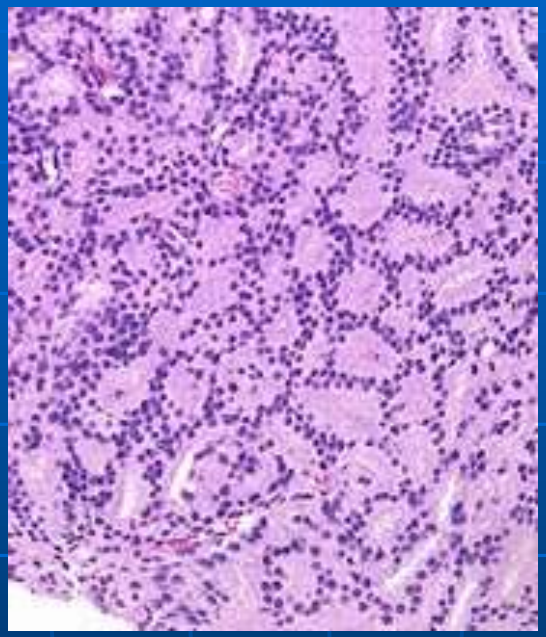
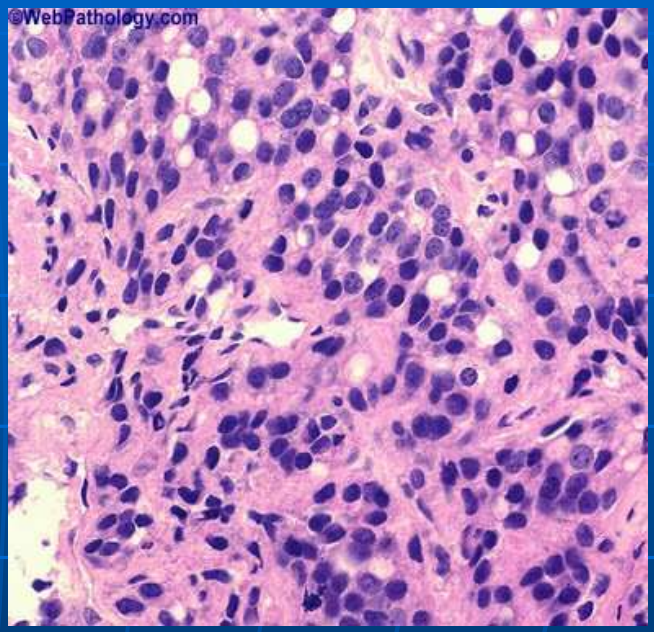


Figure 2 – Extended biopsy.

