

A scenic view of a lake with a large building and mountains in the background under a dramatic sky. The foreground shows a railing with flower boxes. The middle ground features a large, multi-story building with a central tower, surrounded by trees. The background consists of rugged mountains under a sky with heavy, dark clouds and patches of light. The water in the lake is calm, reflecting the sky and the building.

# Updates in Surgical Approaches to PCA

John W. Davis

# So many options and consequences

- Active Surveillance
- Radical Prostatectomy
- Radiation—external, brachy
- Alternatives
  - Alternate XRT—gamma knife, SBRT
  - Focal therapy—several energy sources
  - Cryotherapy
  - HIFU
  - Other ablations
- Oncologic control
  - Relapse—salvage options
- QOL
  - Sexual
  - Bladder
    - Irritation/obstruction
    - Continence
  - Bowel
  - Hormonal
- Cost
- Expertise—volume—learning
- Logistics
- Comparative data



# Areas of Discussion

- Emphasis on strategies for intermediate to high risk disease
- Decision on lymph nodes
- Decision on nerve sparing
- Technical choices—
  - Open
  - Robotic
  - Novel robotic—single port
    - Future of “small space” RP—perineal, transvesical
- Optimizing outcomes, minimizing f/u therapies



# Favorable vs. Unfavorable Intermediate Risk

## FAVORABLE

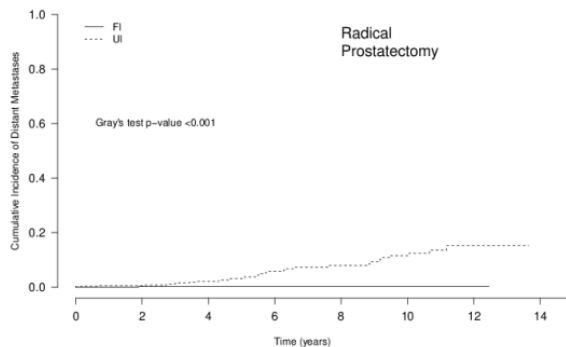
- Bx Primary Gleason pattern 3
- Proportion of positive bx cores <50%
- Single NCCN intermediate risk factor

## UNFAVORABLE

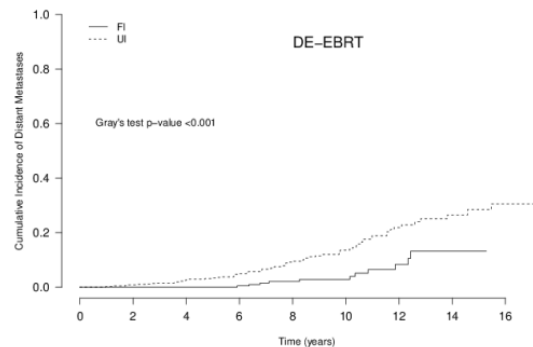
- Bx primary Gleason pattern 4
- Proportion of positive bx cores  $\geq 50\%$
- >1 NCCN intermediate risk factor (i.e. PSA 10-20 or cT2b-c)

# Favorable vs. Unfavorable Intermediate Risk

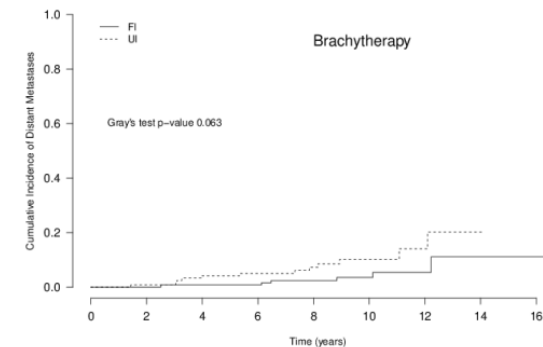
## Cumulative Incidence Distant Metastasis



No. at Risk								
FI	522	433	342	151	79	47	3	0
UI	605	499	385	207	133	94	15	0



No. at Risk								
FI	399	343	271	194	119	72	28	6
UI	744	638	505	362	217	120	53	23



