

Improving Outcomes in Clinically Localized Prostate Cancer



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Disclosures

- Paid Consultant
 - HIFU Prostate Services
 - Angiodynamics
 - Exact Sciences
 - Sonablate

What Are Patients Reading?

THE WALL STREET JOURNAL.

The New York Times

OPINION
GUEST ESSAY

Not Everything We Call Cancer Should Be Called Cancer

Aug. 30, 2023

HEALTH | WELLNESS | YOUR HEALTH

The Cancer That Doctors Don't Want to Call Cancer

Renaming the lowest-risk prostate cancer would cut down on overly aggressive treatment, some doctors say



By [Sumathi Reddy](#) [Follow](#)

Jan. 24, 2024 9:00 pm ET



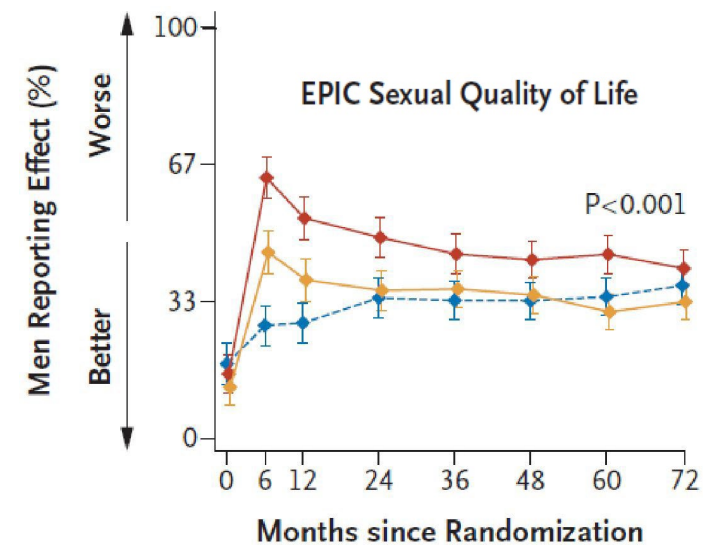
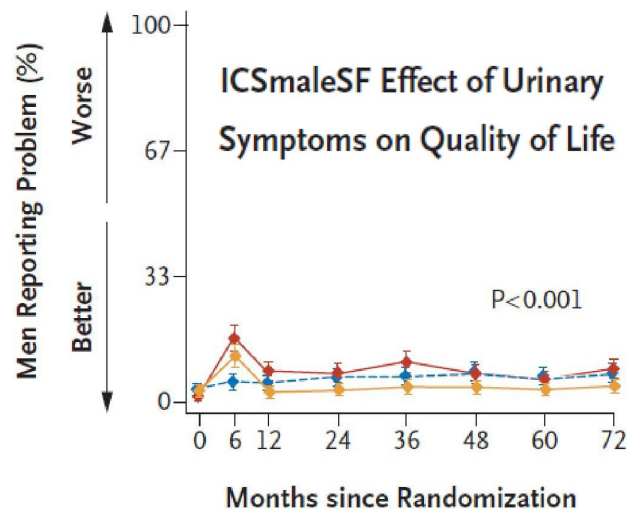
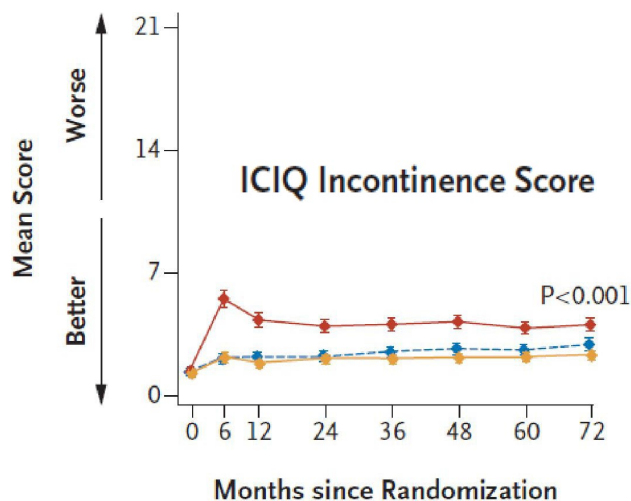


**HOW DOES TREATMENT
EFFECT PATIENTS?**

Patient-Reported Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer


J.L. Donovan, F.C. Hamdy, J.A. Lane, M. Mason, C. Metcalfe, E. Walsh, J.M. Blazeby, T.J. Peters, P. Holding, S. Bonnington, T. Lennon, L. Bradshaw, D. Cooper, P. Herbert, J. Howson, A. Jones, N. Lyons, E. Salter, P. Thompson, S. Tidball, J. Blaikie, C. Gray, P. Bollina, J. Catto, A. Doble, A. Doherty, D. Gillatt, R. Kockelbergh, H. Kynaston, A. Paul, P. Powell, S. Prescott, D.J. Rosario, E. Rowe, M. Davis, E.L. Turner, R.M. Martin, and D.E. Neal, for the ProtecT Study Group*

- ◆— Radical prostatectomy
- ◆— Radical radiotherapy
- ◆— Active monitoring



What are Patients Saying?




 stmmotor · 9d

I had my RALP on 9/25/23. My incontinence is terrible. I go through 6-10 pads a day. My groin is continuously soaked in urine. I've been outsourced to an external PT group.

I'm tired of the medical professionals asking me "are you doing kegels?". That's all I'm doing!


Basically, I'm f**ked. There's not a damn thing the urologist can do for me now. Sure, they removed the cancer, but it's just me and my urine soaked underwear now.

... [Reply](#) [Upvote](#) 11 [Downvote](#)


 415z · 7d

I had mine end of August and also had pretty bad incontinence for several months, and I'm only 48. Now I'm dry. It varies from person to person. All I can say is you're only 4 months post op and still have some time left on the recovery curve. It's actually a little too early to be saying you're totally screwed. But I get it, it was very distressing for me as well.

... [Reply](#) [Upvote](#) [Downvote](#)

 auswild100 · 7d

Add a comment

 AndrewW1111 · 3d

Need helping to deal with severe aftereffects of ADT!

Self Post

I'm 18 months post RT and ADT (I had a 6-month course of Lupron and 26 Low Dose RT sessions). Currently I'm experiencing these debilitating side effects although thankfully my PSA is 0.1!

1. Needing 10 hours plus sleep. Otherwise, I feel very ill.
2. Muscle pain and soreness. Joint pain as well.
3. Muscle weakness (I have cut my resistance training in half!)
4. Brain fog

Has anyone experienced this so long after stopping ADT? Has anything helped? I'm desperate for some advice! Thanks

[Upvote](#) 3 [Downvote](#) [Comments](#) 3 [Share](#)

 Frosty-Growth-2664 · 3d

What's your Testosterone level now?
Do you know what it was before starting ADT?