Gleason 3,4,5

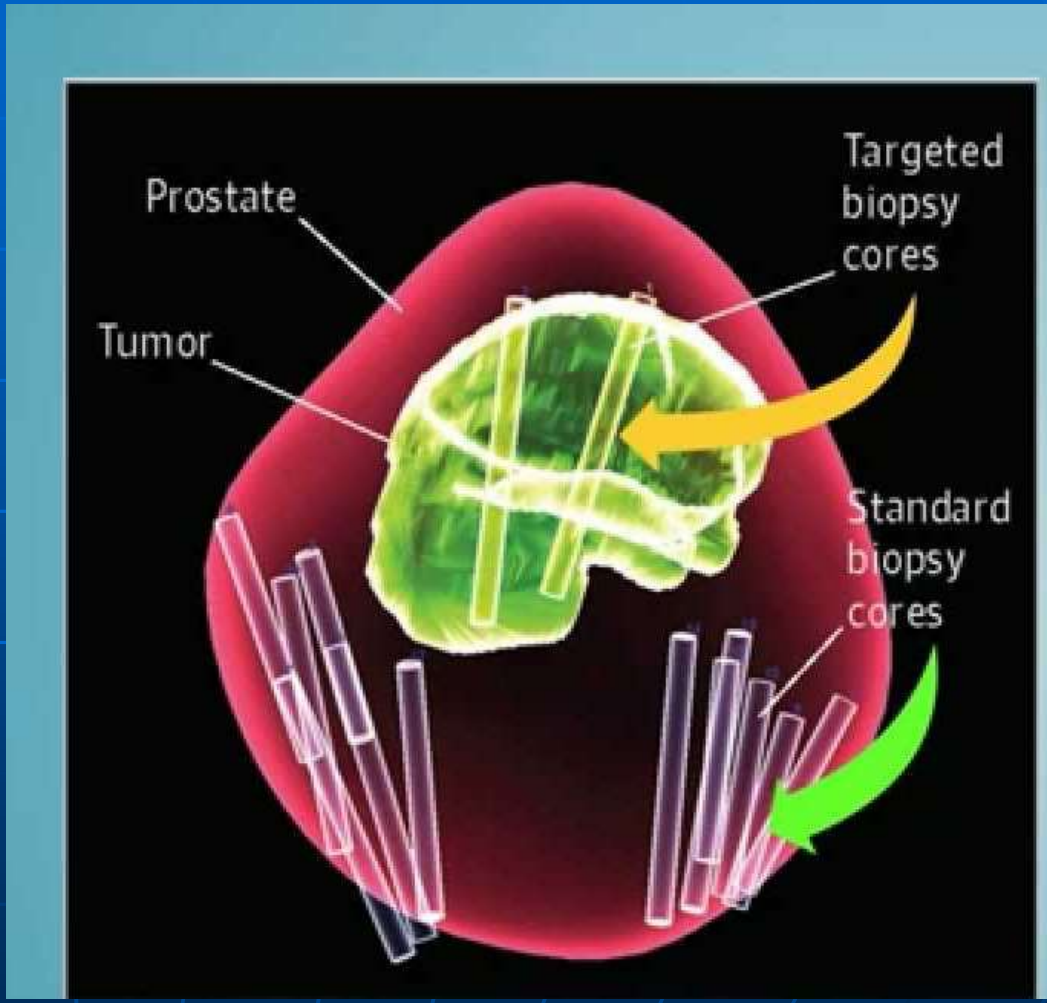




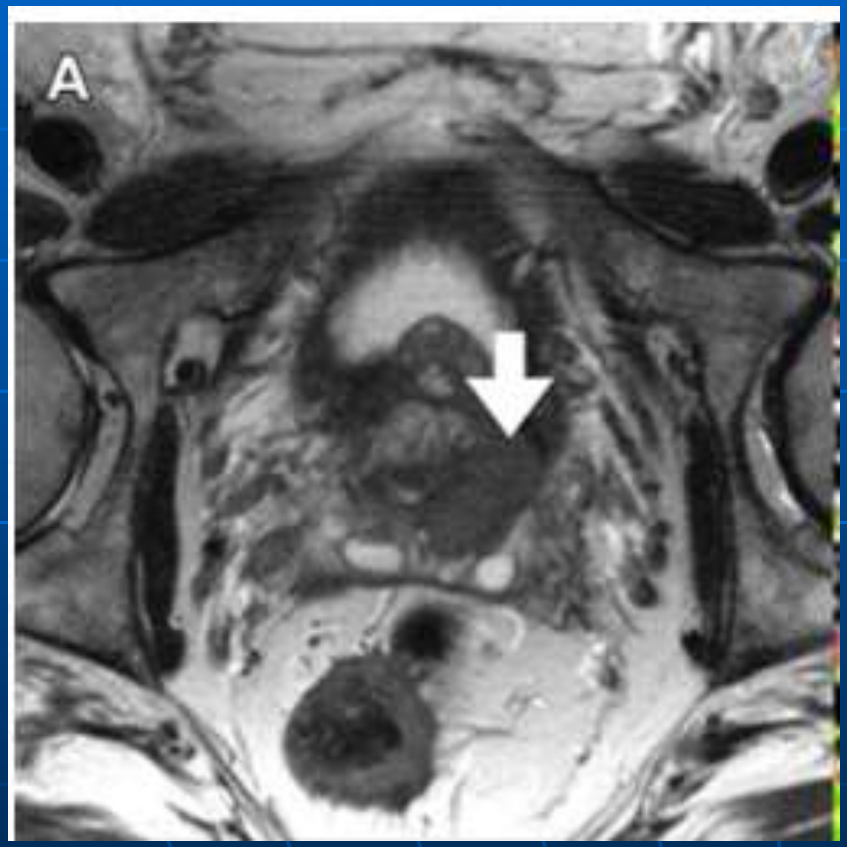


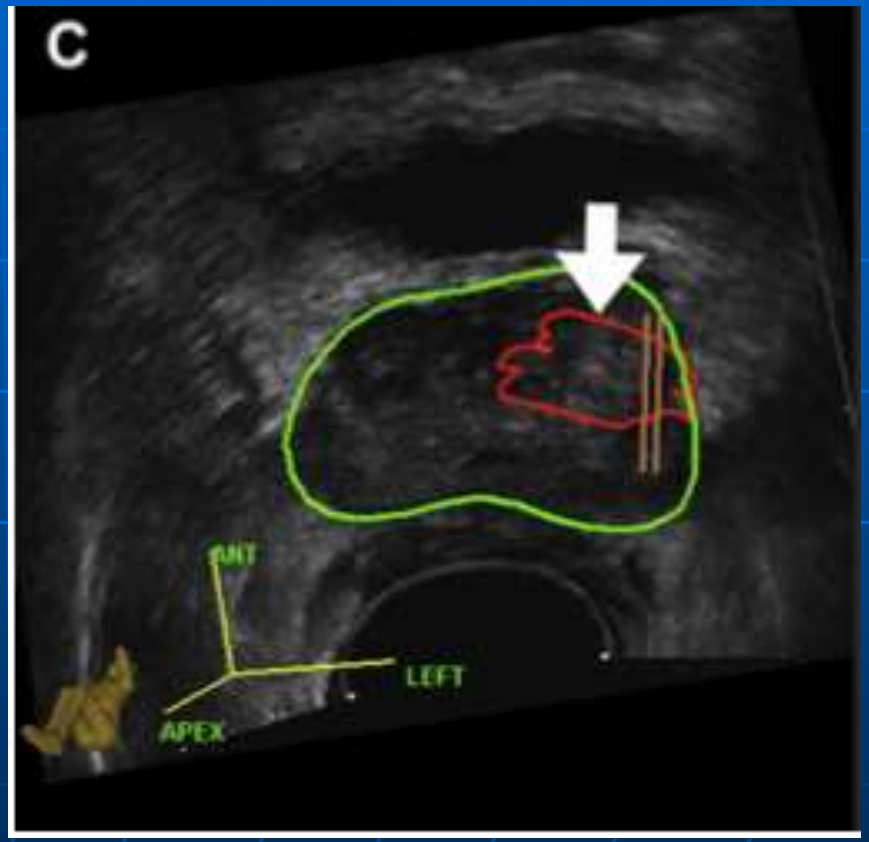
MRI Fusion Rationale

- Target lesion specifically
- Identify Gl7
-
- avoid Gl6



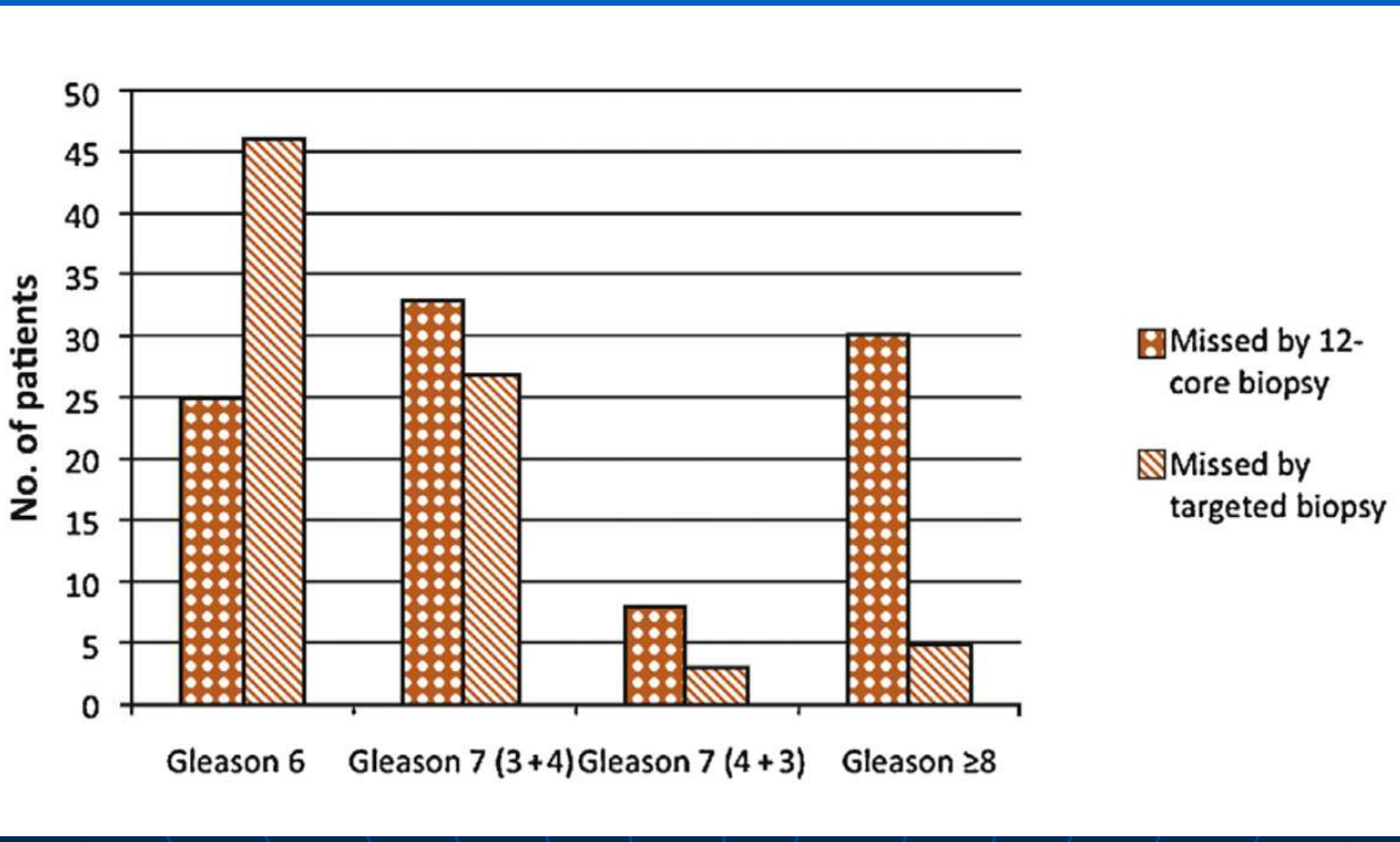
MRI Fusion Bx





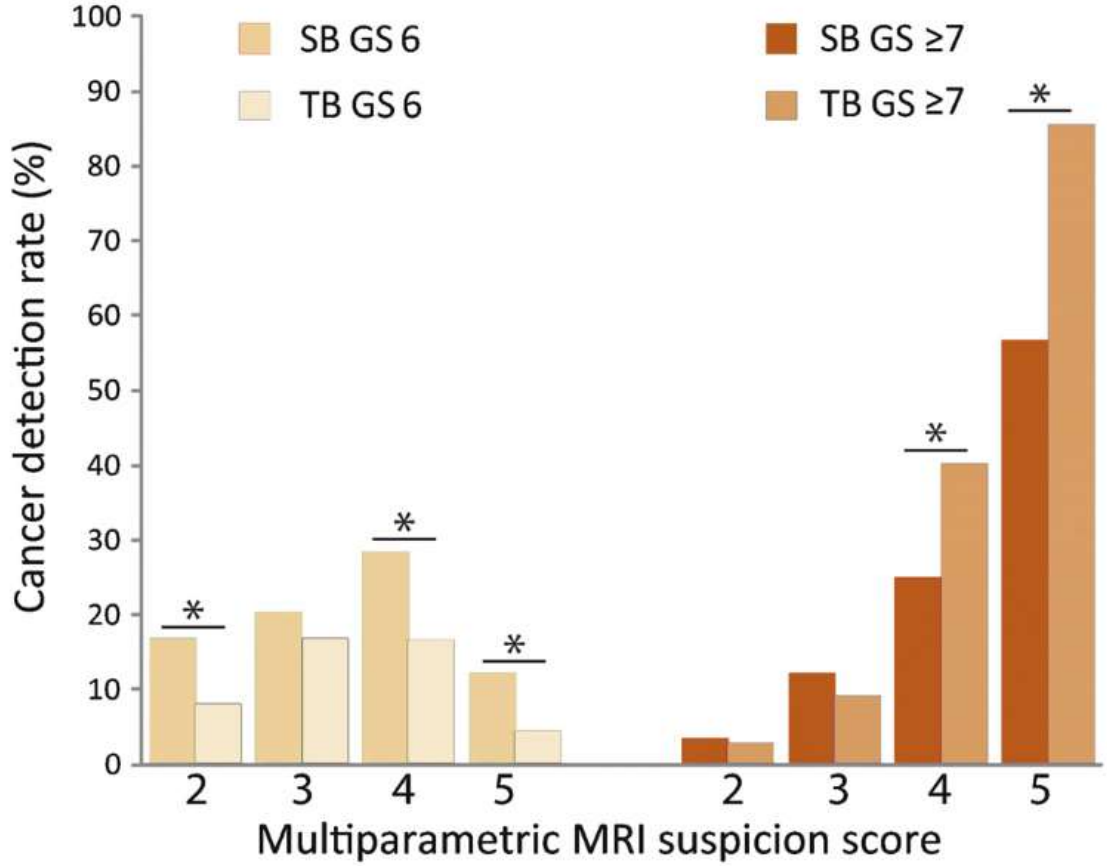
Magnetic Resonance Imaging/Ultrasound–Fusion Biopsy Significantly Upgrades Prostate Cancer Versus Systematic 12-core Transrectal Ultrasound Biopsy

M. Minhaj Siddiqui [a], Soroush Rais-Bahrami [a], Hong Truong [a], Lambros Stamatakis [a], Srinivas Vourganti [a], Jeffrey Nix [a], Anthony N. Hoang [a], Annerleim Walton-Diaz [a], Brian Shuch [a], Michael Weintraub [a], Jochen Kruecker [d], Hayet Amalou [c], Baris Turkbey [b], Maria J. Merino [e], Peter L. Choyke [b], Bradford J. Wood [c], Peter A. Pinto [a,c,]*



Relationship Between Prebiopsy Multiparametric Magnetic Resonance Imaging (MRI), Biopsy Indication, and MRI-ultrasound Fusion–targeted Prostate Biopsy Outcomes

Xiaosong Meng [a], Andrew B. Rosenkrantz [b], Neil Mendhiratta [c], Michael Fenstermaker [c], Richard Huang [a], James S. Wysock [a,e], Marc A. Bjurlin [a,f], Susan Marshall [a], Fang-Ming Deng [d], Ming Zhou [d], Jonathan Melamed [d], William C. Huang [a], Herbert Lepor [a], Samir S. Taneja [a,b,]*



- Thoughts on Treatment for Local Disease?

Therapie Standard

- Radiation
- surgery
  - Open
  - Lap
  - Robot

Dan Lewinshtein 2014

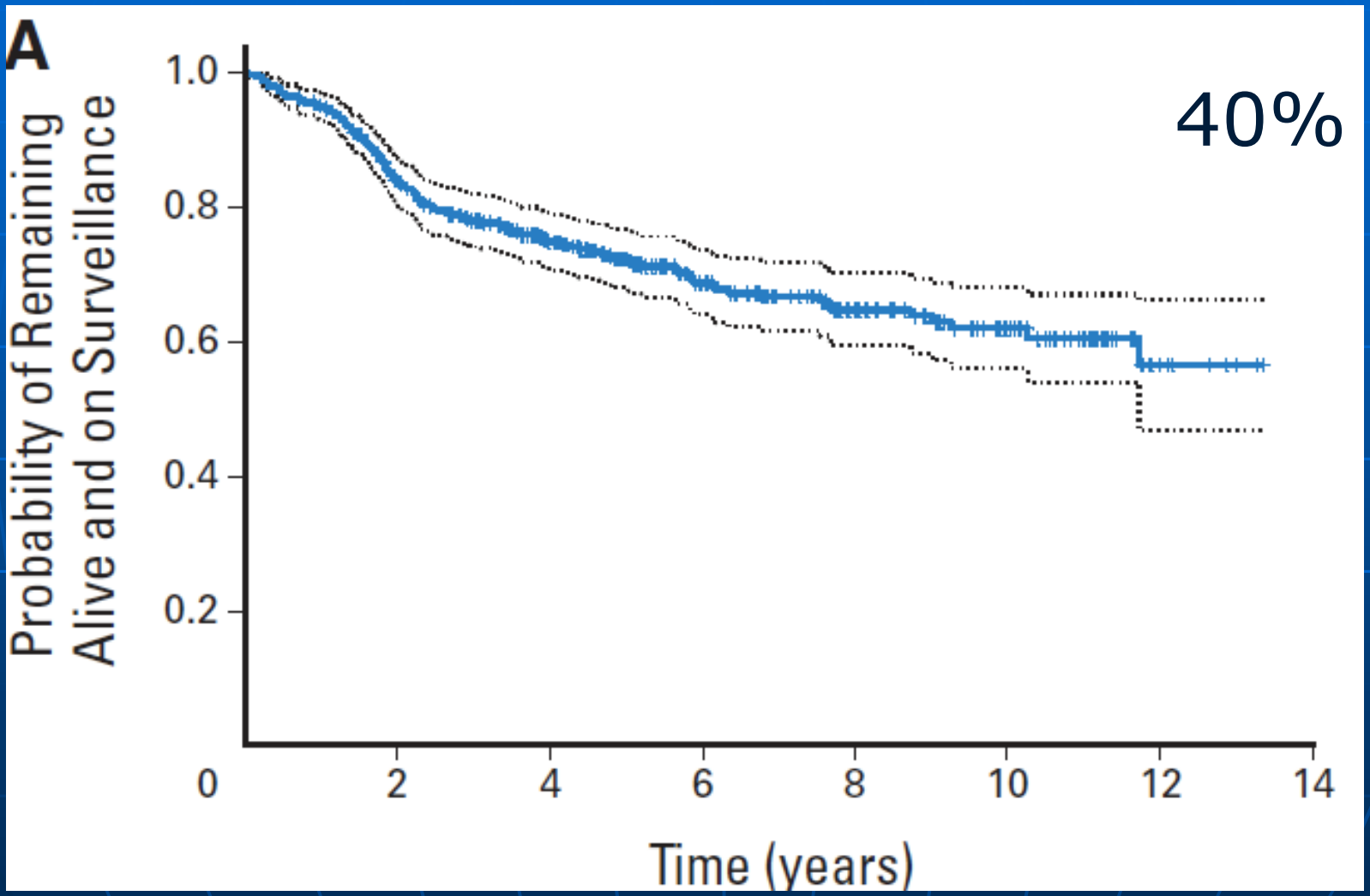
UofT & Klotz: Active Surveillance (AS)

