

To Treat or not to Treat:  
Discerning the Duds from the Time Bombs

*Active Surveillance for Prostate Cancer*

*MA Prostate Cancer Coalition Annual Conference  
May 16, 2009*

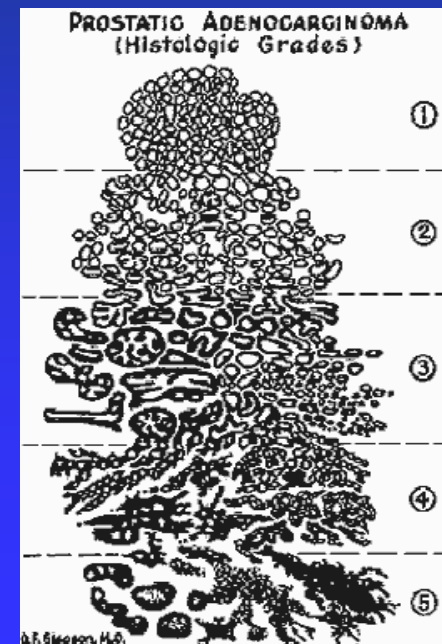
*Martin G. Sanda, M.D. and Neil Rofsky, M.D.  
Prostate Care Center at BIDMC*

# Measuring Prostate Cancer Severity: Stage, Gleason, PSA and “Risk Groups”

Early Stage Prostate Cancer (Stage T1-2) Severity Category	Gleason Score	Serum PSA
Low risk	$\leq 6$	$\leq 10$
Intermediate risk	$\leq 6$	10-20
	7	<20
High risk	$\leq 7$	>20
	8-10	Any PSA