... [Reply](#) [Upvote](#) 1 [Downvote](#)

Add a comment





**IS THERE A MORTALITY
BENEFIT WITH TREATMENT**

Randomized Data

- What is the Best Oncologic Option for Clinically Localized Disease Management?
- Do we have randomized trials demonstrating benefits of therapy for prostate cancer?
 - SPCG – 4
 - PIVOT
 - Protect T

Radical Prostatectomy or Watchful Waiting
in Prostate Cancer — 29-Year Follow-up

N ENGL J MED 379;24 NEJM.ORG DECEMBER 13, 2018

SPCG – 4

- Inclusion Criteria

- Date of Enrollment 10/89 to 2/99
- Age < 75 years
- 10 year life expectancy
- PSA <50 ng/mL
- Localized disease (negative bone scan)

- ALL 695 PATIENTS FOLLOWED UNTIL 12/31/17

- None lost to FU

	Radical Prostatectomy (N=347)	Watchful Waiting (N=348)
Age — yr	64.6±64.6	64.5±64.5
Mean PSA level — ng/ml	13.5	12.3
Tumor stage — no. (%)†		
T1b	33 (9.5)	50 (14.4)
T1c	43 (12.4)	38 (10.9)
T2	270 (77.8)	259 (74.4)
Gleason score of biopsy specimen — no. (%)§		
2–4	45 (13.0)	46 (13.2)
5 or 6	165 (47.6)	166 (47.7)
7	77 (22.2)	82 (23.6)
8 or 9	14 (4.0)	21 (6.0)
Missing data¶	46 (13.3)	33 (9.5)

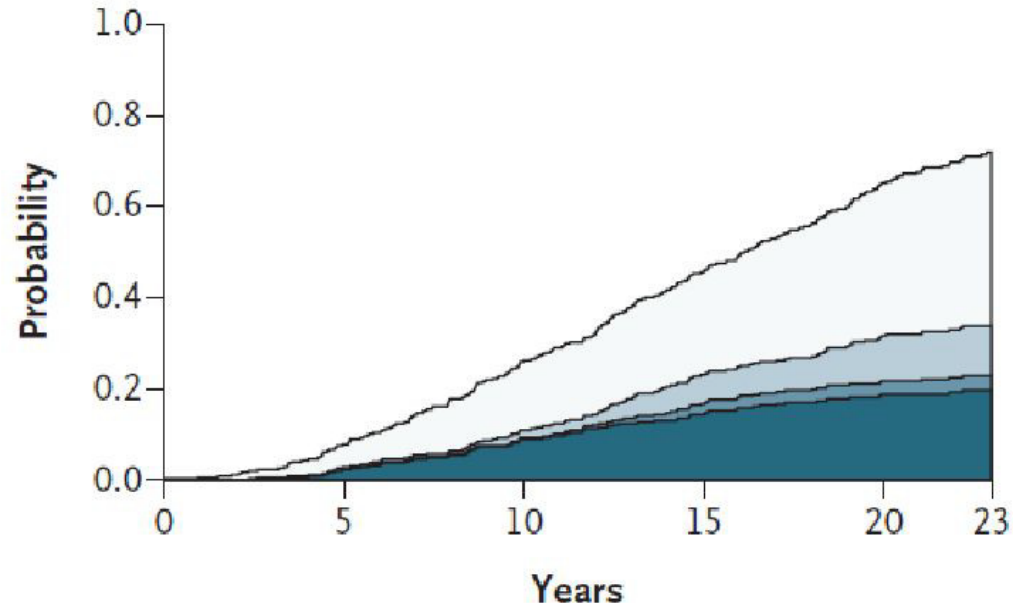
□ Other main cause, without androgen-deprivation therapy

■ Other main cause, with androgen-deprivation therapy

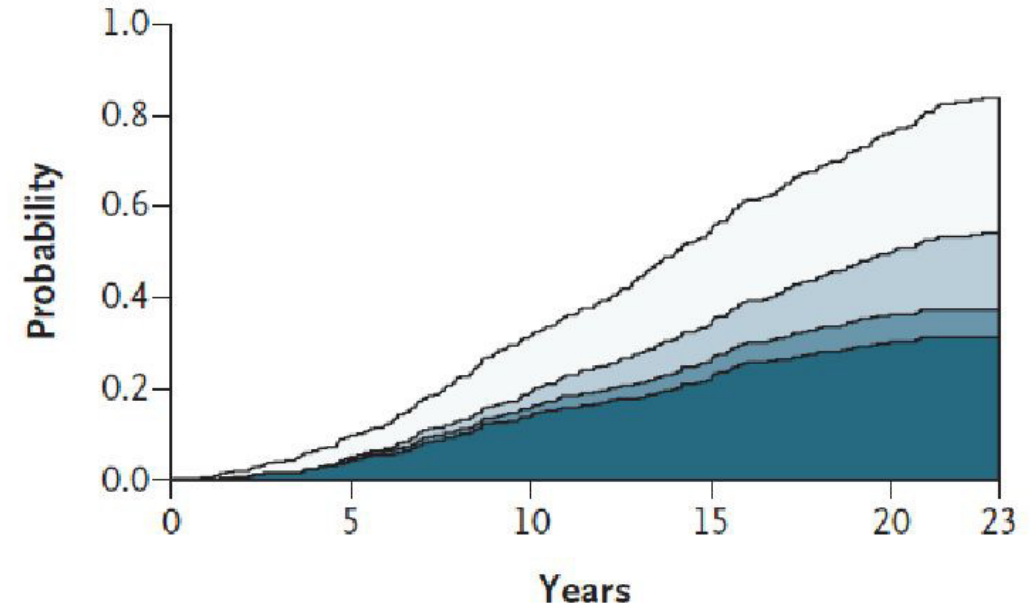
■ Other main cause, with metastasis

■ Prostate cancer

A Radical Prostatectomy, Any Age



B Watchful Waiting, Any Age



- Overall Death Incidence 71.9% vs 83.8%
 - RR 0.74 (95% CI 0.62 - 0.87, p<0.001)
- Death from Prostate Cancer – 19.6% vs 31.3%
 - OR 0.55 (95% CI 0.41 – 0.74, p<0.001)
- Distant Metastases 26.6% vs 43.3%
 - OR 0.54 (95% CI, 0.42 to 0.70; P<0.001)

Follow-up of Prostatectomy versus Observation for Early Prostate Cancer

Timothy J. Wilt, M.D., M.P.H., Karen M. Jones, M.S., Michael J. Barry, M.D.,
Gerald L. Andriole, M.D., Daniel Culkin, M.D., Thomas Wheeler, M.D.,
William J. Aronson, M.D., and Michael K. Brawer, M.D.

- 731 men with localized prostate cancer (Goal 2000)
- Enrollment time: November 1994 - January 2002
- Inclusion Criteria:
 - PSA value of less than 50 ng/nL
 - Age < 75 years
 - Negative results on a bone scan
 - Life expectancy of at least 10 years