- Gleason 6[1]
- -
  - Risk of progression
- +
  - Avoid ED et incontinence

⑩↓cost

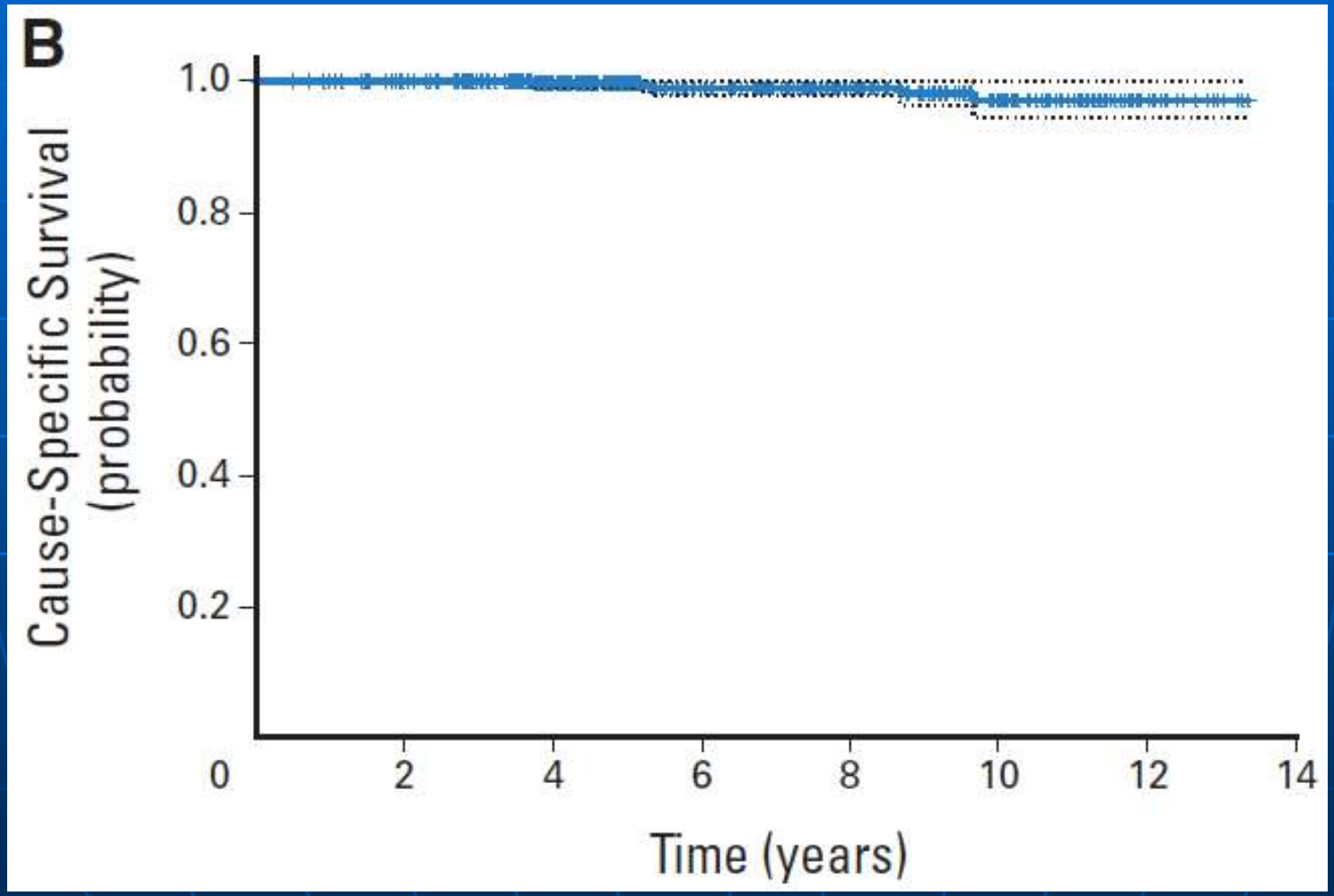
1:JCO 28:126

Klotz: AS failure



Dan Lewinshtein 2014

Klotz AS: Cancer specific Survival



Dan Lewinshtein 2014

PIVOT: RRP vs. AS

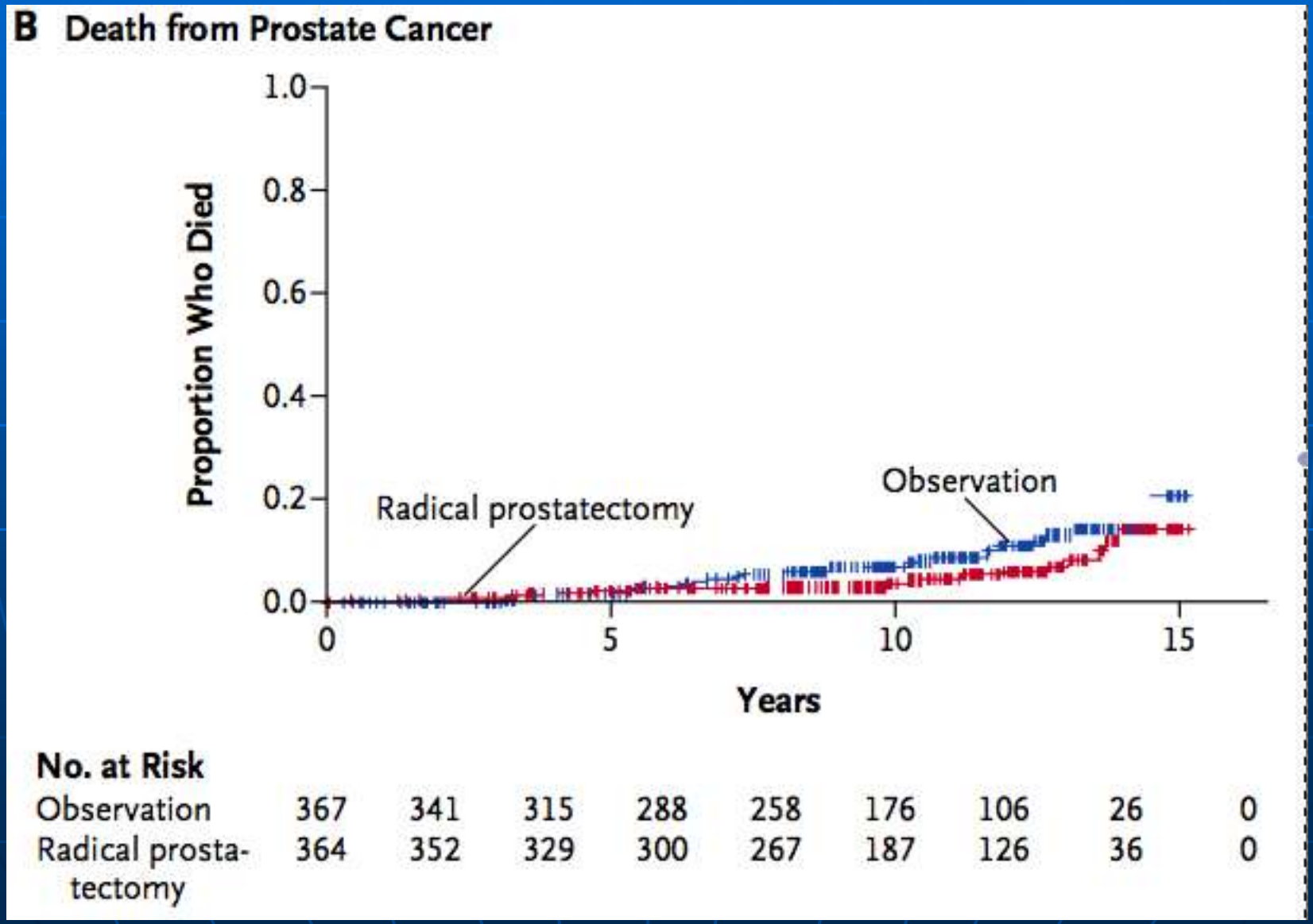
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 19, 2012 VOL. 367 NO. 3

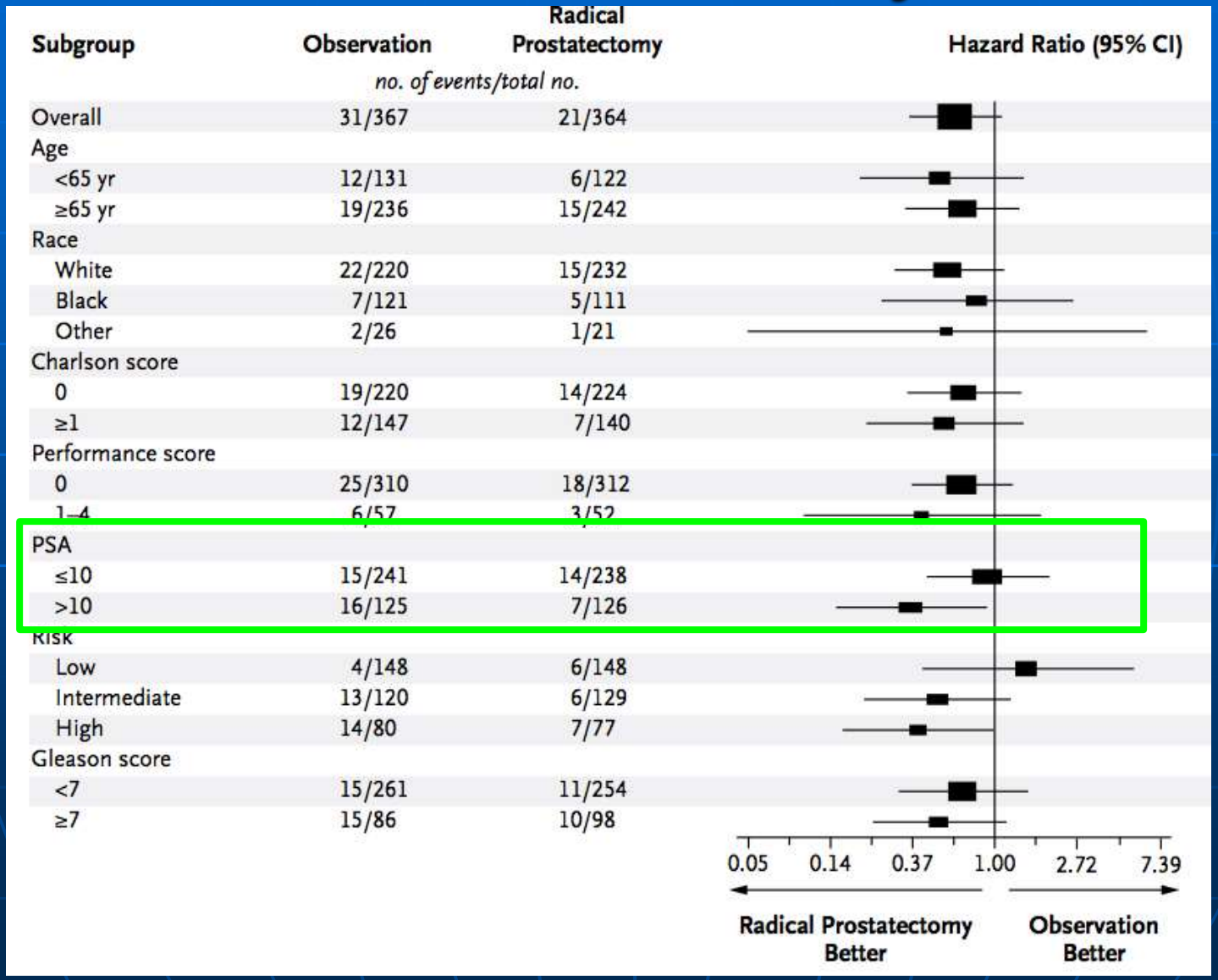
Radical Prostatectomy versus Observation for Localized Prostate Cancer

Timothy J. Wilt, M.D., M.P.H., Michael K. Brawer, M.D., Karen M. Jones, M.S., Michael J. Barry, M.D., William J. Aronson, M.D., Steven Fox, M.D., M.P.H., Jeffrey R. Gingrich, M.D., John T. Wei, M.D., Patricia Gilhooly, M.D., B. Mayer Grob, M.D., Imad Nsouli, M.D., Padmini Iyer, M.D., Ruben Cartagena, M.D., Glenn Snider, M.D., Claus Roehrborn, M.D., Ph.D., Roohollah Sharifi, M.D., William Blank, M.D., Parikshit Pandya, M.D., Gerald L. Andriole, M.D., Daniel Culkin, M.D., and Thomas Wheeler, M.D., for the Prostate Cancer Intervention versus Observation Trial (PIVOT) Study Group

PIVOT: RRP vs. AS

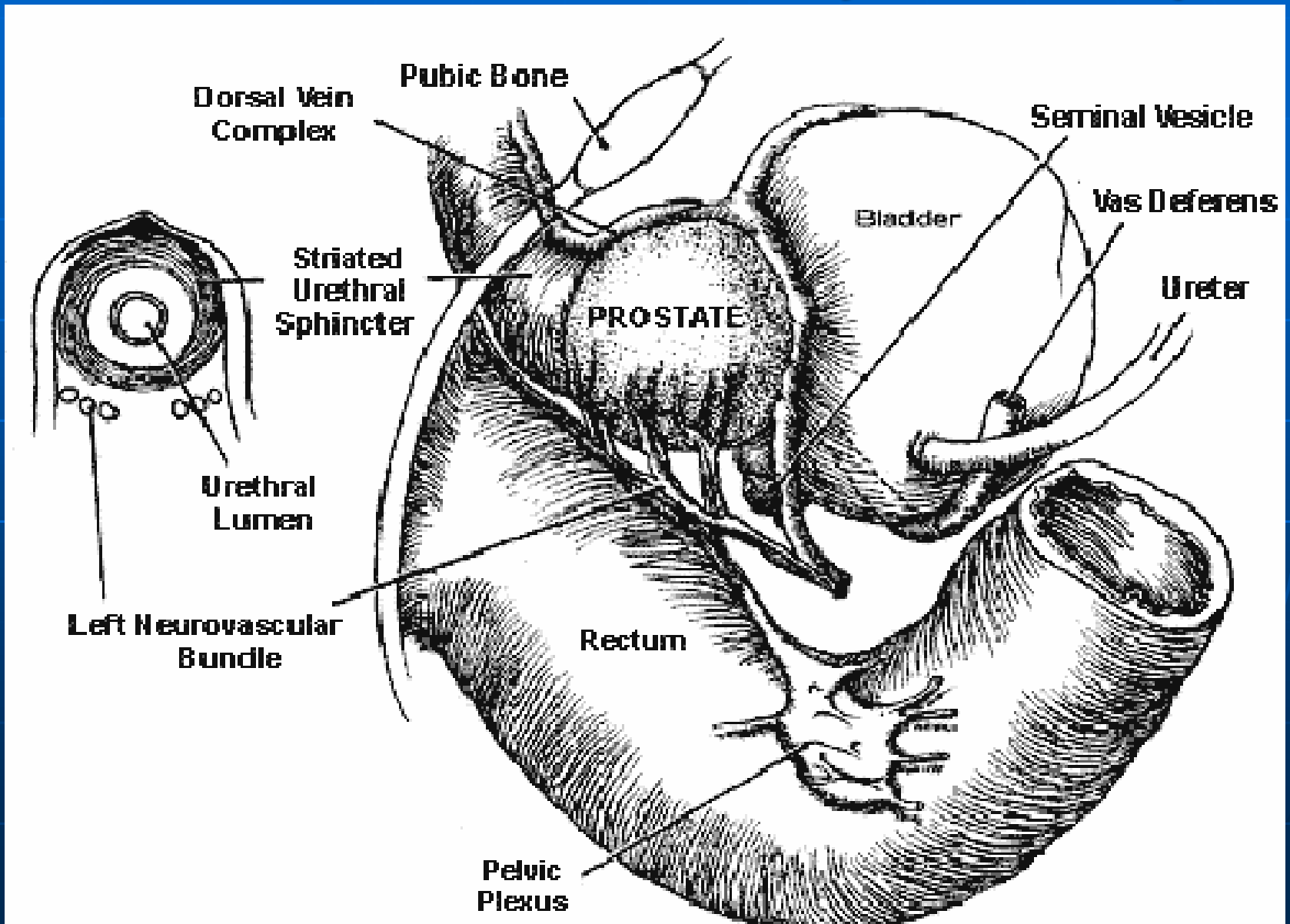


Pivot:Sub Analysis

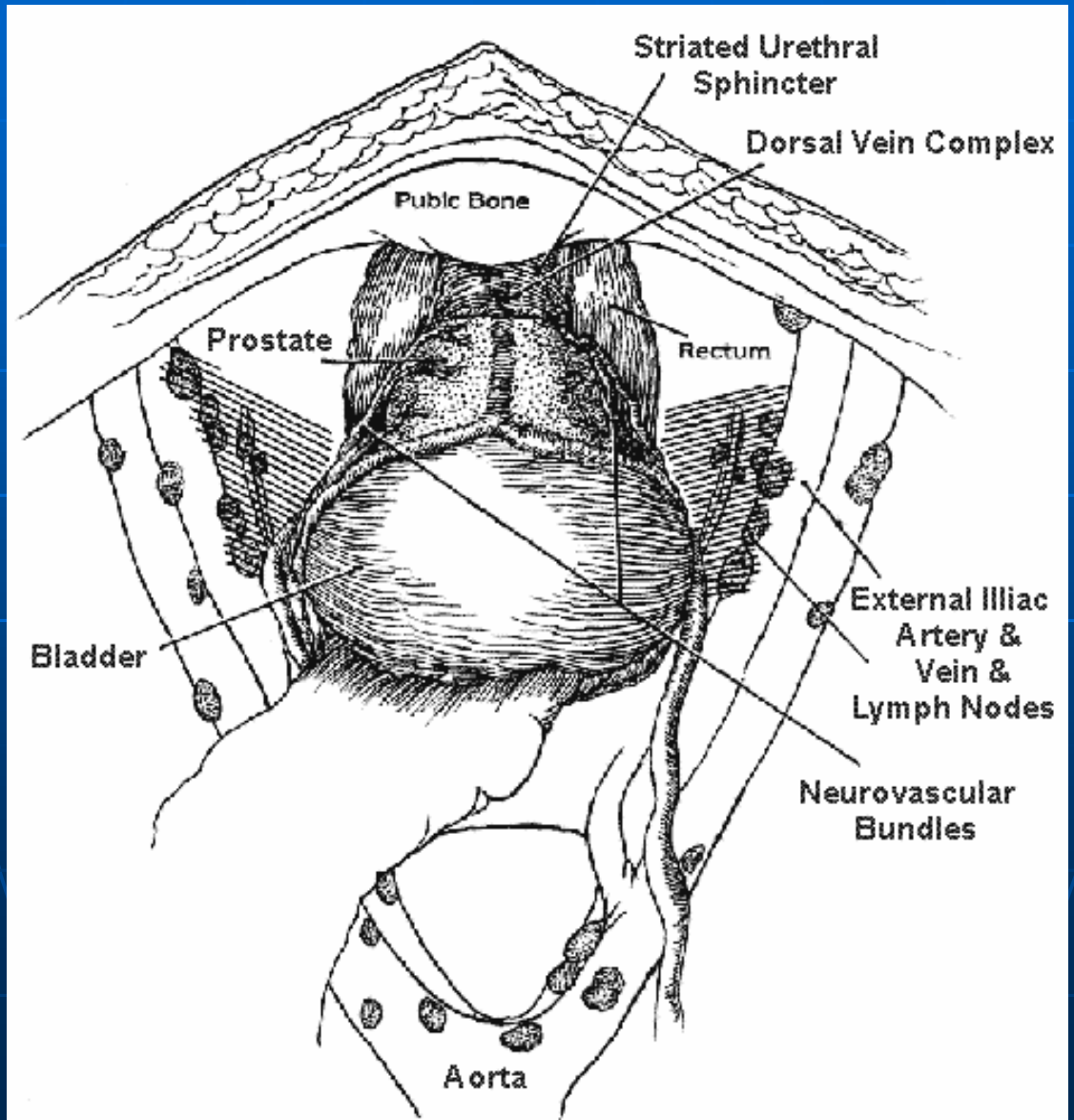


Subgroup	Observation	Radical Prostatectomy
	no. of events/total no.	
Overall	31/367	21/364
Age		
<65 yr	12/131	6/122
≥65 yr	19/236	15/242
Race		
White	22/220	15/232
Black	7/121	5/111
Other	2/26	1/21
Charlson score		
0	19/220	14/224
≥1	12/147	7/140
Performance score		
0	25/310	18/312
1–4	6/57	3/52
PSA		
≤10	15/241	14/238
>10	16/125	7/126
Risk		
Low	4/148	6/148
Intermediate	13/120	6/129
High	14/80	7/77
Gleason score		
<7	15/261	11/254
≥7	15/86	10/98