No. at Risk								
FI	132	129	120	115	90	50	16	4
UI	126	123	109	100	69	35	12	1

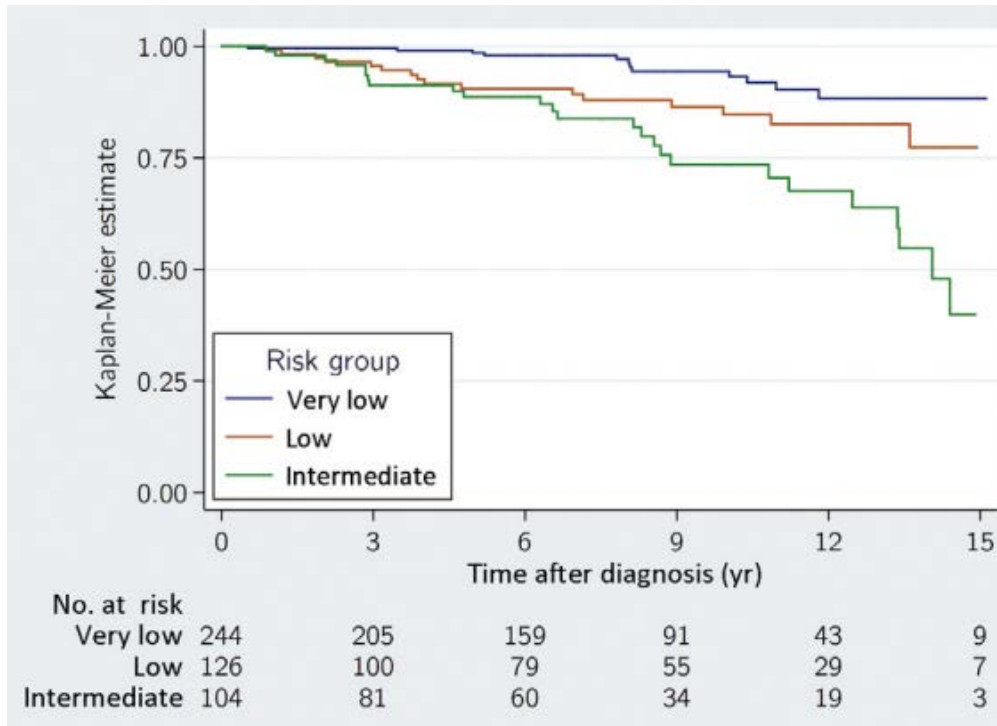
# AS in Intermediate Risk

## Active Surveillance for Intermediate Risk Prostate Cancer: Survival Outcomes in the Sunnybrook Experience

Hima Bindu Musunuru, Toshihiro Yamamoto, Laurence Klotz, Gabriella Ghanem,  
Alexandre Mamedov, Peraka Sethukavalan, Vibhuti Jethava, Suneil Jain,  
Liyang Zhang, Danny Vesprini and Andrew Loblaw\*

- 213 Intermediate risk patients
- Median Age 72
- Median FU 6.7 years
- GI 7 = 60% of cohort
- 15 yr MFS estimate for 3+4, PSA <20 =84%
- 15 yr MFS estimate for 4+3 PSA <20 =63%

# Goteborg AS – Treatment Free Survival

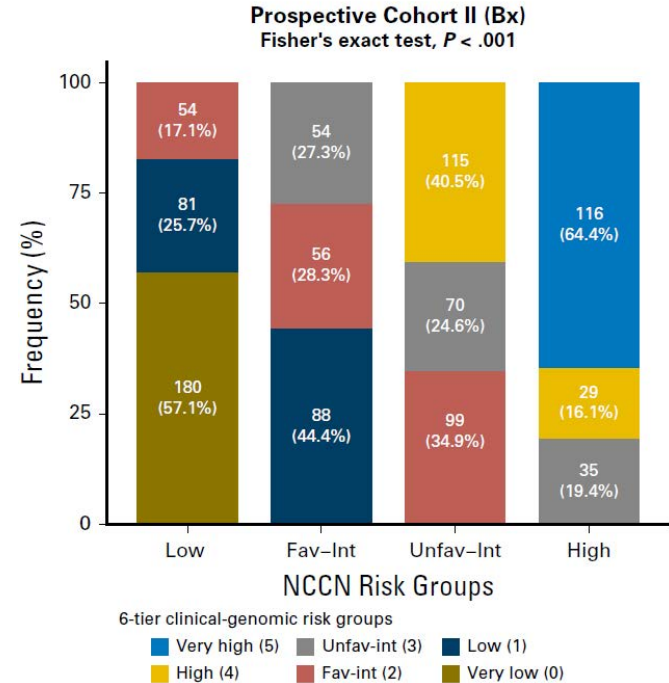


Failure Free Survival	10 years	15 years
Low Risk	85%	77%
Int Risk	73%	40%

Cancer Specific Survival	10 years	15 years
Low Risk	100%	94%
Int Risk	98%	90%

# AS in Intermediate Risk

- 977 pre-treatment biopsy samples
- NCCN alone vs. NCCN + decipher
- C index of 0.84 for 10 year DM in the validation cohort





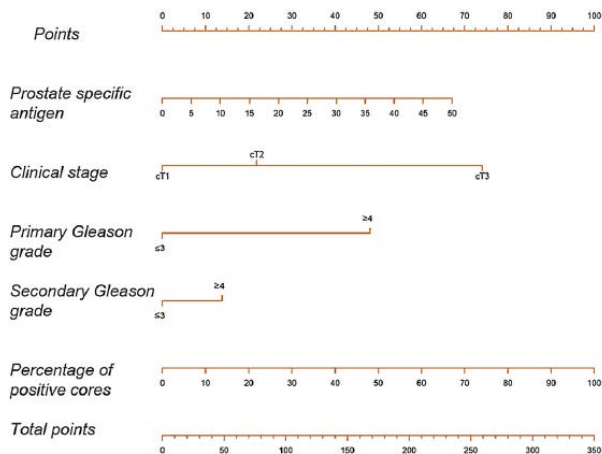
# PLND or Not?