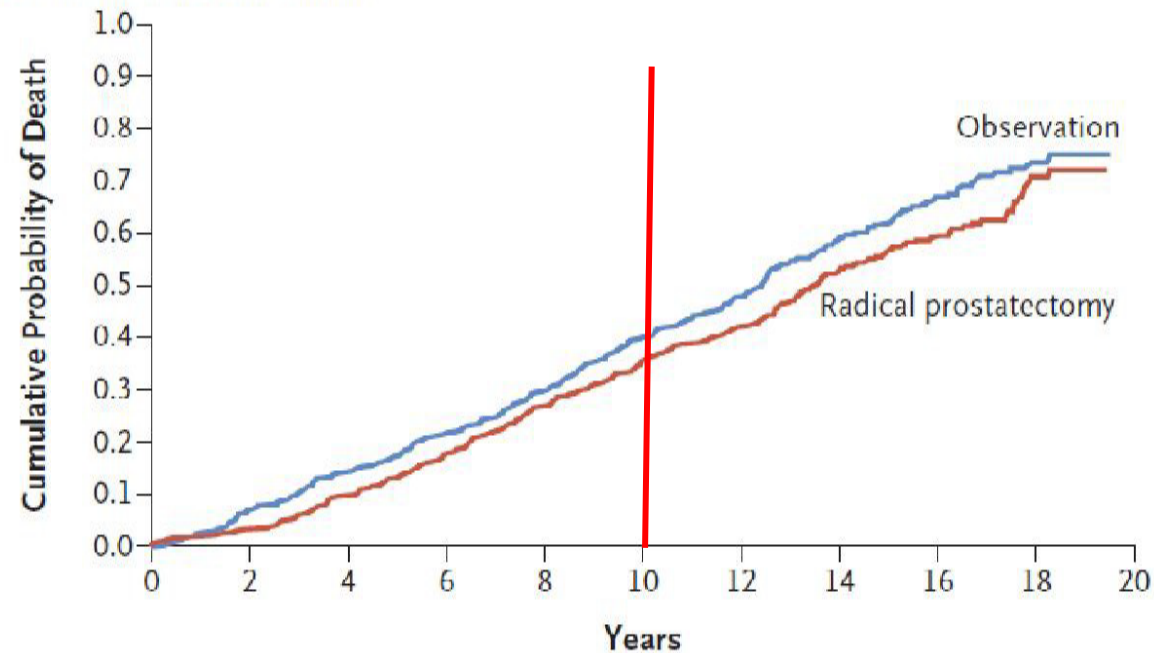
	Observation (n=367)	RP (n=364)	p-value
MEAN AGE years (SD)	66.8 (5.6)	67.0 (5.2)	.60

Tumor Risk Category (%)**			.37
Low risk	148 (40.3)	148 (40.7)	
Intermediate risk	120 (32.7)	129 (35.4)	
High risk	80 (21.8)	77 (21.2)	
7	64 (17.4)	69 (19.0)	
8-10	22 (6.0)	29 (8.0)	

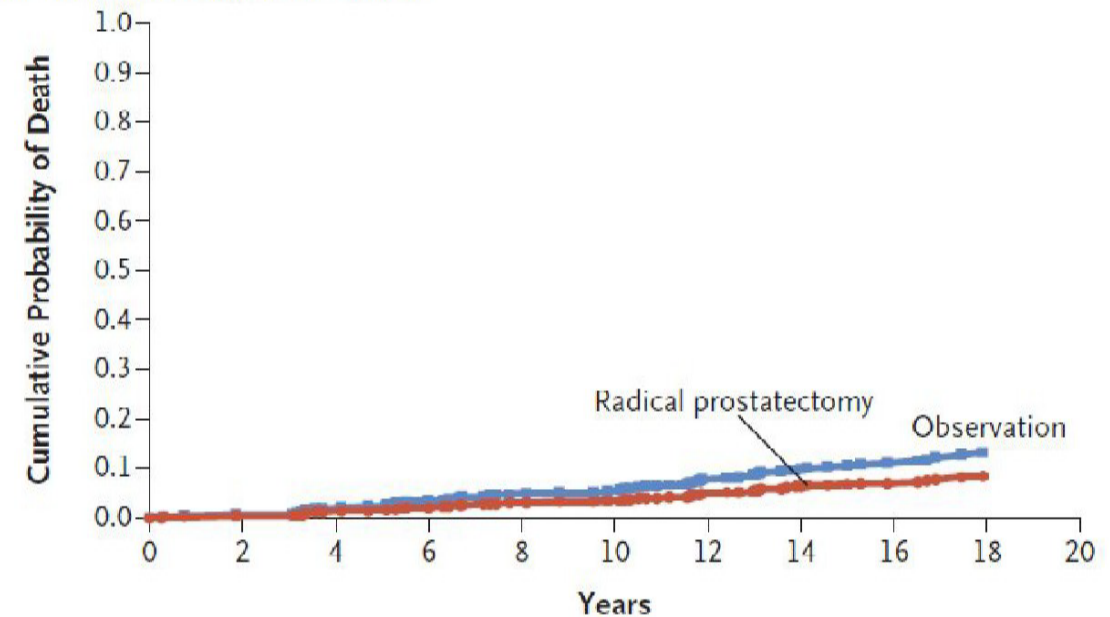
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A Death from Any Cause



B Death from Prostate Cancer



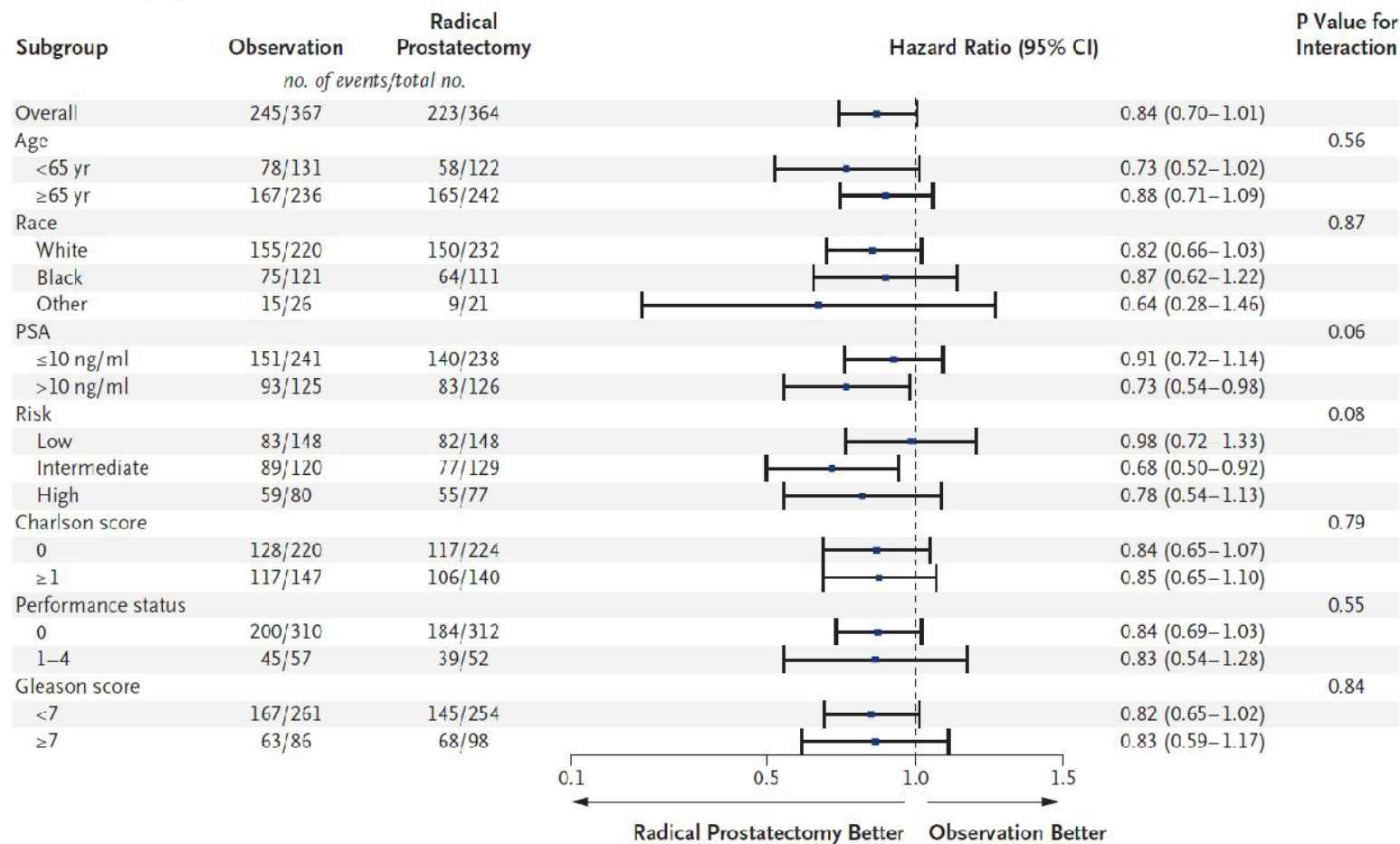
All-cause mortality – 61.3% vs 66.8% (RR 0.92; 95% CI, 0.82 to 1.02, P = 0.06)