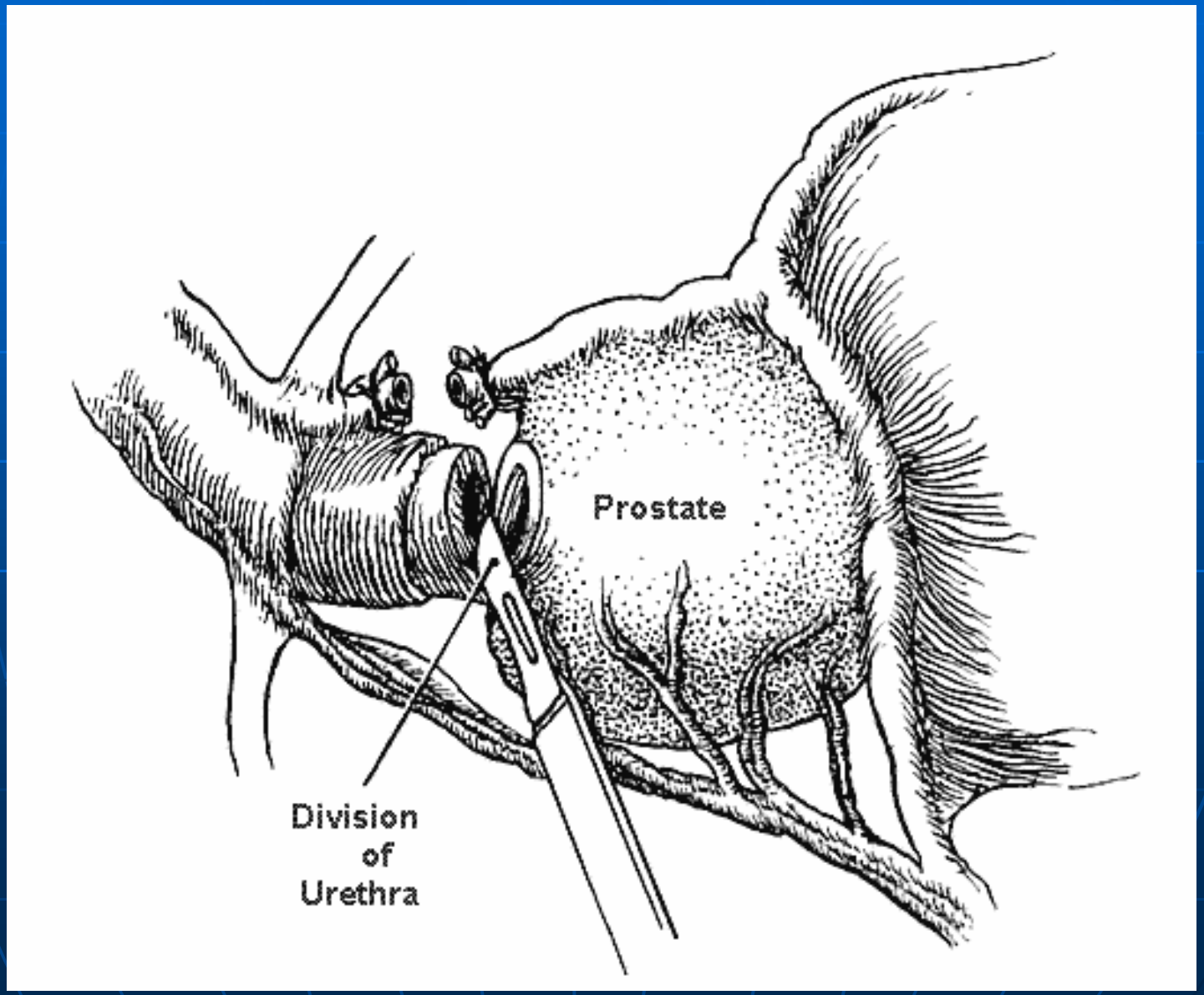
Radical Prostatectomy: Anatomy



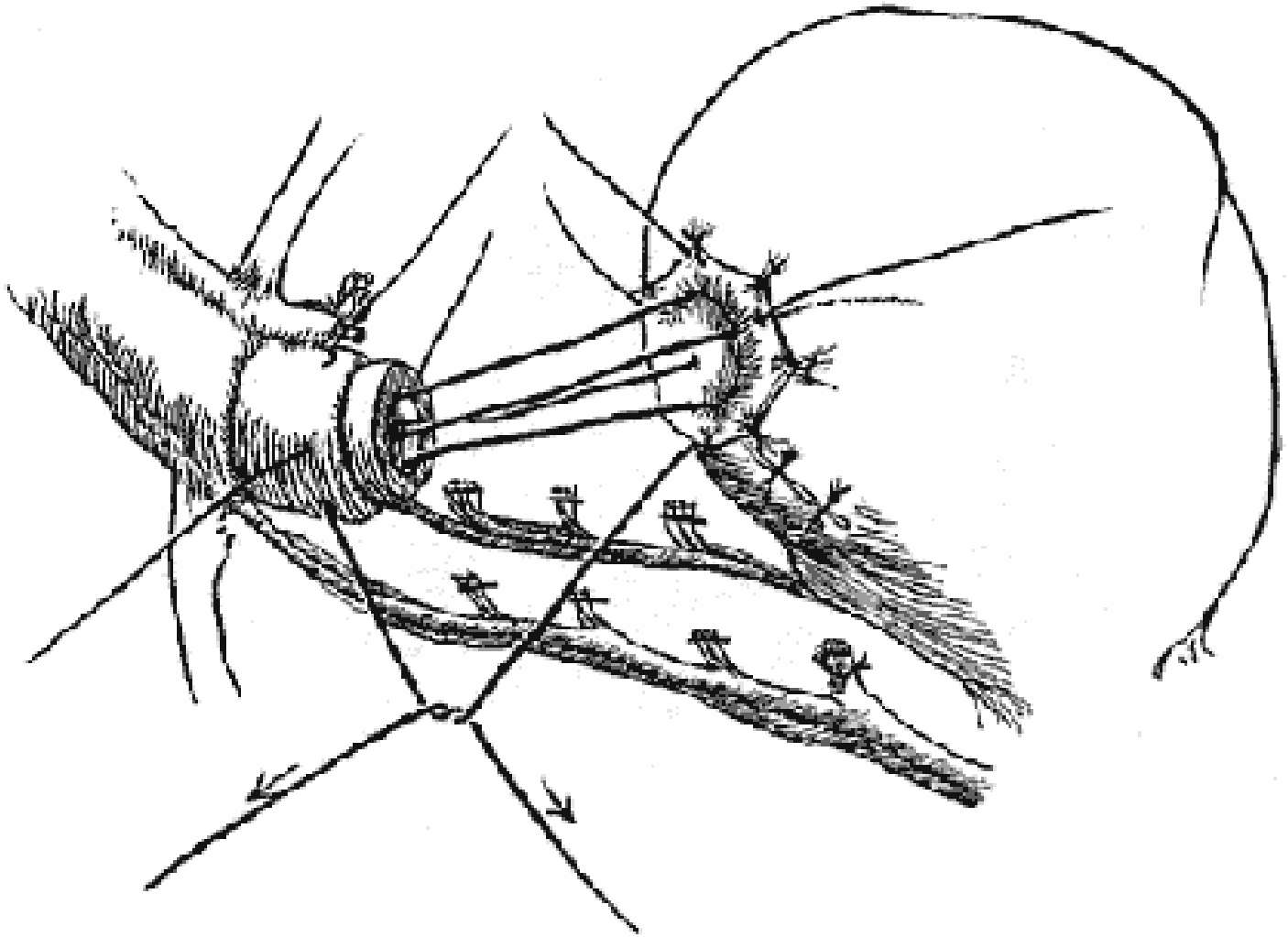
Radical Prostatectomy: LND



Radical Prostatectomy: Urethra Length



Radical Prostatectomy: Nerve Sparing



Robotic Prostatectomy

Robot:Usage

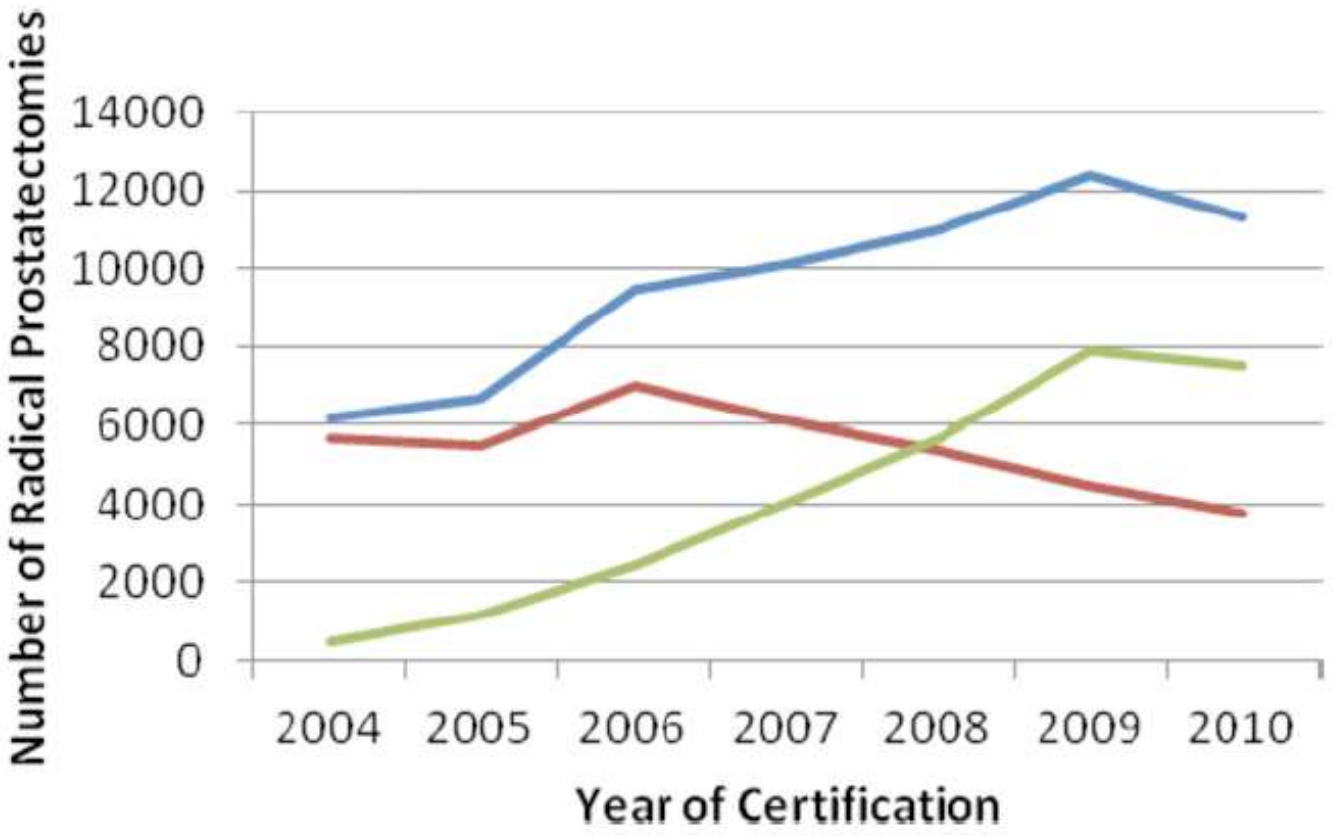


Figure 1. Trends in robotic (green curve) and open (red curve) RP. Blue curve indicates total.