RP<sup>s</sup> ± PLND if predicted  
probability of lymph  
node metastasis ≥2%

<b>Radical prostatectomy (RP)</b>	Offer RP to patients with intermediate-risk disease and a life expectancy > 10 years.	Strong
	Offer nerve-sparing surgery to patients with a low risk of extracapsular disease (refer to nomograms).	strong
<b>Extended pelvic lymph node dissection (ePLND)</b>	Perform an ePLND in intermediate-risk disease if the estimated risk for positive lymph nodes exceeds 5%.	Strong

# Updated Nomogram Predicting Lymph Node Invasion in Patients with Prostate Cancer Undergoing Extended Pelvic Lymph Node Dissection: The Essential Importance of Percentage of Positive Cores

Alberto Briganti<sup>a,\*</sup>, Alessandro Larcher<sup>a</sup>, Firas Abdollah<sup>a</sup>, Umberto Capitanio<sup>a</sup>,  
Andrea Gallina<sup>a</sup>, Nazareno Suardi<sup>a</sup>, Marco Bianchi<sup>a</sup>, Maxine Sun<sup>c</sup>, Massimo Freschi<sup>b</sup>,  
Andrea Salonia<sup>a</sup>, Pierre I. Karakiewicz<sup>c</sup>, Patrizio Rigatti<sup>a</sup>, Francesco Montorsi<sup>a</sup>

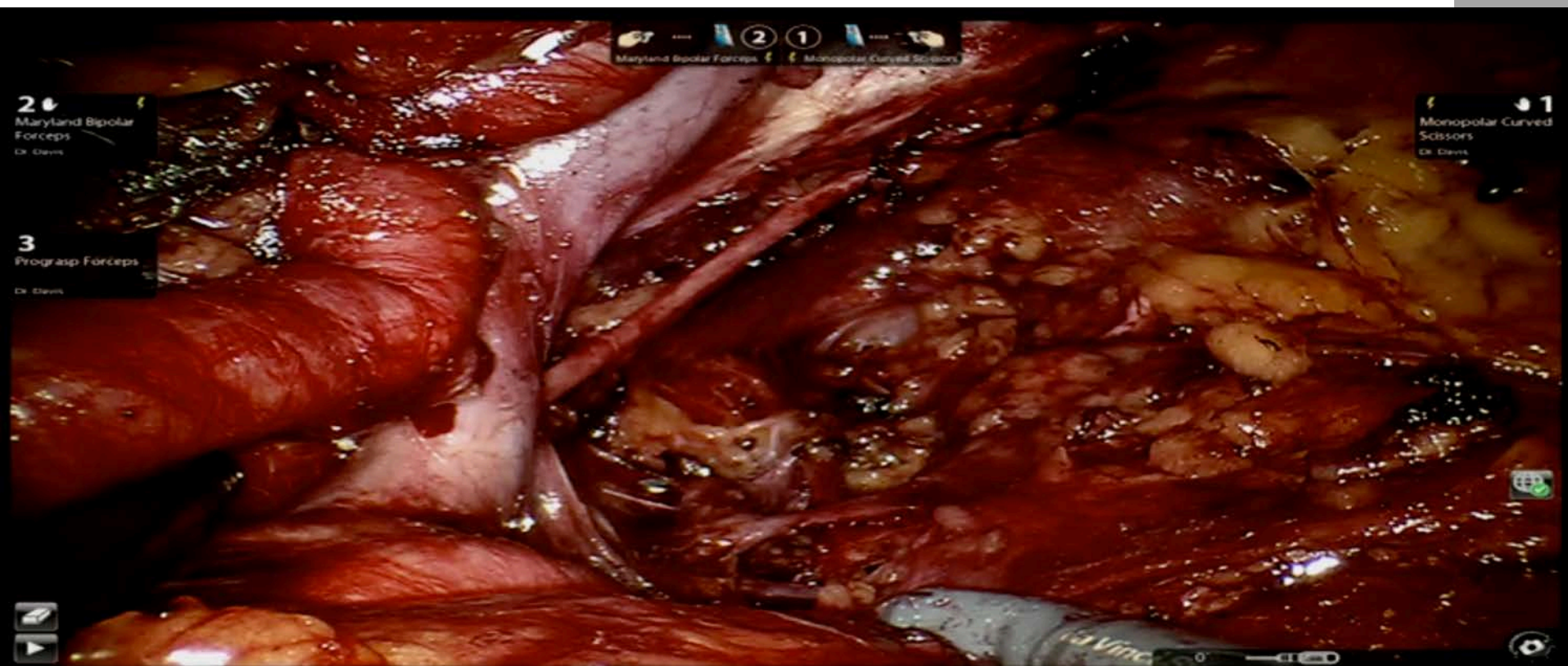


- 5% Cutoff
  - 65.5% of patients spared PLND
  - 1.5 % of patients with LNI missed
  - 98.4% NPV