Death due to prostate cancer 7.4% vs 11.4% (RR 0.63; 95% CI, 0.39 to 1.02; P = 0.06)

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A Death from Any Cause



The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

APRIL 27, 2023

VOL. 388 NO. 17

Fifteen-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer

F.C. Hamdy, J.L. Donovan, J.A. Lane, C. Metcalfe, M. Davis, E.L. Turner, R.M. Martin, G.J. Young, E.I. Walsh, R.J. Bryant, P. Bollina, A. Doble, A. Doherty, D. Gillatt, V. Gnanapragasam, O. Hughes, R. Kockelbergh, H. Kynaston, A. Paul, E. Paez, P. Powell, D.J. Rosario, E. Rowe, M. Mason, J.W.F. Catto, T.J. Peters, J. Oxley, N.J. Williams, J. Staffurth, and D.E. Neal, for the ProtecT Study Group*

- 1643 Men
- 10 year life expectancy
- PSA < 50
- Neg Bone Scan/CT Scan
- Taken from 80,000+ men screening study

All Cause Mortality

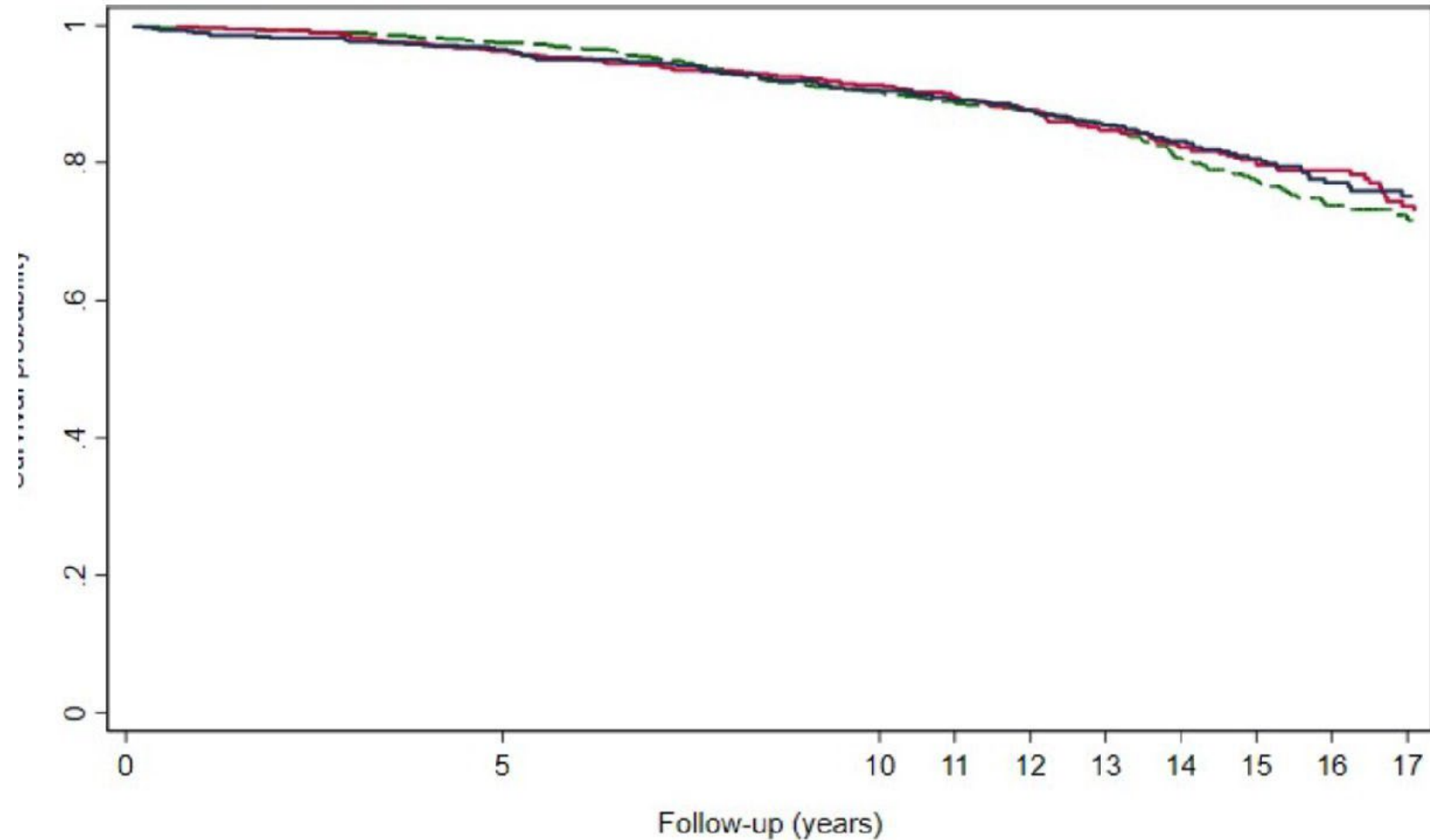
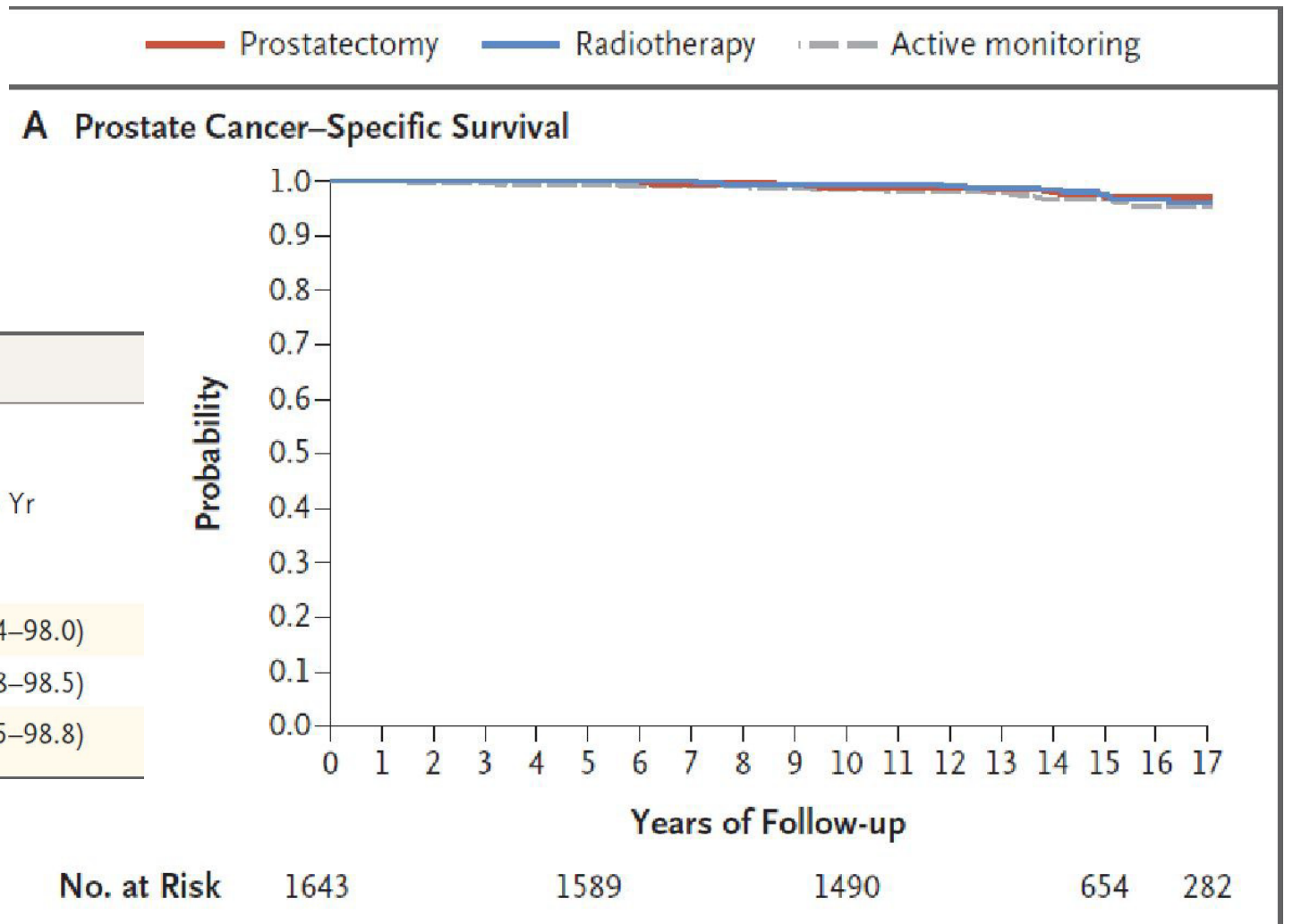