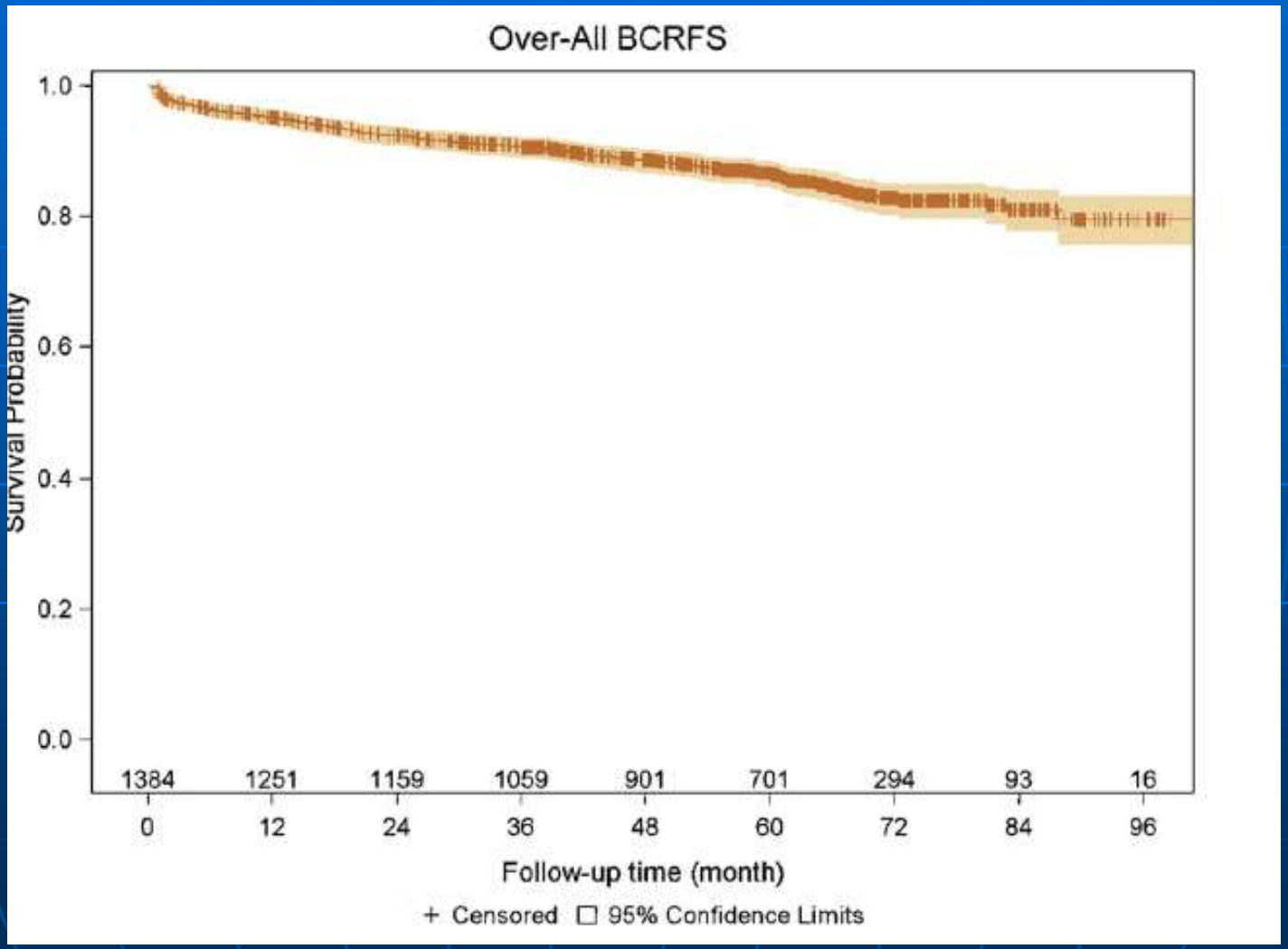
J UROL 187:2087

Robot: Results Peri-op?

Outcomes	MIRP	RRP	MIRP vs RRP, Ratio (95% Confidence Interval)[b]	*P* Value
Length of stay, median (IQR)[c]	2 (1-2)	3 (2-4)	0.67 (0.58-0.72)	<.001
Heterologous blood transfusion, %	2.7	20.8	0.11 (0.06-0.17)	<.001

JAMA 302:1557

Robot: BCR



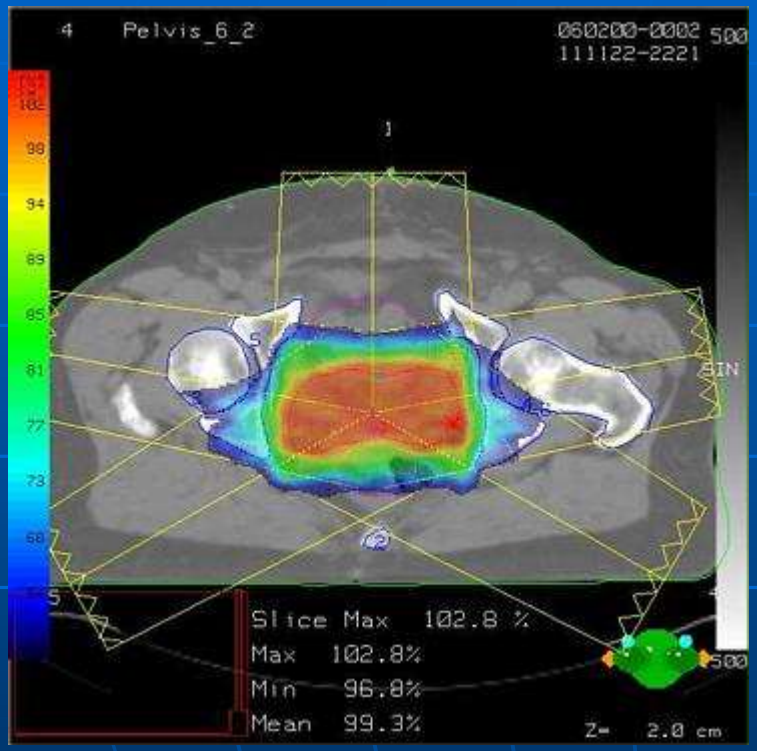
JAMA 302:1557

Robot: Functional Results

Outcomes	MIRP	RRP	MIRP vs RRP, Ratio (95% Confidence Interval)[b]	*P* Value
Incontinence per 100 person-years[e]				
Diagnosis	15.9	12.2	1.3 (1.05-1.61)	.02
Procedures	7.8	8.9	0.87 (0.69-1.1)	.24
Erectile dysfunction per 100 person-years[e]				
Diagnosis	26.8	19.2	1.40 (1.14-1.72)	.009
Procedure	2.3	2.2	1.05 (0.74-1.51)	.78

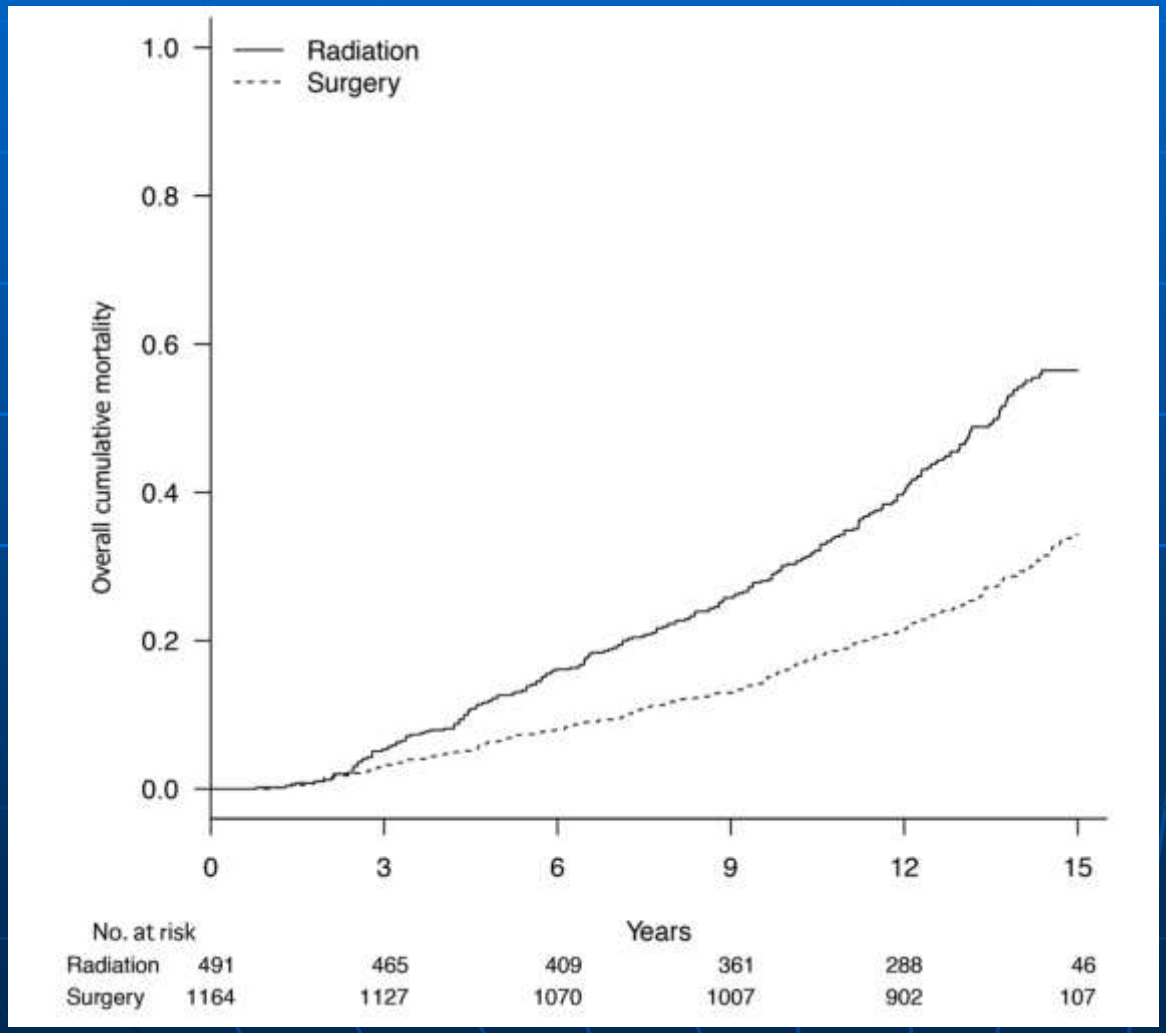
JAMA 302:1557

Radiotherapy



Mortality After Radical Prostatectomy or External Beam Radiotherapy for Localized Prostate Cancer

Richard M. Hoffman, Tatsuki Koyama, Kang-Hsien Fan, Peter C. Albertsen, Michael J. Barry, Michael Goodman, Ann S. Hamilton, Arnold L. Potosky, Janet L. Stanford, Antoinette M. Stroup, David F. Penson