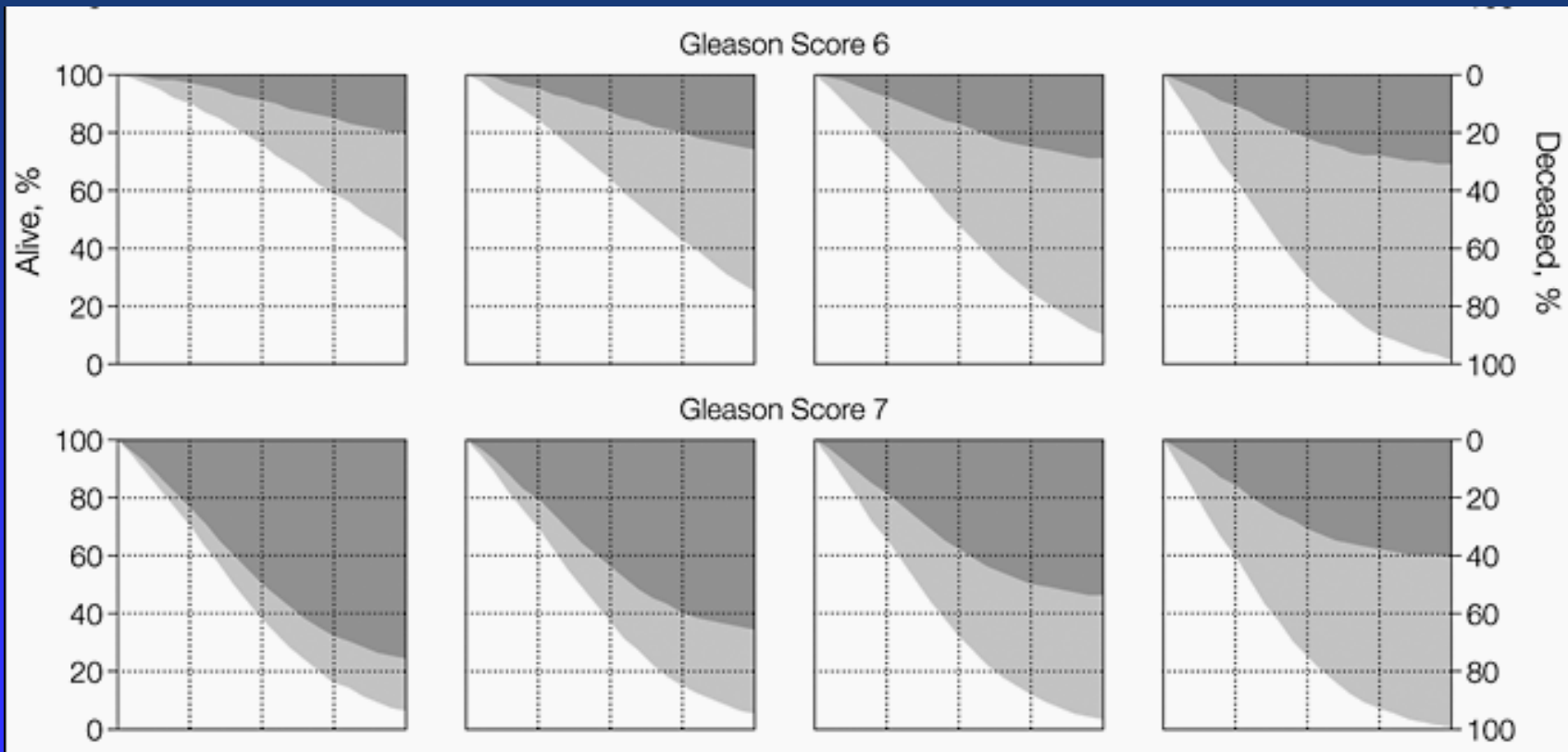
## Gleason Score

2 most common Gleason patterns (each graded 1-5) added together (eg 3+4=7 or 3+3=6)