Table 2. Prostate Cancer Survival.*

Trial Group	Survival (95% CI)	
	At 10 Yr	At 15 Yr
	<i>percentage of patients</i>	
Active monitoring	98.7 (97.2–99.4)	96.6 (94.4–98.0)
Prostatectomy	99.0 (97.7–99.6)	97.2 (94.8–98.5)
Radiotherapy	99.4 (98.2–99.8)	97.7 (95.5–98.8)



Prostate Cancer Deaths

Variable	Active Monitoring (N= 545)	Prostatectomy (N= 553)	Radiotherapy (N= 545)	Hazard Ratio (95% CI)	
				Prostatectomy vs. Active Monitoring	Radiotherapy vs. Active Monitoring
	<i>no. of patients/total no. (%)</i>				
CAPRA risk score‡					
0–2	11/381 (2.9)	6/382 (1.6)	13/388 (3.4)	0.52 (0.19–1.41)	1.10 (0.49–2.46)
3–5	4/143 (2.8)	5/150 (3.3)	2/135 (1.5)	1.23 (0.33–4.58)	0.57 (0.11–3.14)
6–10	2/13 (15.4)	0/8	1/19 (5.3)	NA	0.16 (0.01–1.76)
D'Amico risk score§					
Low	9/328 (2.7)	4/343 (1.2)	6/343 (1.7)	0.44 (0.13–1.42)	0.63 (0.23–1.78)
Intermediate	3/129 (2.3)	2/118 (1.7)	5/122 (4.1)	0.68 (0.11–4.05)	1.64 (0.39–6.86)
High	2/49 (4.1)	6/54 (11.1)	0/44	2.62 (0.53–12.97)	NA

Discordance Between Trials

- Era of Treatment
- Clinical Risk of Patients
- Health of patients
- Patient Selection

Summary

- In intermediate risk and high risk cancer there is probably a cancer specific benefit to treatment
- Counseling patients requires discussion that treatment may be either over or undertreatment
- Identifying the most aggressive tumors will help to improve oncologic outcomes

**Goal should be Treating
Aggressive Intermediate
Risk Disease**

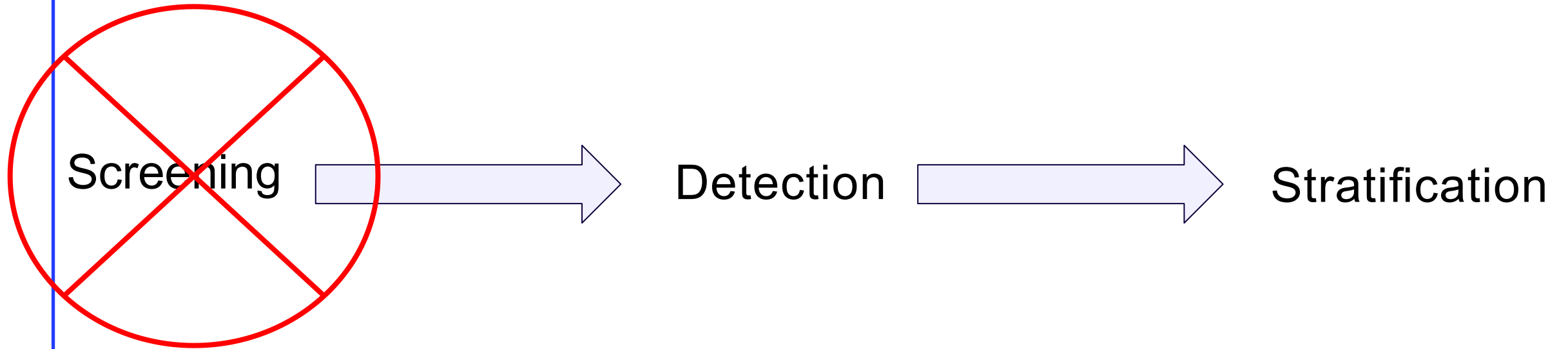
How do we Identify Aggressive Intermediate Risk Prostate Cancer