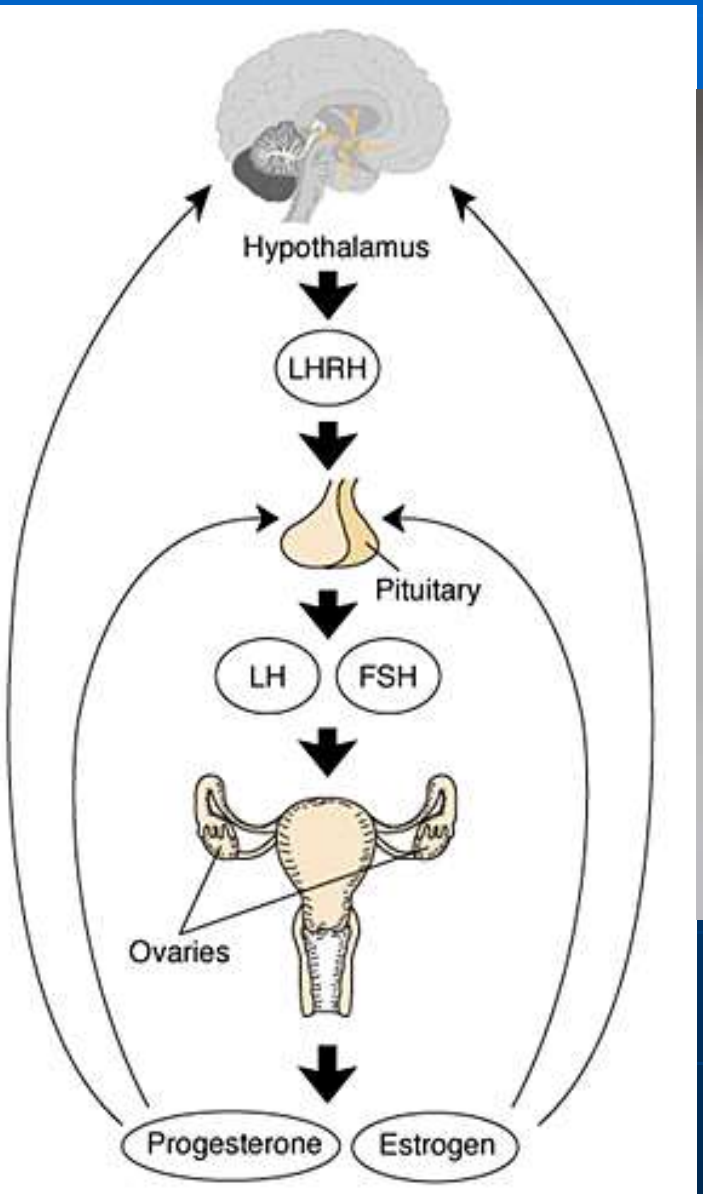


- JNCI 105:711

- Metastatic Disease?
- Mets to death 6 yr

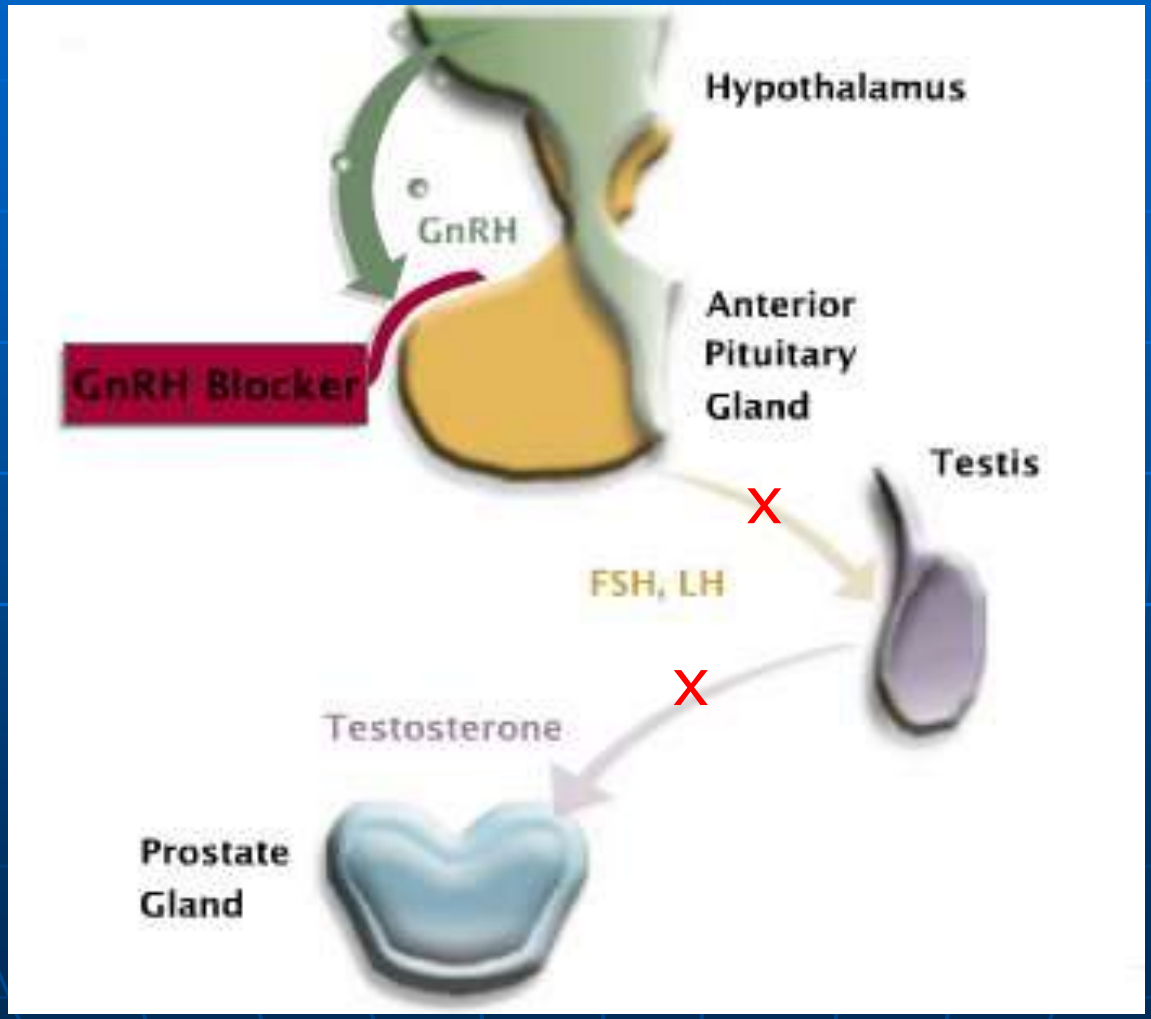
Dan Lewinshtein 2014

Hormones


Hypothalamus
LHRH
Pituitary
LH
FSH
Ovaries
Progesterone
Estrogen

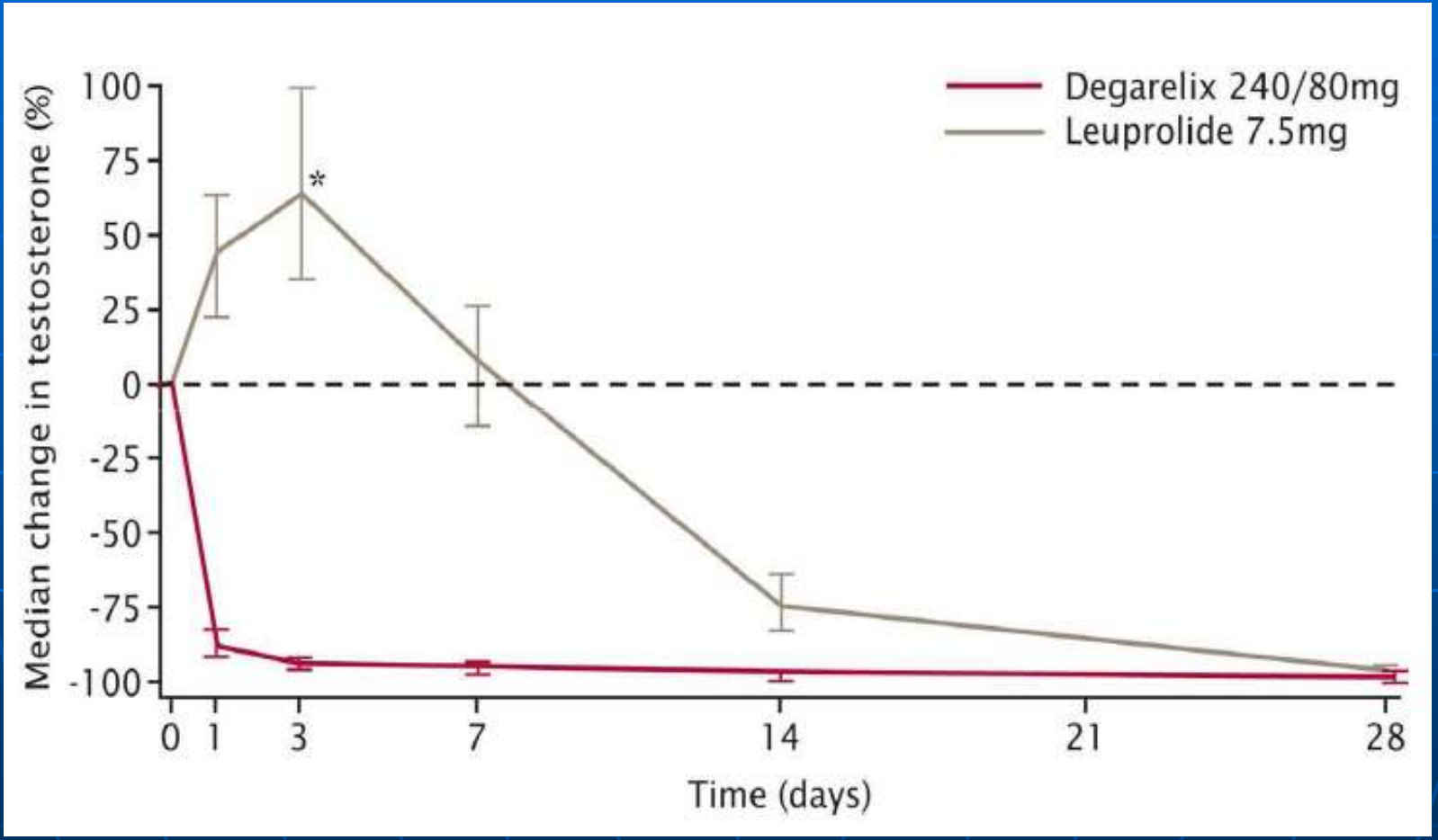

Zoladex LA
Zoladex LA

Firmagon: LHRH Receptor Blocker



Dan Lewinshtein 2014

Firmagon: Rapid Testosterone block

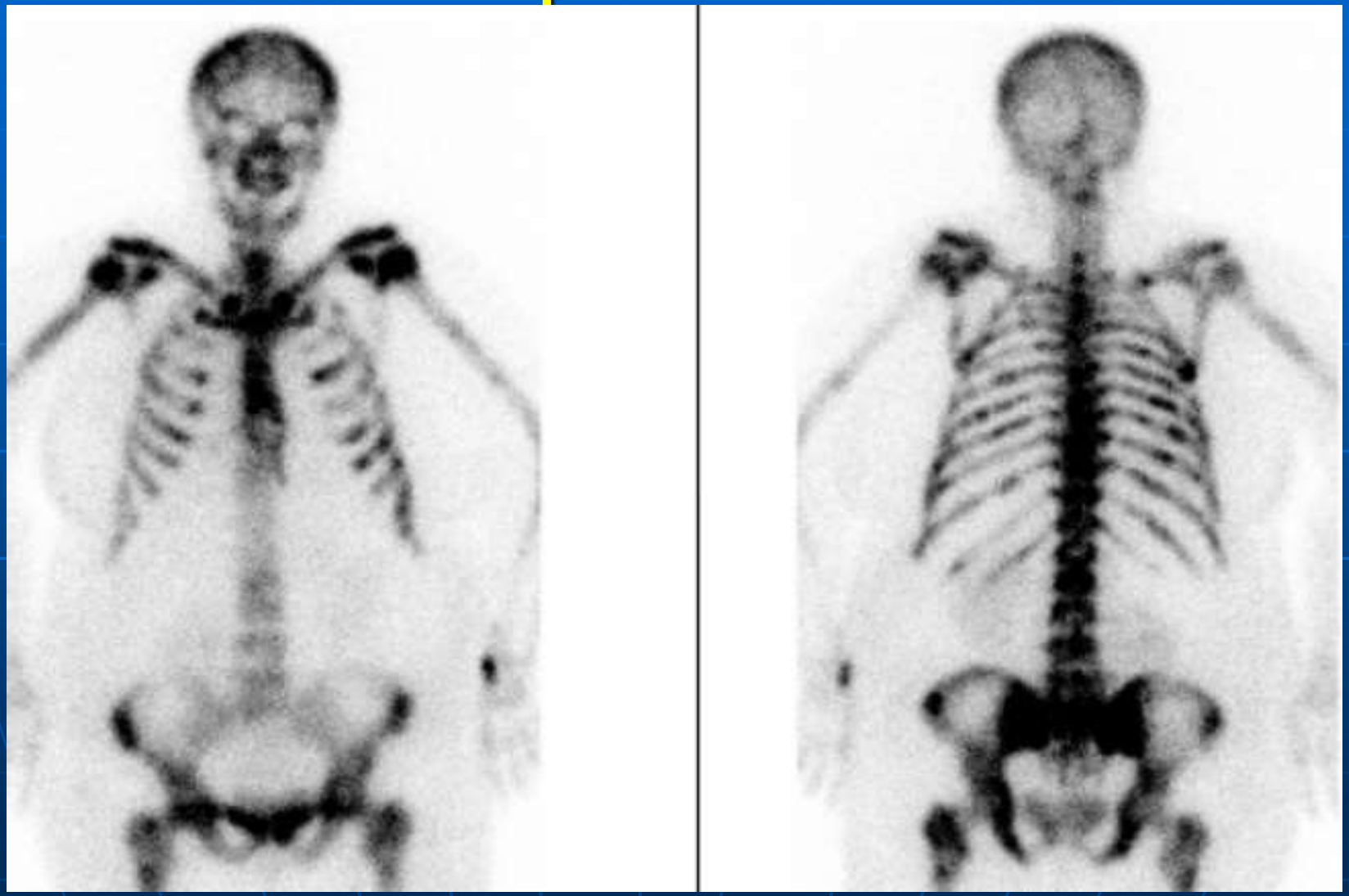


BJU 102:1531

Bone Protection

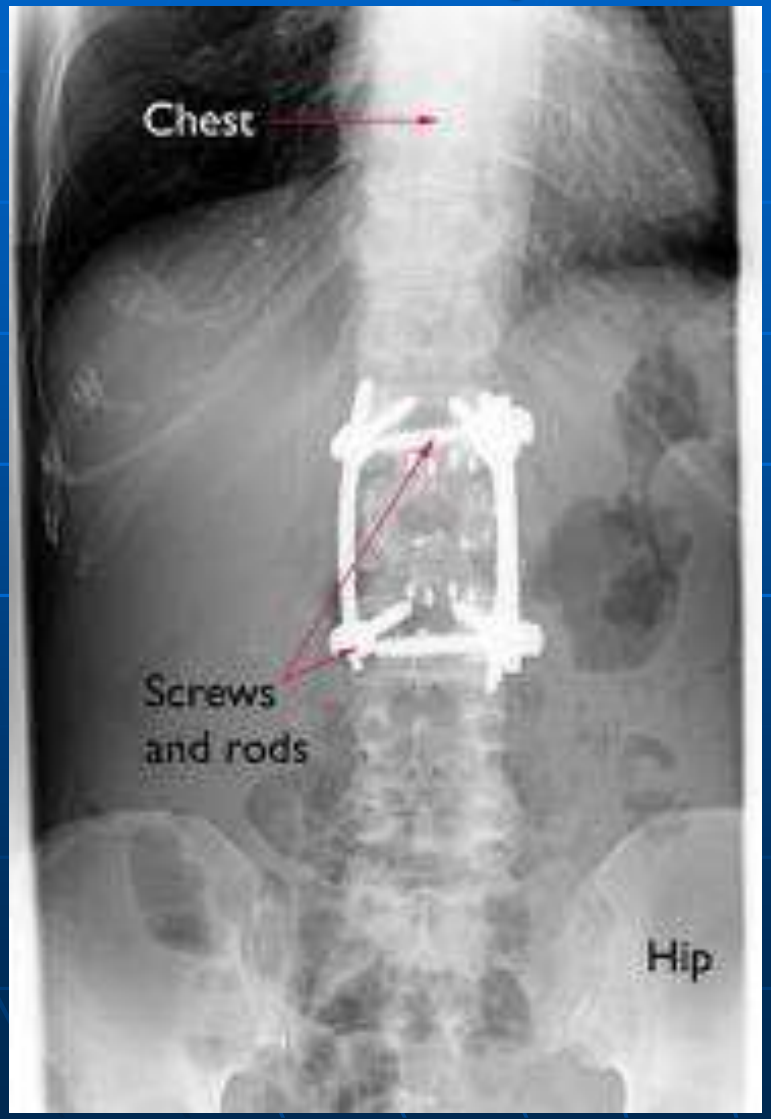
Dan Lewinshtein 2014

Superscan

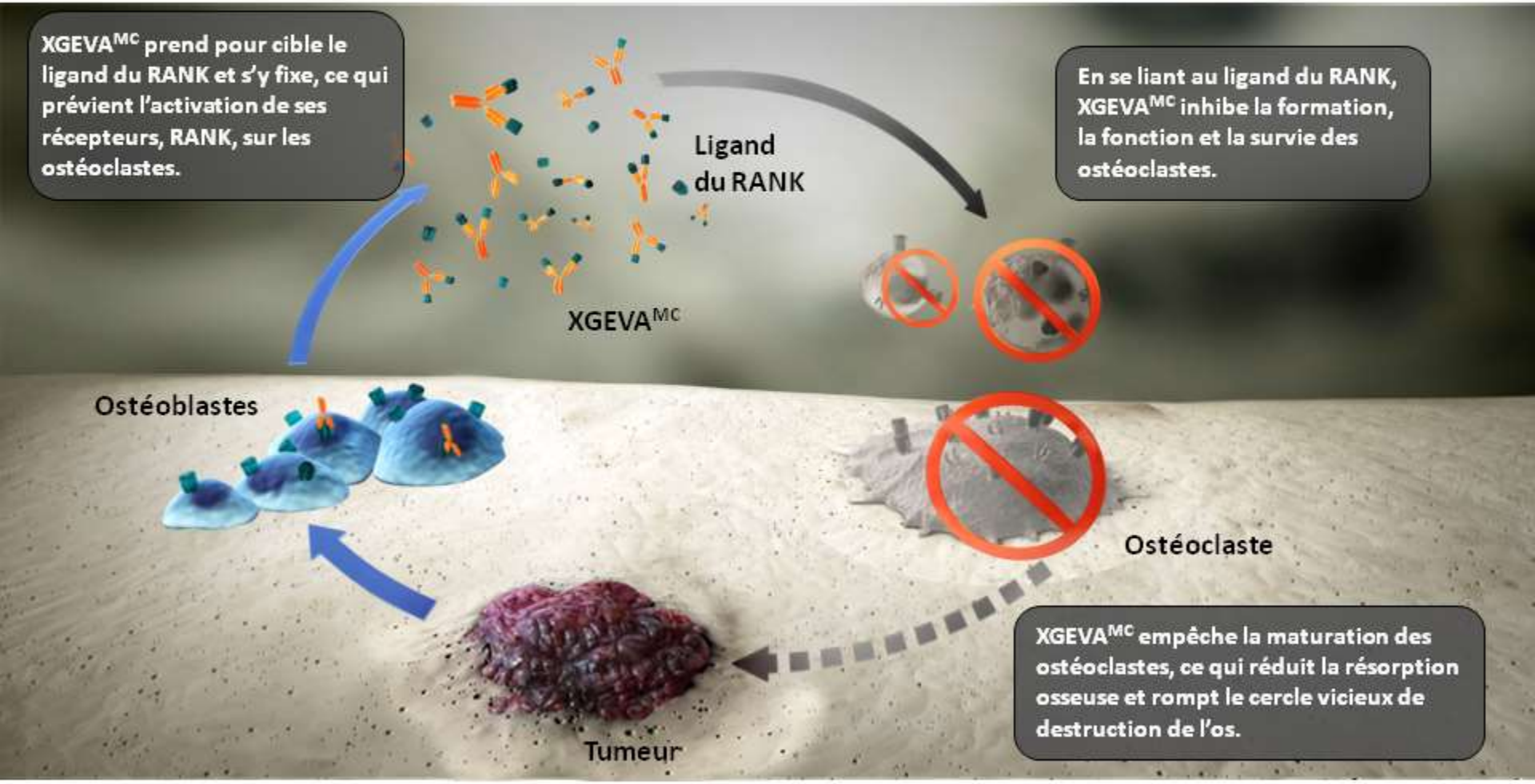