# Impact of Cancer Grade on Natural History of T1-T2 Prostate Cancer: 20-year Mortality in Untreated PCa

Albertsen P et al, JAMA 2005



Age: 55-59

60-64

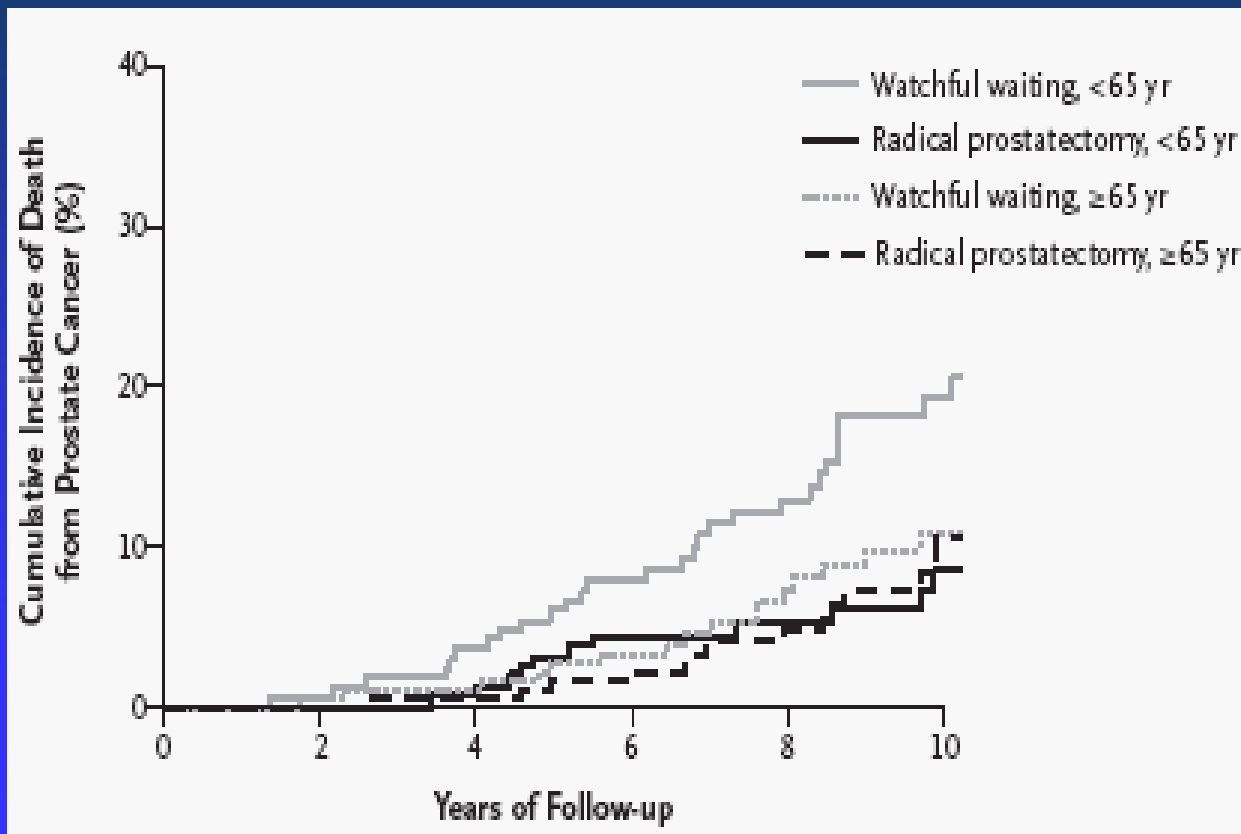
65-69

70-74

# Prostate Cancer Randomized Trials: Treatment

<u>Setting</u>	<u>Study</u>	<u>Survival Benefit ?</u>
High Risk: Lymph nodes involved	Messing et al NEJM 2002	Surgery + Hormones better than surgery alone
High grade early stage	Bolla et al NEJM 1995	XRT + hormones better than XRT alone
Moderate risk early stage	D'Amico et al JAMA 2004	XRT + hormones better than XRT alone
Low to Moderate risk early stage	Bill-Axelsson et al NEJM 2005	Surgery better than watchful waiting (in men < 65)

# Swedish Prostatectomy vs Watchful Waiting: Cancer-Specific Survival



1. Prostate ca death reduced by prostatectomy in younger men (< 65yo)

2. Prostatectomy not beneficial in older men due to death from other causes

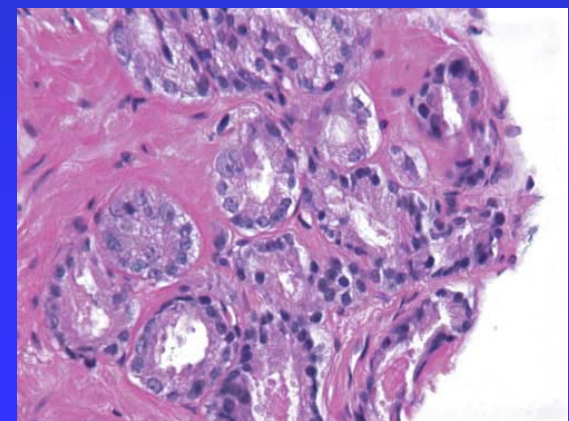
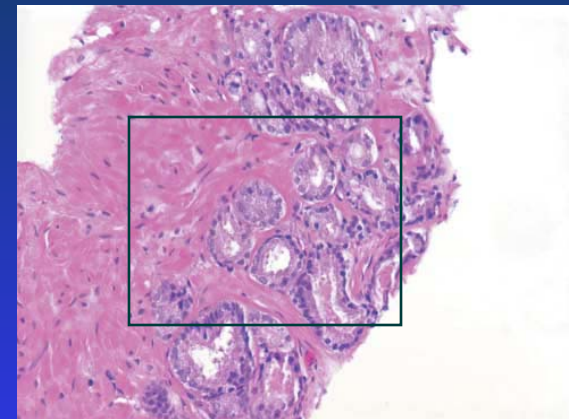
# Randomized Trials of Prostate Cancer Screening

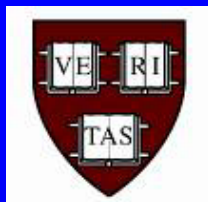
- Randomized trials (NEJM April 2009)
  - Trial: half get PSA/DRE (rectal exam), half don't – then follow for overall survival
  - 8 yr f/u
- Prostate, Lung, Colon and Ovarian Screening Trial 'PLCO'
  - No survival benefit BUT >52% screening contamination in controls
- European Randomized Screening trial in Prostate Cancer (ERSPC): **Significant survival benefit detected BUT:**
  - 1400 patients screened for each life saved
  - 40 treated for each life saved

# Biopsy Features Suggesting Minimal Risk Indolent/Dormant Prostate Cancer

Minimal risk cancers – those with minimal chance of extraprostatic extension - the 'Epstein Criteria'

- Gleason score  $\leq 6$
- No perineural invasion
- Not more than 3 cores involved (based on 6 total cores, 1994 standard care)
- Not more than 50% of any core is Ca
- PSA Density  $< 0.15$  (eg PSA  $< 10$  for 60 gm prostate)





## Discerning Risk of Clinically Significant Versus Indolent Prostate Cancer Prior to Biopsy: Predictive Model From a Multi-Center Cohort



Williams SB, Regan M, Wei JT, Kearney M, DeWolf WC,  
Tang J, Bueti G, Rubin MA, Genega E, Eyre A and Sanda MG

Beth Israel Deaconess Medical Center, DFCI,  
Cornell University, and University of Michigan

### Study Design

- ◆ 635 men undergoing biopsy at 5 Urology practices in Boston and Michigan
- ◆ Biopsy histopathology: Aggressive PCa (26%) vs non-ca or indolent CaP