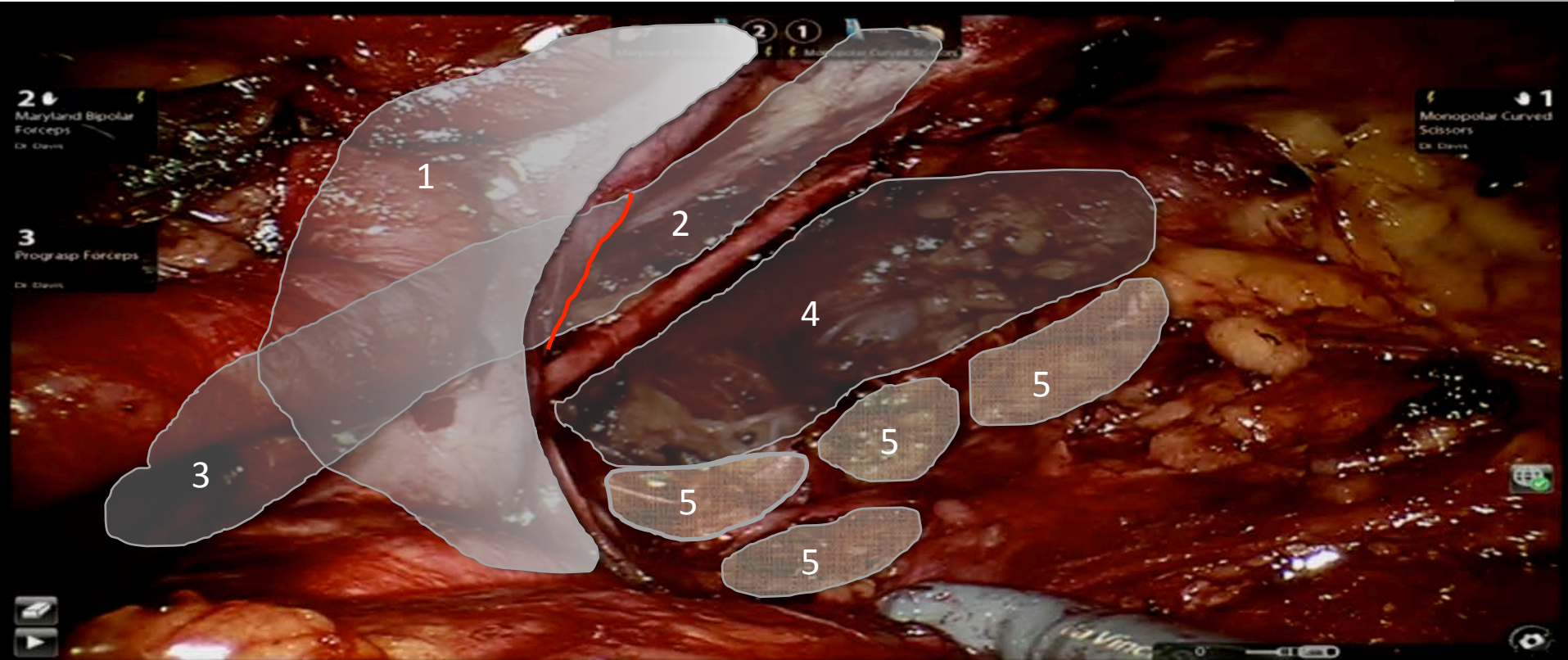
# “Davis Team” Publications

---

- Extended PLND:
  - Doubles LN count
  - Yields—0% low risk, 10-12% intermediate, 35% HR
  - Without trial—no clear therapeutic
  - In review—low-favorable risk disease omitting PLND—no difference in BCR rates
  - Complications trend higher but NS
  - Standard PLND—fairlyl useless—makes it harder to go back
  - Current triage “all or none” approach and tell the “none” patients a small chance of having to go back









# Biochemical Recurrence Free Survival

	Gleason 3+4=7	Gleason 4+3=7
2 years	90.6%	79.9%
5 years	80.7%	63.7%



Urological Oncology | [Free Access](#)