Dan Lewinshtein 2014

Pathologic Fracture & Spinal Compression

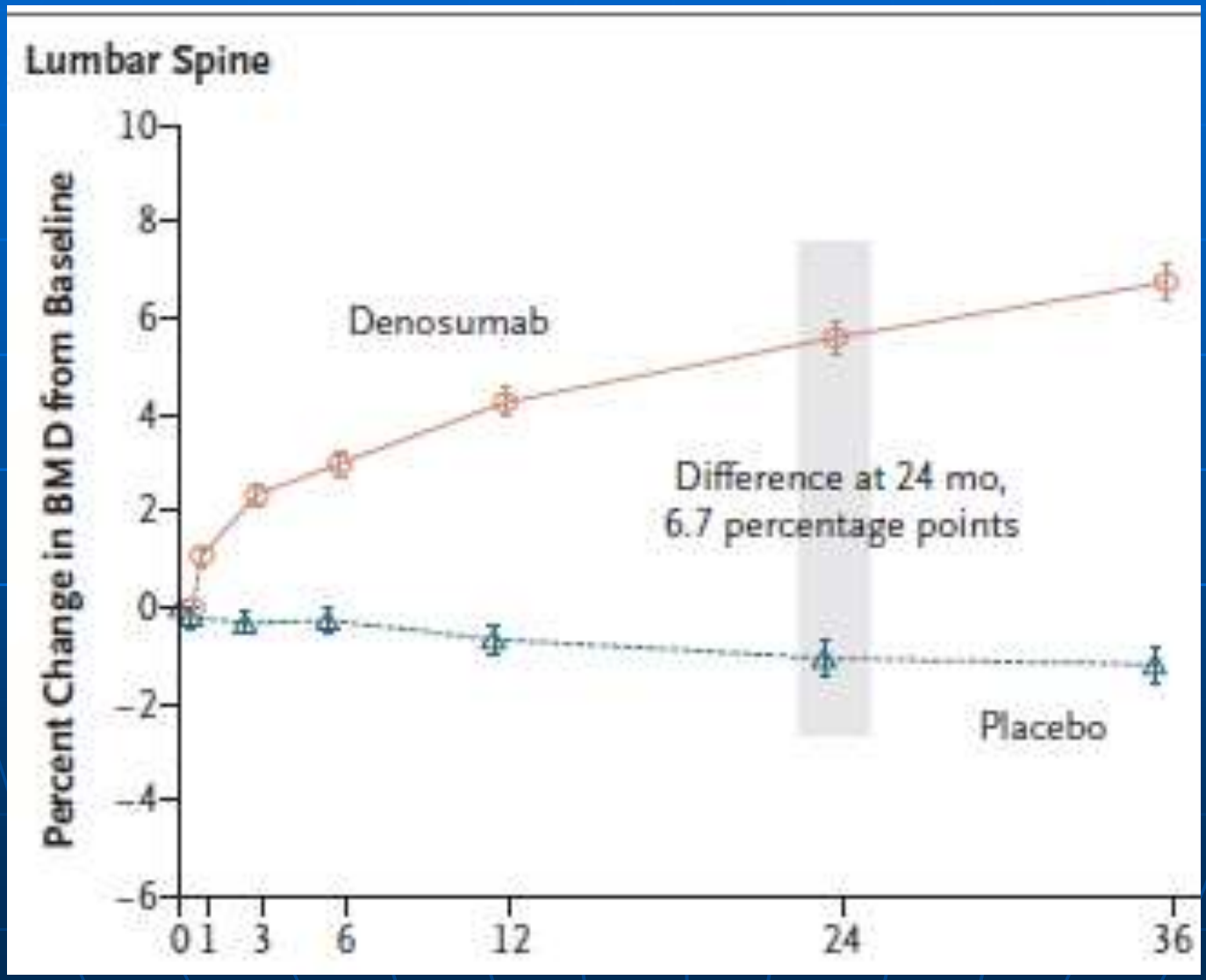


XGEVA[MC] : Prend pour cible et inhibe le ligand du RANK pour briser le cercle vicieux de destruction de l'os et prévenir les complications osseuses.



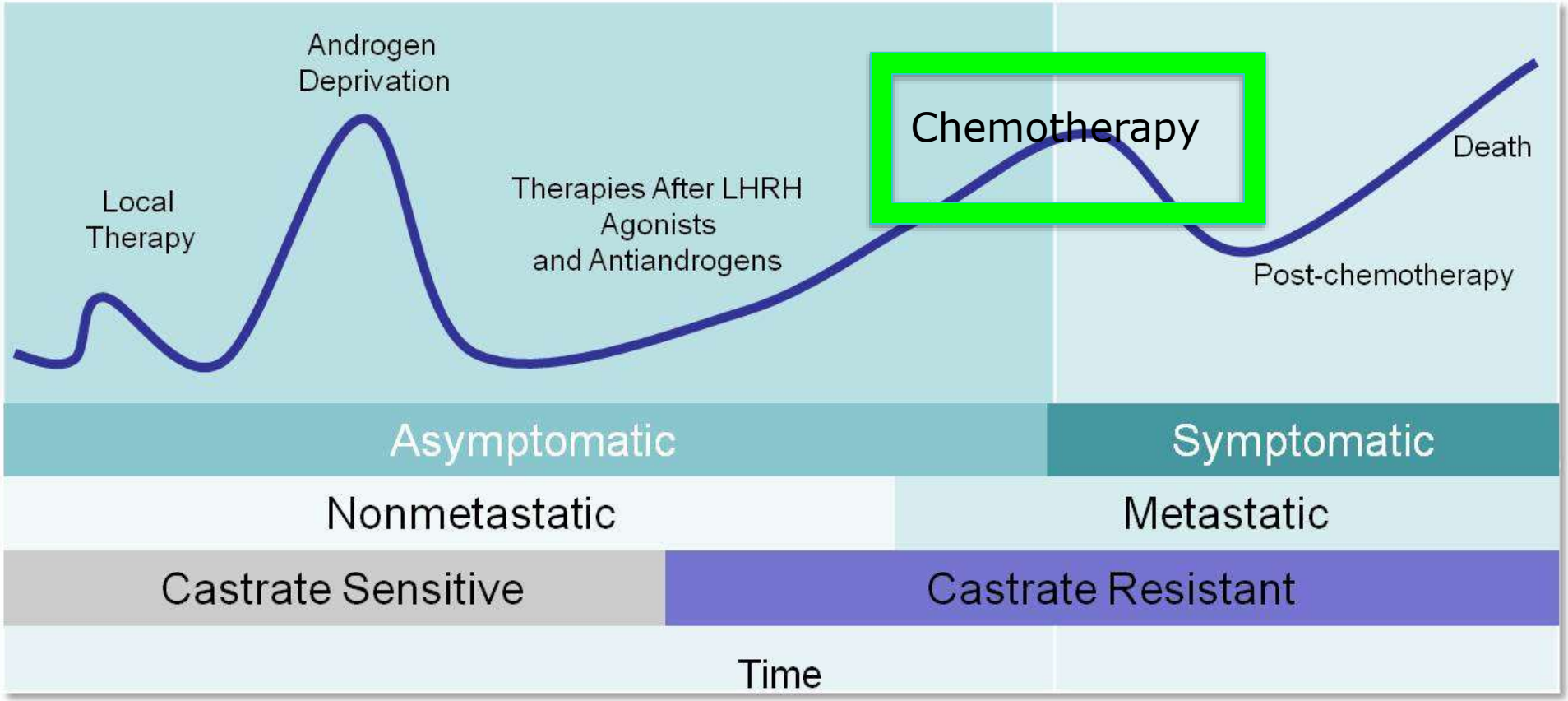
1. Adapté d'après : Roodman, GD. *N Engl J Med*. 2004;350:1655-1664.
2. Monographie de XGEVA[MC] (denosumab) Amgen Canada Inc. Mai 2011

Denosumab: Bone Protection

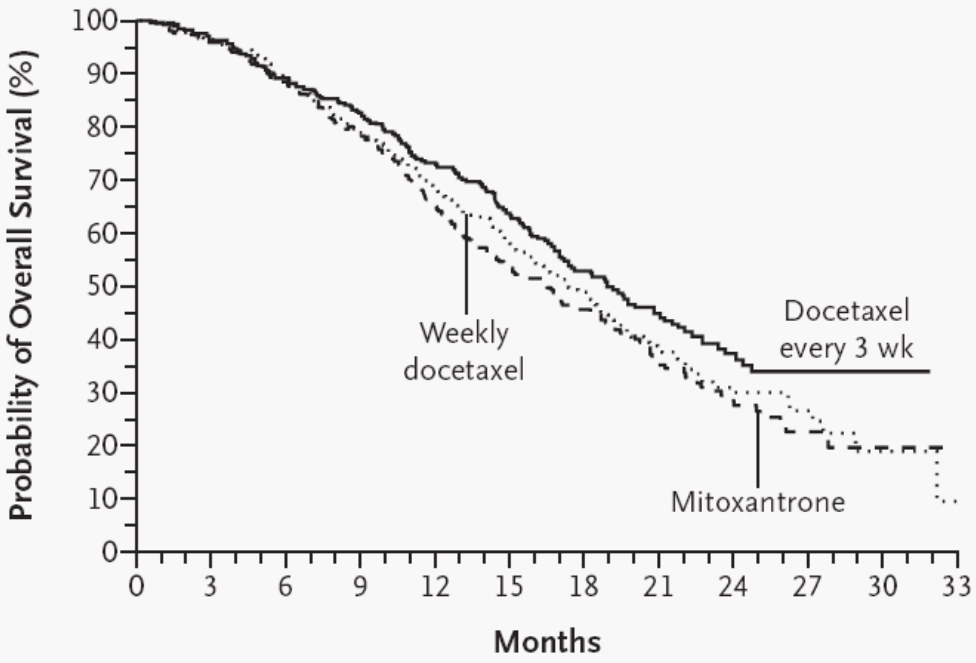


Dan Lewinshtein 2014

Hormone Refractory Disease (CRPC)