FHx	BMI	PSA/Prostate Size (PSA Density)		
		0.07	0.10	0.16
No	25	4%	8%	15%
	30	6%	10%	19%
Yes	25	10%	18%	30%
	30	12%	22%	35%

### Conclusion:

Combination of Age, Fam Hx, DRE, PSA, Prostate Size (PSA Density) is superior to PSA alone to **identify men at high risk despite normal / low PSA, and those at low risk despite high PSA**

# Active Surveillance / Deferred Treatment in the Health Professionals Follow-Up Study (HPFS)

W Shappley, S Keinfeld, J Kaspercyk, M Stampfer, J Chan, & M Sanda

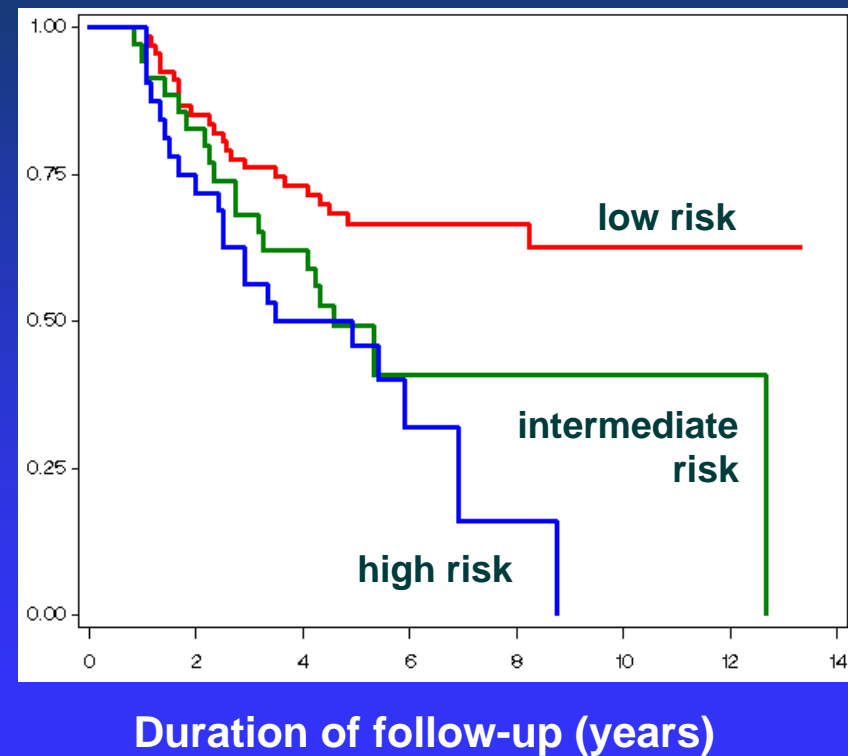
## Study Design

- Health study of 51,529 American men nationwide
- 3,331 developed prostate ca from 1986 to 2007; 8yrs median follow-up
- 'surveillance' = 342 who deferred treatment for > 1yr