## Prognostic Gleason grade grouping: data based on the modified Gleason scoring system

Phillip M. Pierorazio, Patrick C. Walsh, Alan W. Partin, Jonathan I. Epstein

Platinum Priority – Prostate Cancer

Editorial by Markus Graefen, Thorsten Schlomm, Guido Sauter and Hartwig Huland on pp. 436–437 of this issue

## A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score

Jonathan I. Epstein <sup>a,✉</sup>, Michael J. Zelefsky <sup>b</sup>, Daniel D. Sjoberg <sup>b</sup>, Joel B. Nelson <sup>c</sup>, Lars Egevad <sup>d</sup>, Cristina Magi-Galluzzi <sup>e</sup>, Andrew J. Vickers <sup>b</sup>, Anil V. Parwani <sup>e</sup>, Victor E. Reuter <sup>b</sup>, Samson W. Fine <sup>b</sup>, James A. Eastham <sup>b</sup>, Peter Wiklund <sup>d</sup>, Misop Han <sup>a</sup>, Chandana A. Reddy <sup>a</sup>, Jay P. Ciezki <sup>e</sup>, Tommy Nyberg <sup>d</sup>, Eric A. Klein <sup>a</sup>

— <sup>a</sup> —

# Cancer Specific Survival

	Gleason 3+4=7	Gleason 4+3=7
5 year CSS	98.9%	88.6%
10 year CSS	92.1%	76.5%

## Prostate Cancer Specific Mortality and Gleason 7 Disease Differences in Prostate Cancer Outcomes Between Cases With Gleason 4 + 3 and Gleason 3 + 4 Tumors in a Population Based Cohort

Jonathan L. Wright,\* Claudia A. Salinas, Daniel W. Lin, Suzanne Kolb,  
Joseph Koopmeiners, Ziding Feng and Janet L. Stanford

*From the Departments of Urology (JLW, DWL) and Epidemiology (JLS), University of Washington School of Public Health and Division of Public Health Sciences, Fred Hutchinson Cancer Research Center (JLW, CAS, DWL, SK, JK, ZF, JLS), Seattle, Washington*



PI: John W Davis  
Co-Investigators:  
Christopher  
Logothetis  
Brian Chapin  
Patricia Troncoso  
Eleni Efstathio

# A Single Arm Study of 6 Months Neoadjuvant ARN-509 Prior to Radical Prostatectomy in Intermediate Risk Patients to Reduce the Frequency of Pathologic Risk Features That Drive a Post-operative Radiation Therapy Recommendation



# PCa Disease Mortality

- In the PSA era—incidence greater than mortality<sup>1</sup>
- Mortality predicted by high-grade disease, and absence of short to intermediate term threats to survivorship<sup>2</sup>
- Intermediate Risk is more commonly diagnosed by screening than high risk<sup>3</sup>
  - Recent MDACC cohort = 70% of RARP's

1. Siegel R, et al. Cancer Statistics, 2012. CA Cancer J Clin 2012; 62: 10-29.
2. Albertsen PC et al. Competing risk analysis of men aged 55 to 74 years at diagnosis managed conservatively for clinically localized prostate cancer. JAMA 1998 280: 975-80.
3. Falzarano SM, et al. Prostate cancer staging and grading at radical prostatectomy over time. Adv Anat Pathol 2011 18: 159-64.

# BCR after RARP—Which Risk Group?

## Hypothetical 1000 Cases

	Low	Intermediate	High
RARP Fraction	15%	70%	15%
Typical BCR	3%	15%	30-50%
#BCR/1000	5	<b>105</b>	45-75



# Biologic High Risk Pathology After RP for Intermediate Risk

519 Intermediate Risk RARP with Extended PLND from  
1/1/9 to 11/30/12

Pathologic Finding	Number	Percent
N1	54	10%
pT3 N0	132	25%
Gleason 8-10	24	5%
Tertiary 5 pattern	50	10%
Lymphovascular Invasion		Estimated 10%
Higher Risk Features Absent	270	52%
<b>Higher Risk Features Present</b>	<b>249</b>	<b>48%</b>

# Primary Objective

- To determine whether 6 months of neoadjuvant ARN-509 prior to prostatectomy for intermediate risk prostate cancer results in a reduction of aggregate pathologic risk features that drive post-operative radiotherapy recommendations from 35% to 15%.