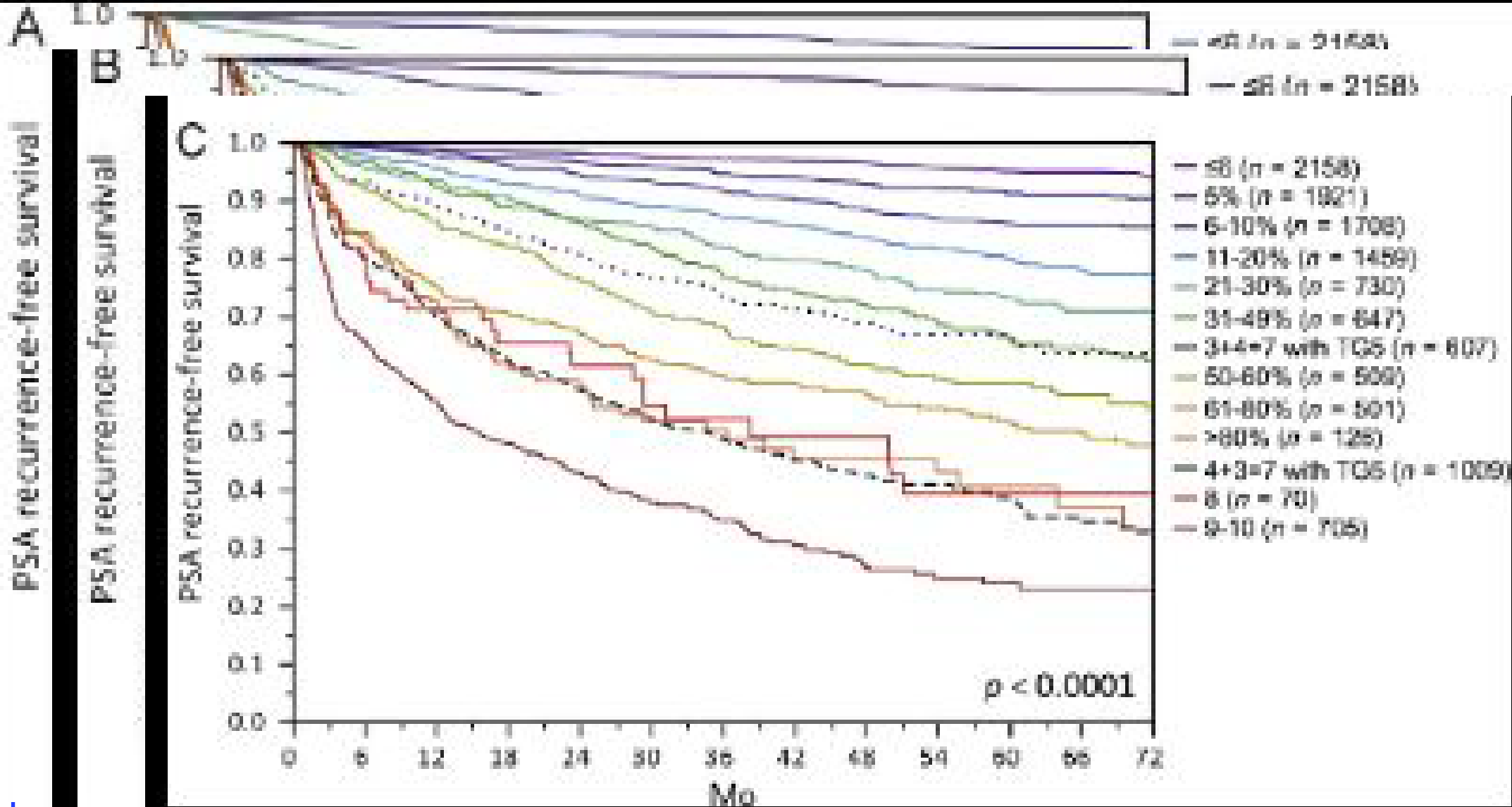


Prostate Cancer Screening

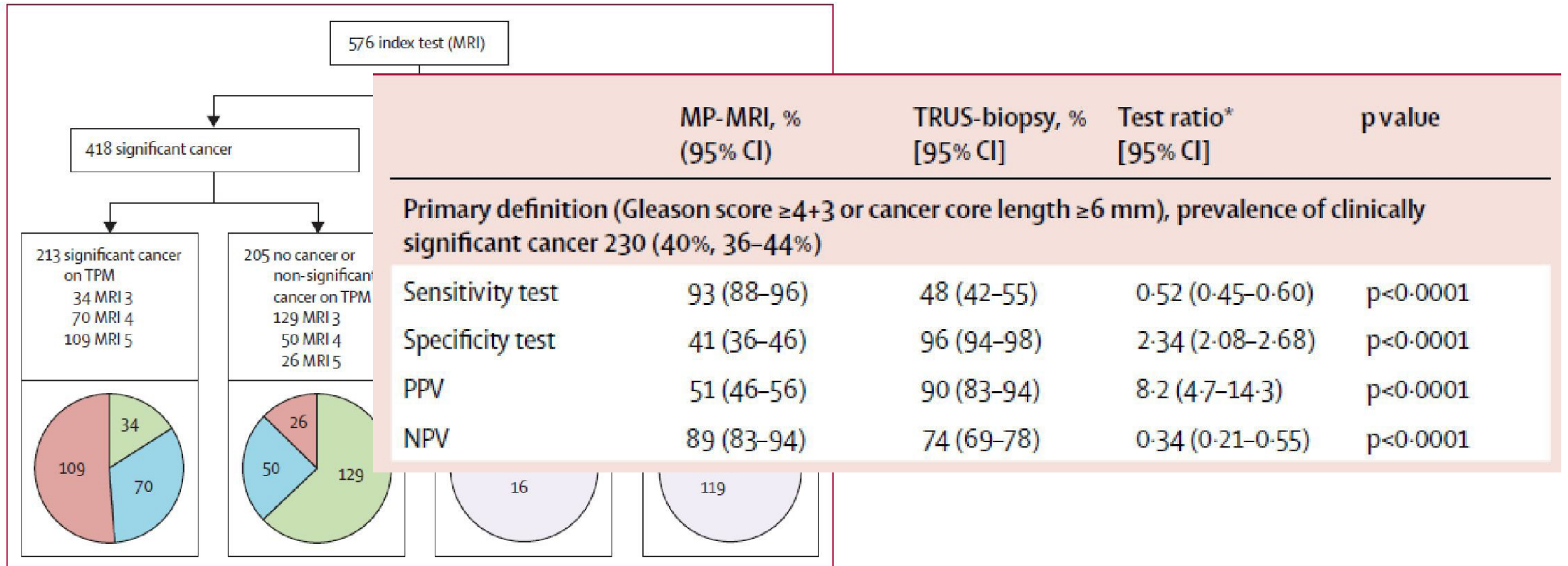


How do we Identify Aggressive Intermediate Risk Prostate Cancer



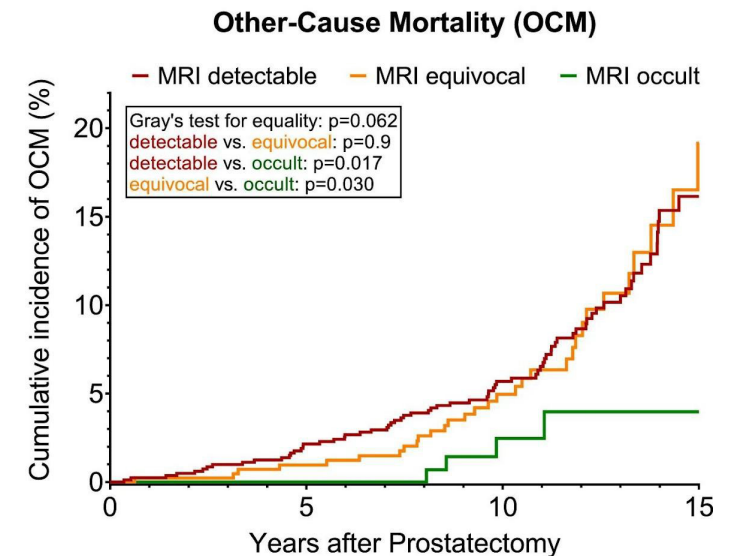
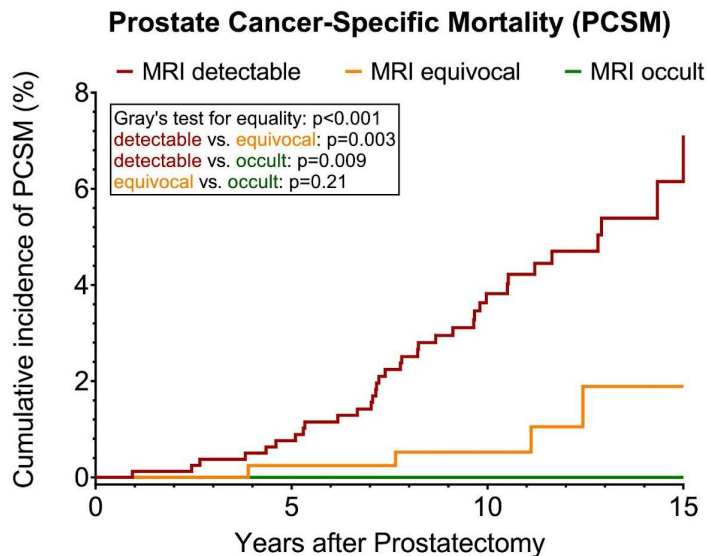
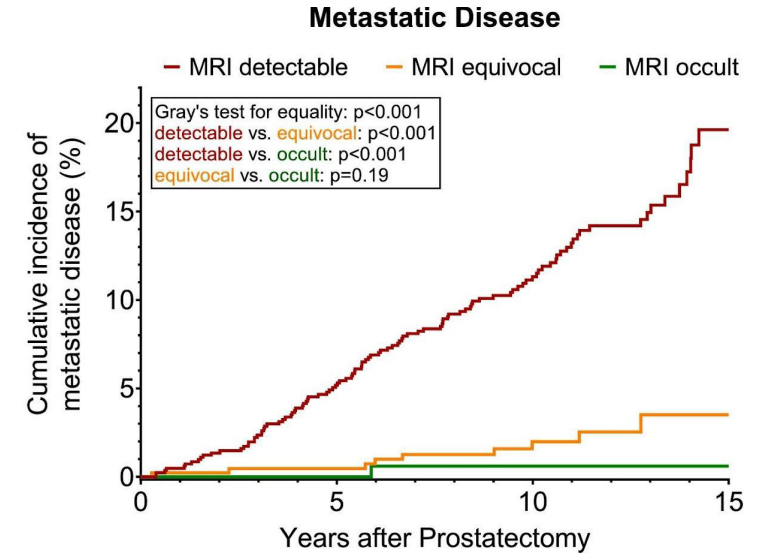
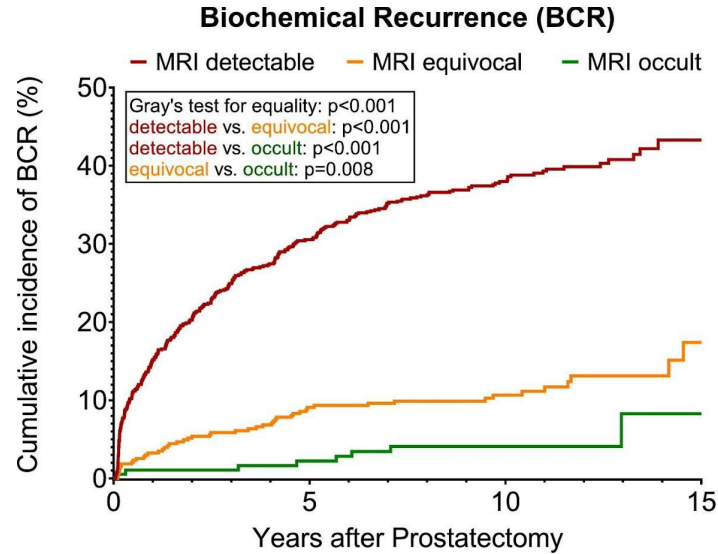


Using MRI to find Aggressive Disease

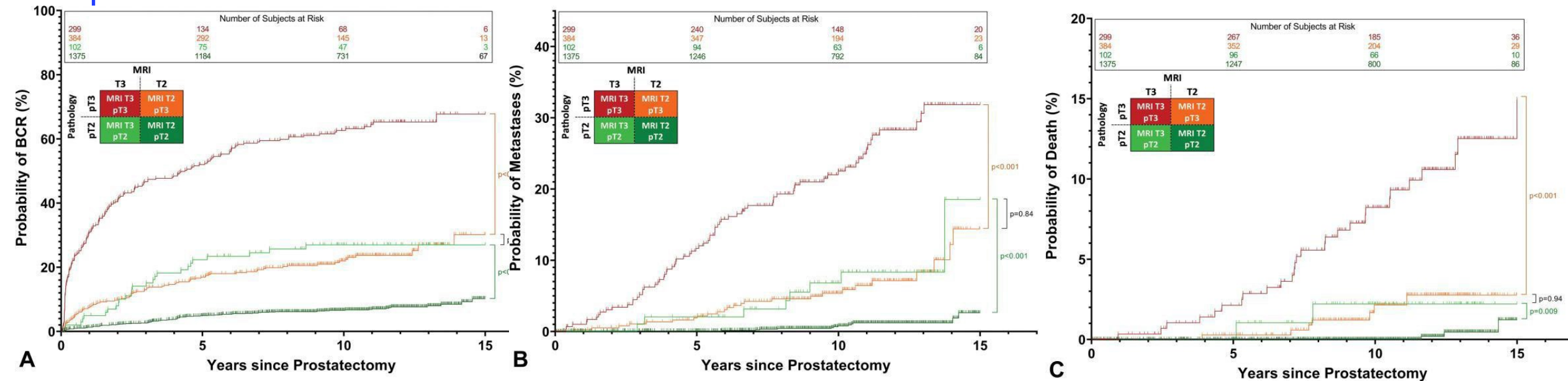


MRI Predicts Cancer Biology

- 1449 MSKCC patients with an MRI < 180 Days prior to Radical Prostatectomy
- PIRADS 1 or 2 – Occult
- PIRADS 3 – Equivocal
- PIRADS 4/5 – Detectable
- 100% PC Specific Survival in occult disease



MRI Predicts Cancer Biology



Tumor stage on prostatectomy specimens

pT2	1477 (68)
pT3a	535 (25)
pT3b	148 (6.9)

Tumor extent at MRI

Organ confined	1759 (81)
Extraprostatic extension	344 (16)
Seminal vesicle invasion	57 (2.6)