## Results:

*Most Low Risk Patients Remain Treatment-Free at >10 Yrs Follow-Up*

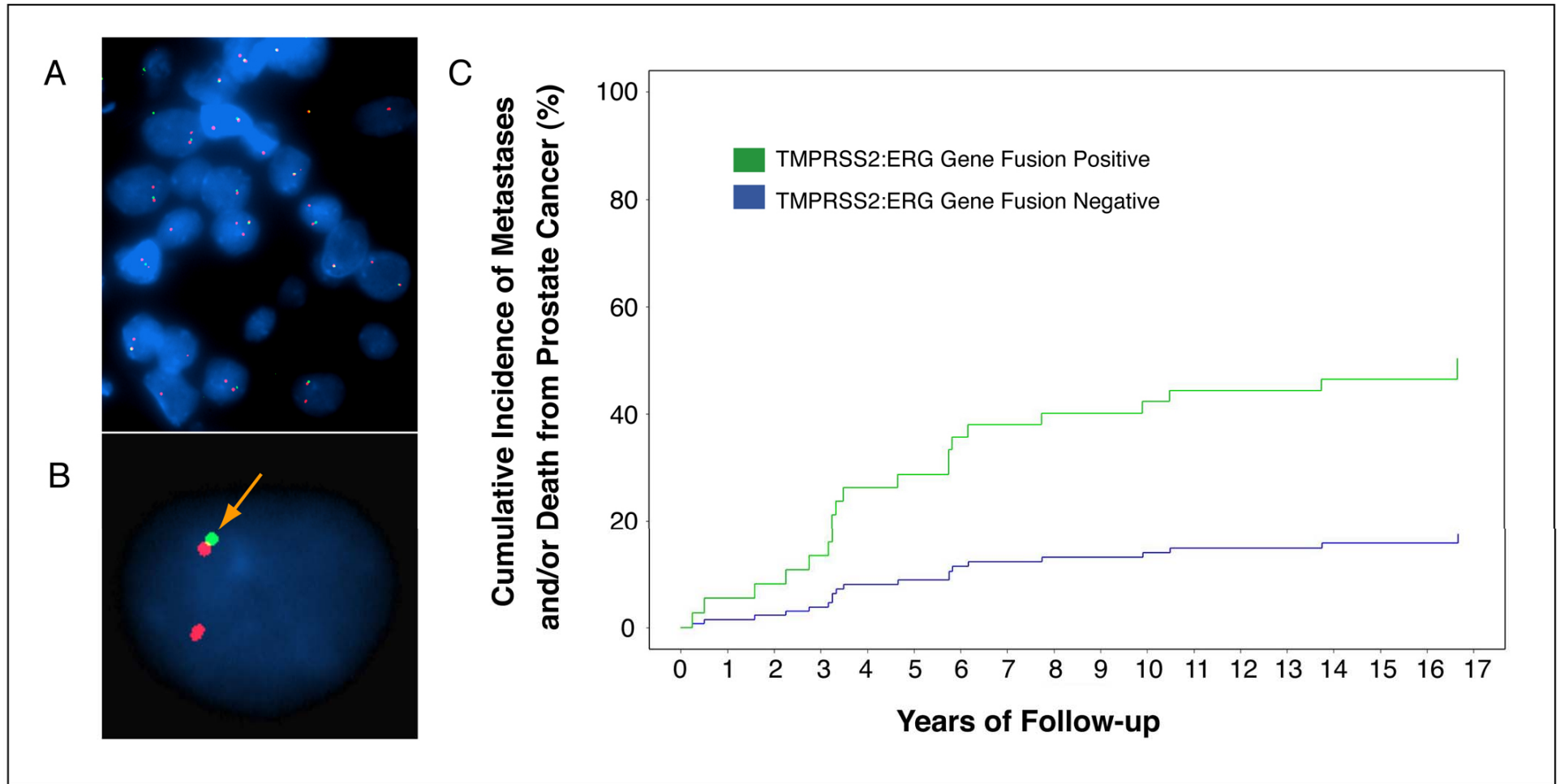
Proportion Treatment Free



## Similar Rates of Metastases or Cancer Death Among Low Risk PCa Patients who Deferred Treatment as Those Initially Treated In the HPFS Cohort

Event	Surveillance/ Deferred Treatment	Immediate Treatment
Metastasis	5.0% (7/139)	2.6% (33/1252)
Prostate Cancer Death	2.1% (3/139)	0.7% (9/1252)

# Presence of TMPRS2-ERG Gene Fusion Predicts Aggressive Cancer Growth/Metastases in Swedish Watchful Waiting Study



FUSION STATUS

Cumulative Incidence Ratio: 3.644 (p-value=0.004)

Rubin et al, Oncogene 2007

Swedish cohort

## Prostate Cancer Active Surveillance with Intent to Treat when Aggressive Features Become Evident

- PSA every 4 to 6 months
  - increase less than 2 ng/ml/year
- Repeat biopsy every 1 to 2 years
  - Gleason score 6 or less
  - Cancer involving less than 50% of biopsy cores
- Prostate MRI every 1 to 2 years (3T magnet)
  - Alternate with biopsy



## Case 1

- 49 yo African American Man
- No urinary symptoms; sexually active, single
- PSA 4.5, Normal prostate exam
- Biopsy – Gleason 6 in less than 20-30% of 2 cores (12 total biopsy cores)

# Case 1 - MRI

## Case 2

- 54 yo man with no family history of PCa; otherwise fit
- No urinary symptoms; no erectile dysfunction
- PSA 3.5, Normal prostate exam
- Biopsy – Gleason 6 in 10% of 1 cores (12 total biopsy cores)

## Case 2 - MRI

# Thank You

[www.bostonprostate.org](http://www.bostonprostate.org)

[www.bidmc.org/prostate](http://www.bidmc.org/prostate)