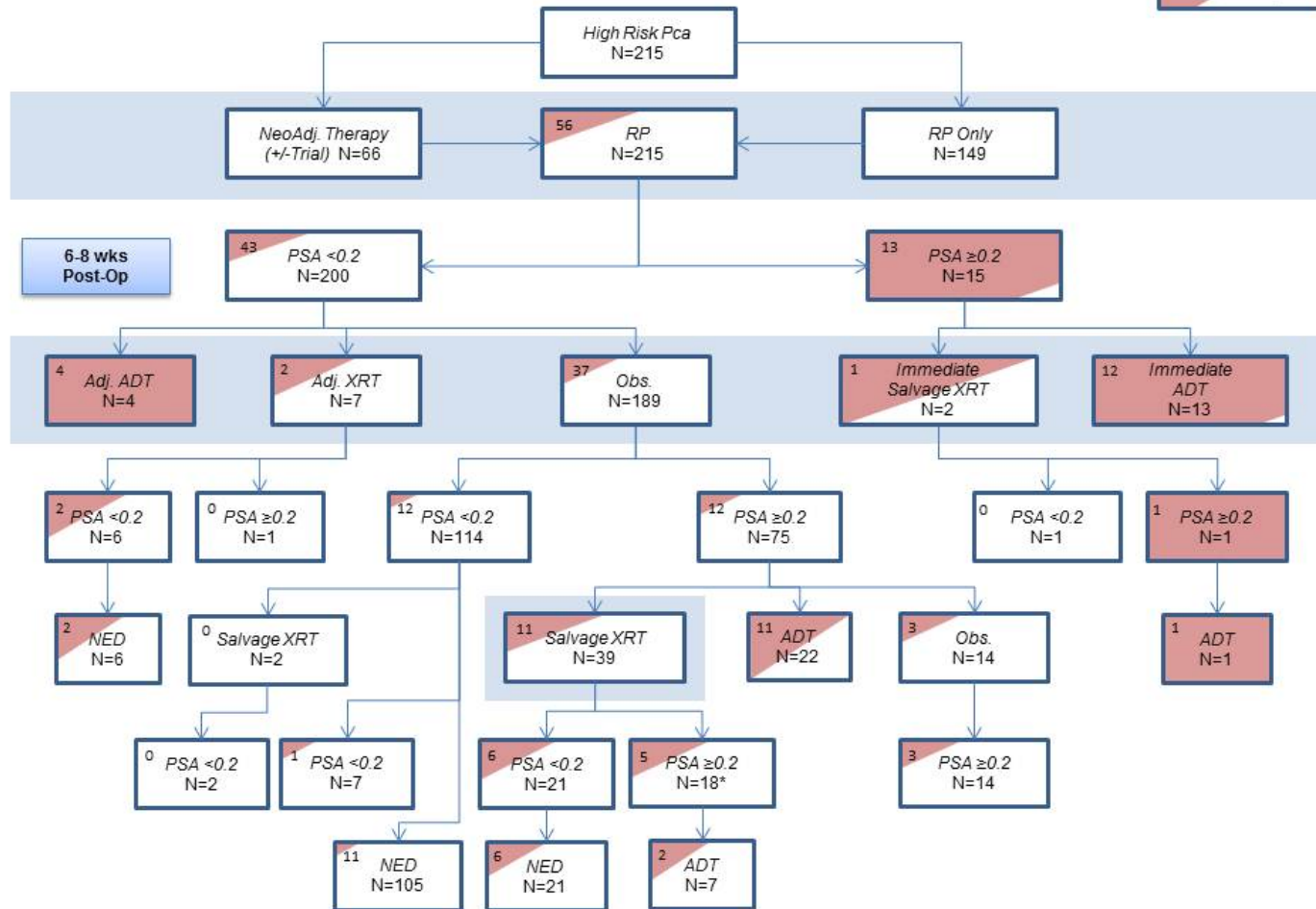
# HR: So many options and consequences

---

- ~~Active Surveillance~~
- Radical Prostatectomy
- Radiation—external, brachy
  - w/more ADT
- Alternatives
  - Alternate XRT—gamma knife, SBRT
  - ~~Focal therapy—several energy sources~~
  - Cryotherapy
  - HIFU
  - Other ablations
- Oncologic control
  - Relapse—salvage options
- QOL
  - Sexual
  - Bladder
    - Irritation/obstruction
    - Continence
  - Bowel
  - Hormonal
- Cost
- Expertise—volume—learning
- Logistics
- Comparative data