Chemotherapy: Docetaxel



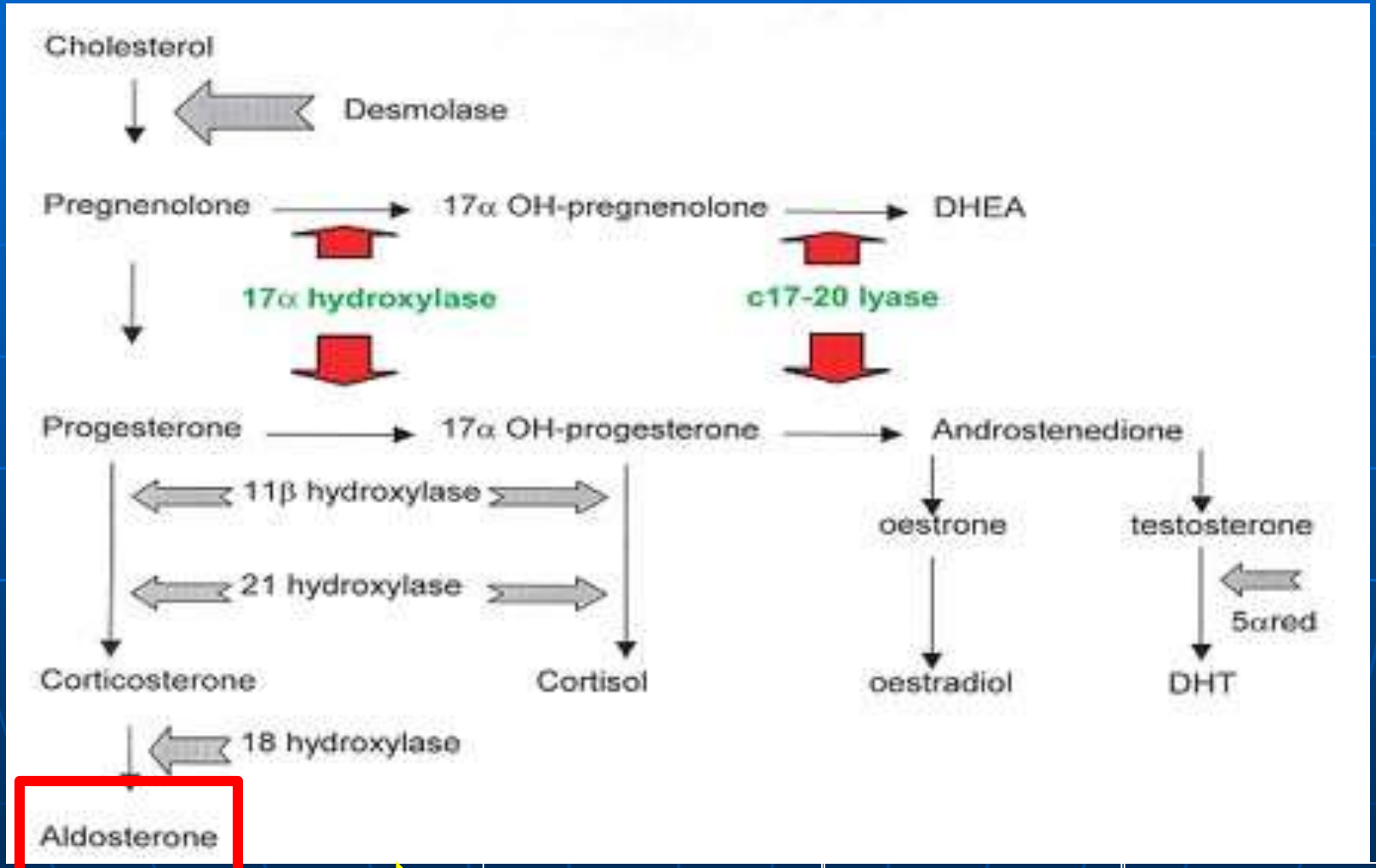
No. at Risk						
Docetaxel every 3 wk	335	296	217	104	37	5
Weekly docetaxel	334	297	200	105	29	4
Mitoxantrone	337	297	192	95	29	3

Figure 1. Kaplan–Meier Estimates of the Probability of Overall Survival in the Three Groups.

Abiraterone: 10X ketoconazole

Dan Lewinshtein 2014

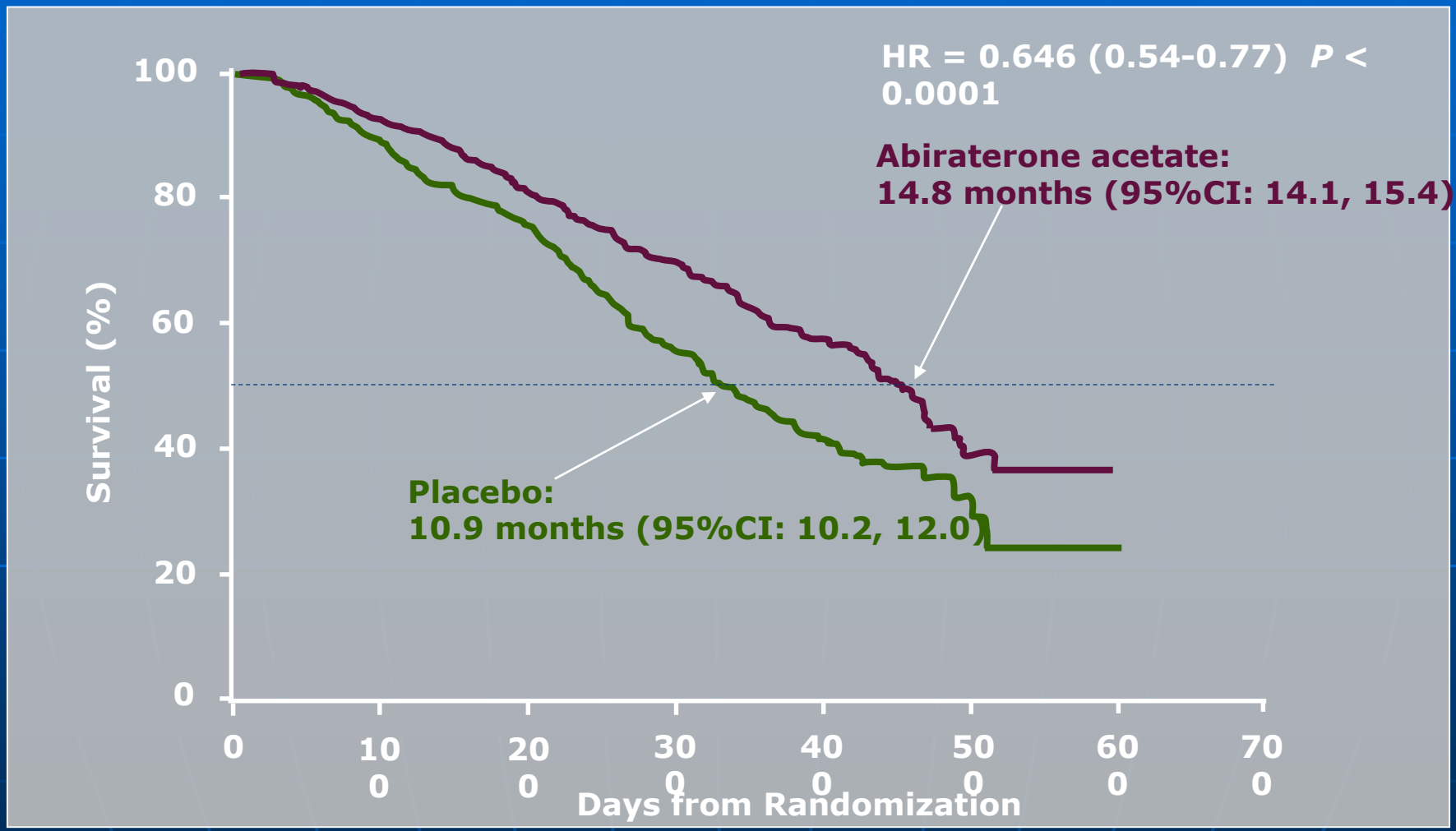
Abiraterone: mechanism



Hypokalemia | **Hypertension** | **Fluid overload**

Dan Lewinshtein 2014

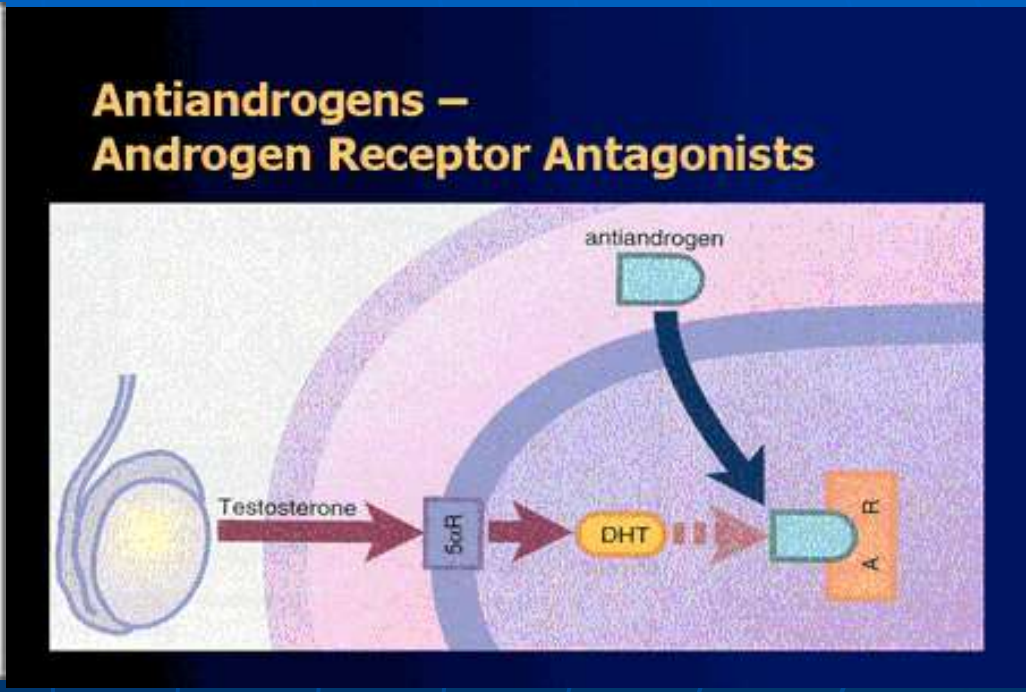
Abiraterone in CRPC post-docetaxel



De Bono et al , ESMO 2010

Dan Lewinshtein 2014

Enzalutamide



Dan Lewinshtein 2012

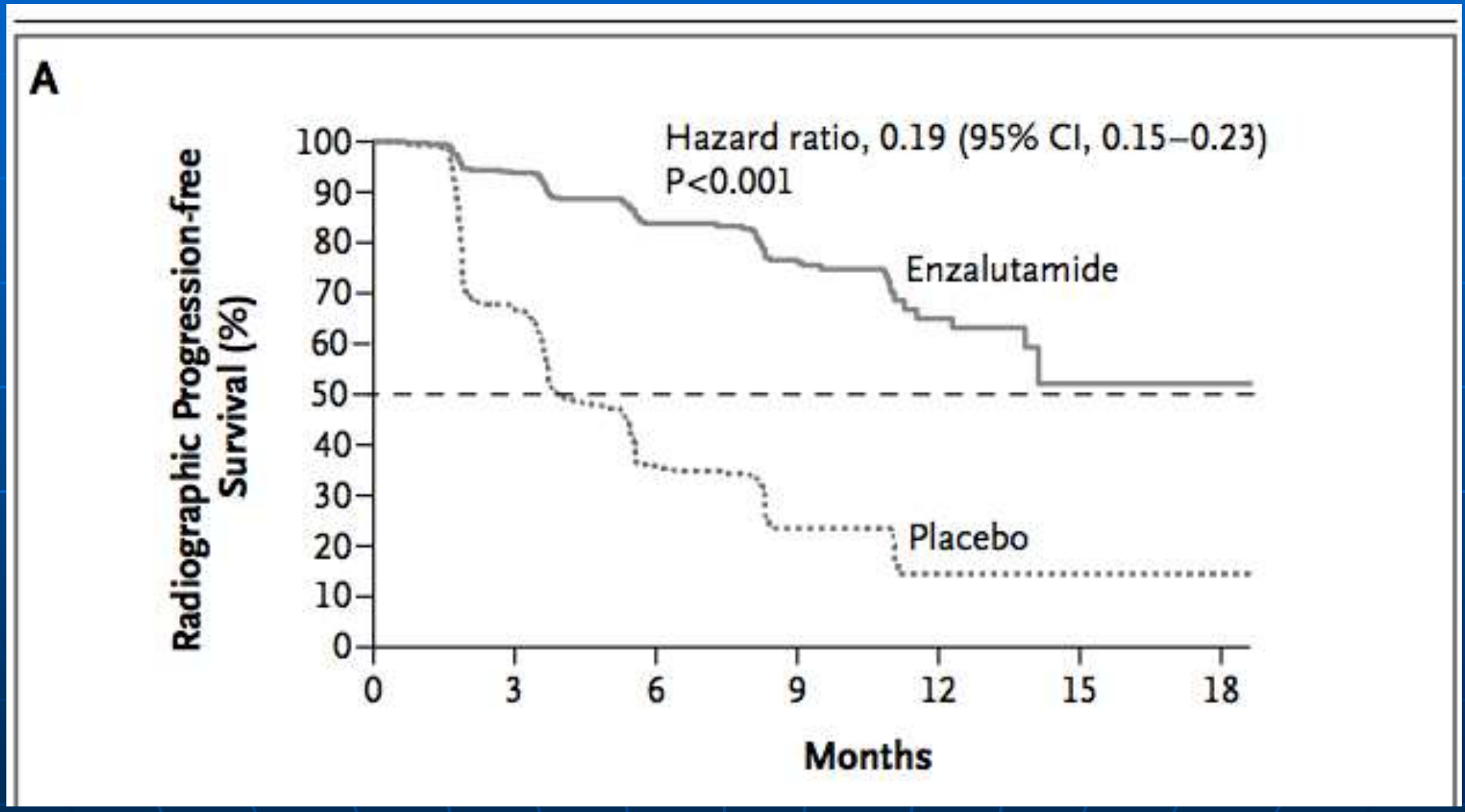
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Enzalutamide in Metastatic Prostate Cancer before Chemotherapy

T.M. Beer, A.J. Armstrong, D.E. Rathkopf, Y. Loriot, C.N. Sternberg, C.S. Higano, P. Iversen, S. Bhattacharya, J. Carles, S. Chowdhury, I.D. Davis, J.S. de Bono, C.P. Evans, K. Fizazi, A.M. Joshua, C.-S. Kim, G. Kimura, P. Mainwaring, H. Mansbach, K. Miller, S.B. Noonberg, F. Perabo, D. Phung, F. Saad, H.I. Scher, M.-E. Taplin, P.M. Venner, and B. Tombal, for the PREVAIL Investigators*

Enzalutamide: Progression Free Survival



- THANK YOU!