# Potential Disease Pathway

pN1  
pN0



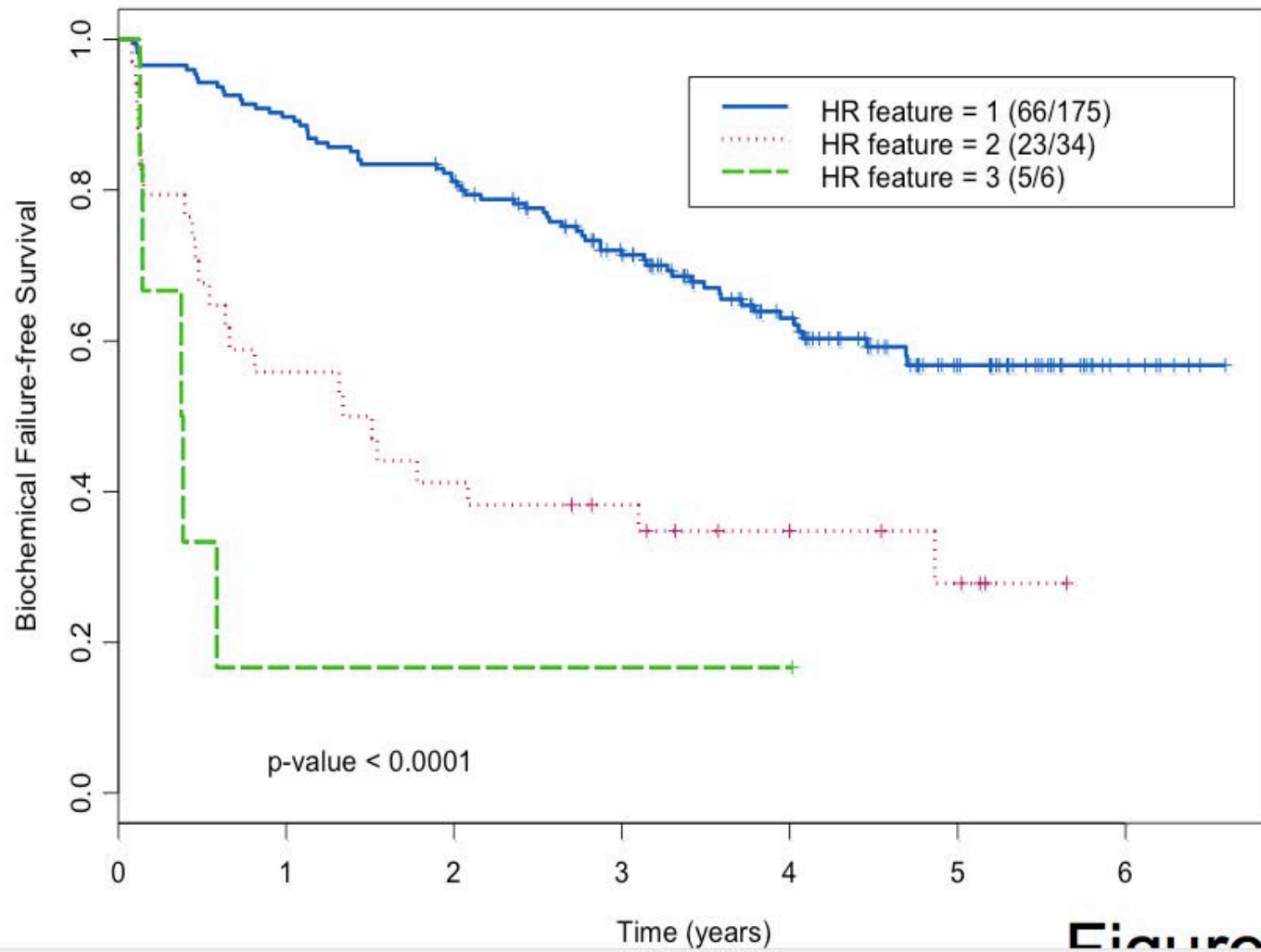
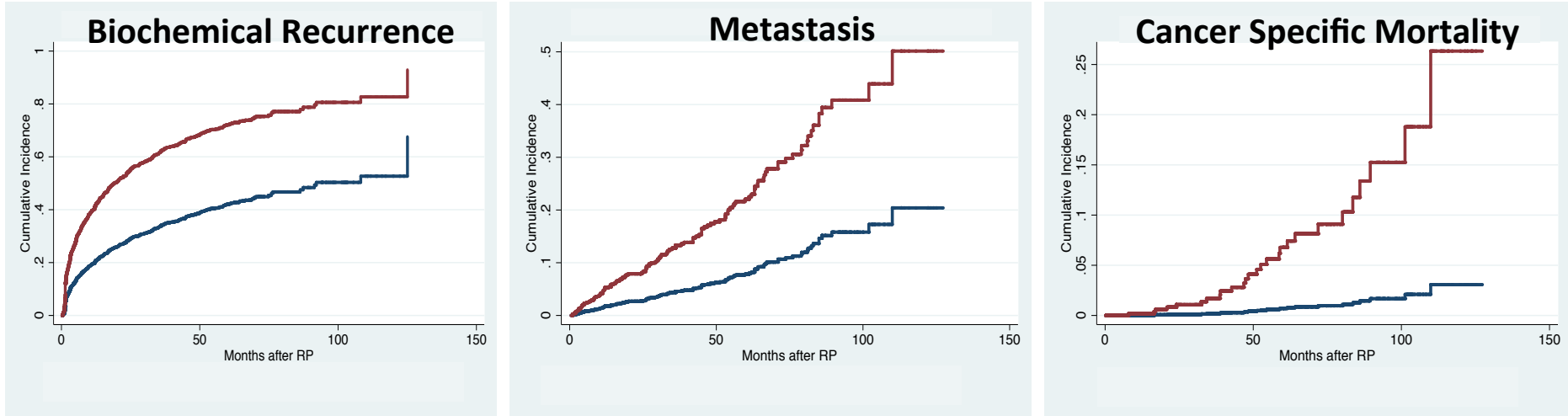


Figure 6



# High/Very High Risk Stratification



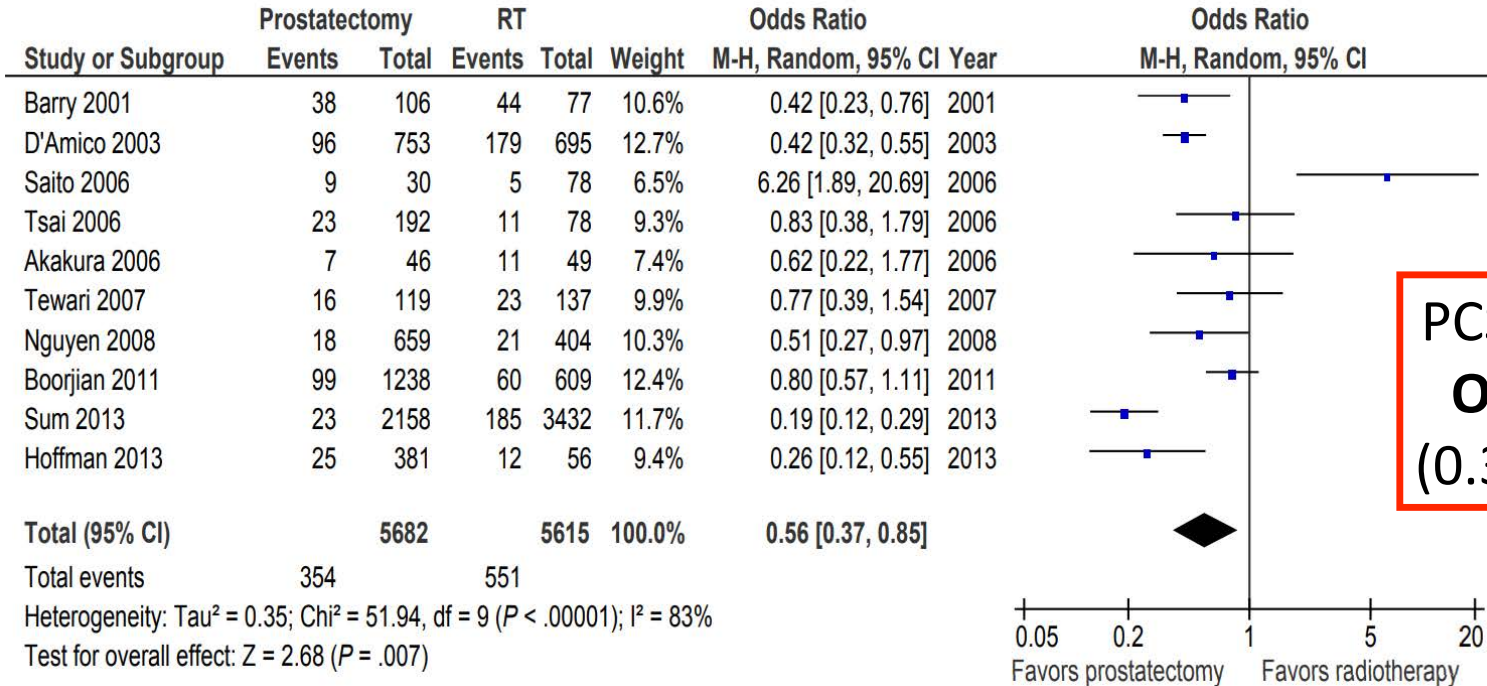
N=1776  
2004-20015 at 3 centers  
Median F/U 41 months

— High-risk (non VHR) — VHR

# Surgery as the First Step in the Treatment of High Risk Prostate Cancer

- Surgery → post-op radiation has less toxicity than radiation → salvage prostatectomy
- Lymph nodes are positive in up to 40% of Very High Risk Pca
- Pathologic evaluation provides the data for deciding on which secondary therapies

# High Risk Prostate Cancer: Surgery or Radiation



# Do we really have a “best” treatment?

- High risk/locally advanced prostate cancer has lethal potential
- Surgery as the initial step in multimodality therapy provides informed application of subsequent therapies
- Multimodality therapy is necessary in a large proportion of patients with High Risk prostate cancer