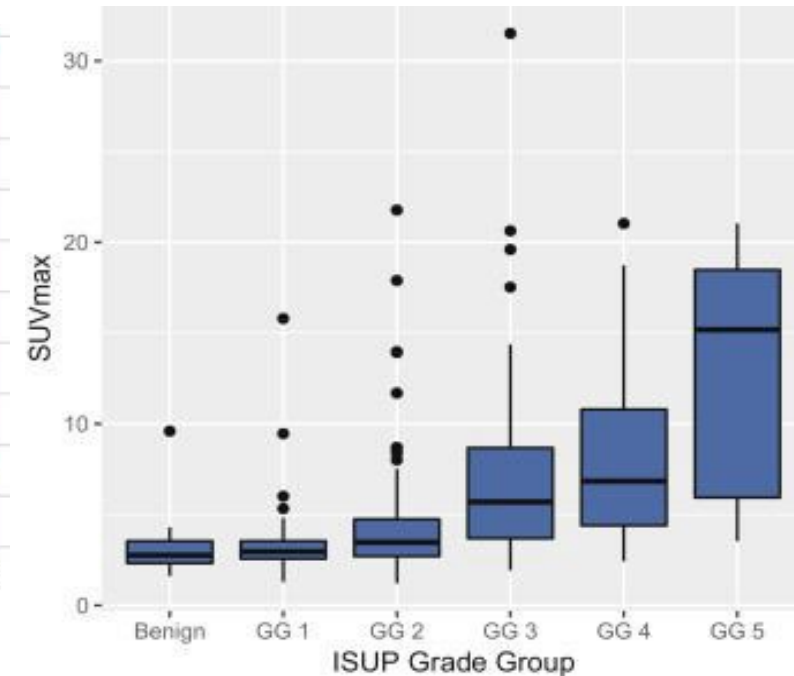
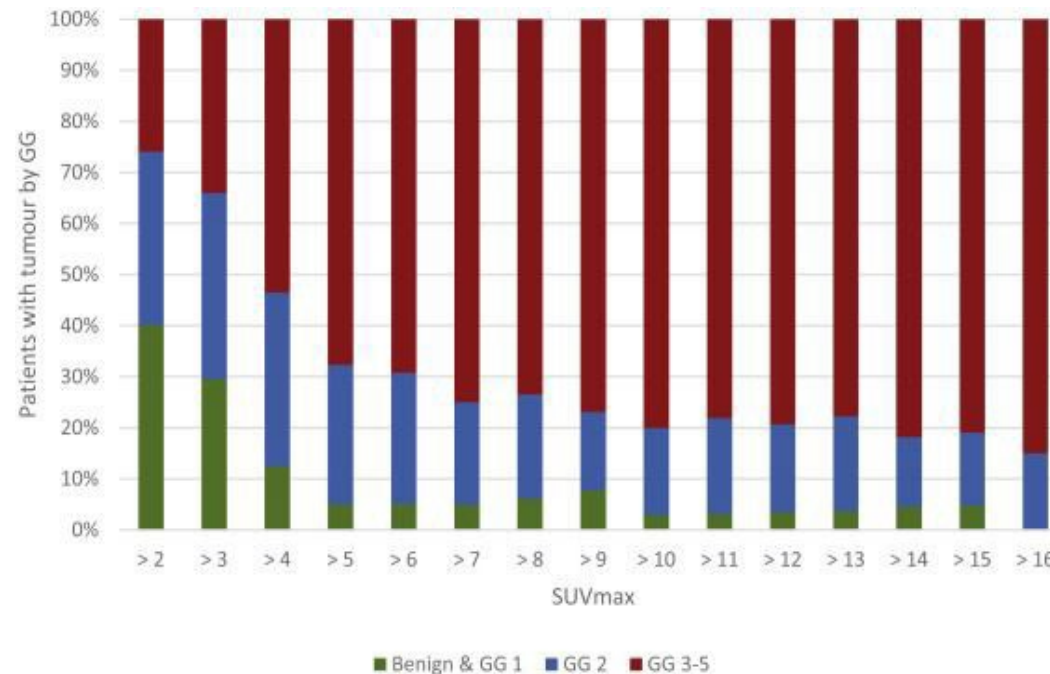
Can we add other Imaging Modalities?

200 Australian Men

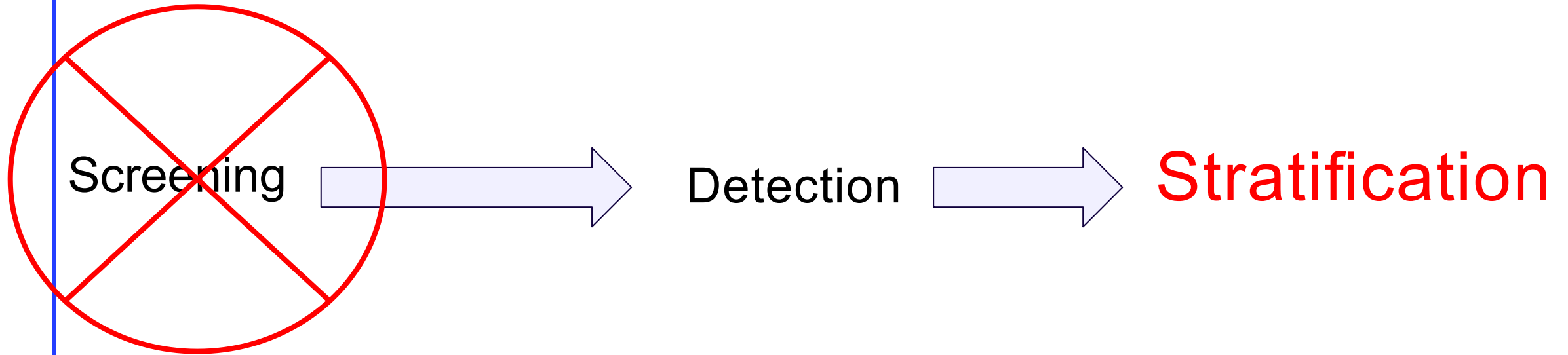
All underwent TP biopsies

Benign tissue and GG 1-2 - SUV 3.14 (2.55-3.91)

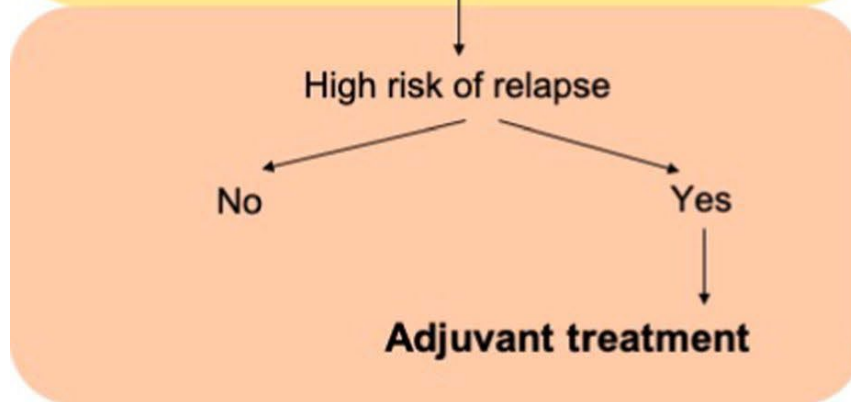
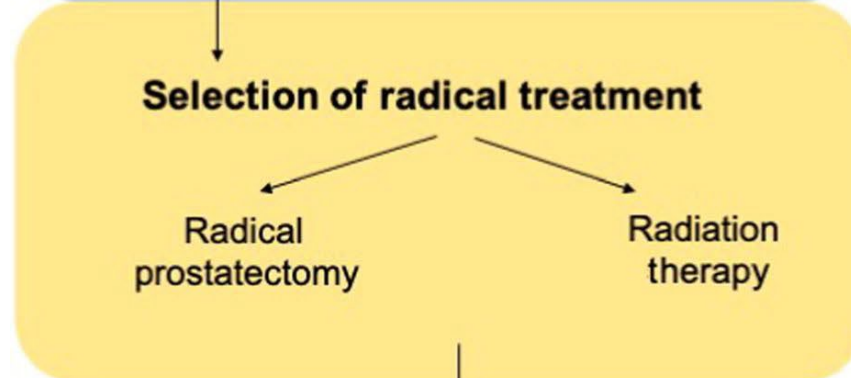
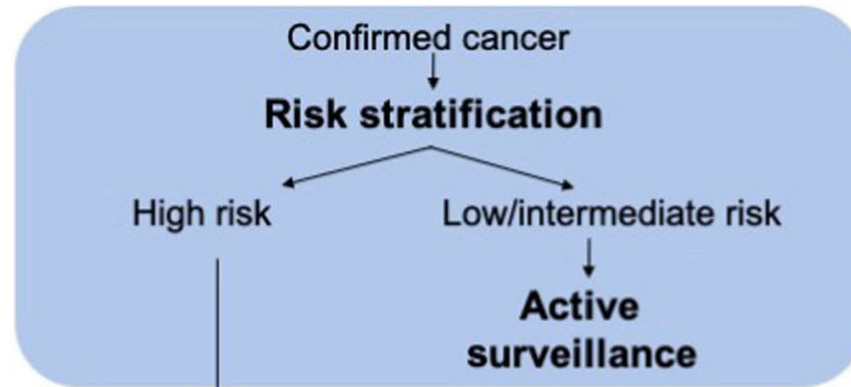
GG 3-5 6.40 (4.47-11.0)



How do we Identify Aggressive Intermediate Risk Prostate Cancer



Biomarkers



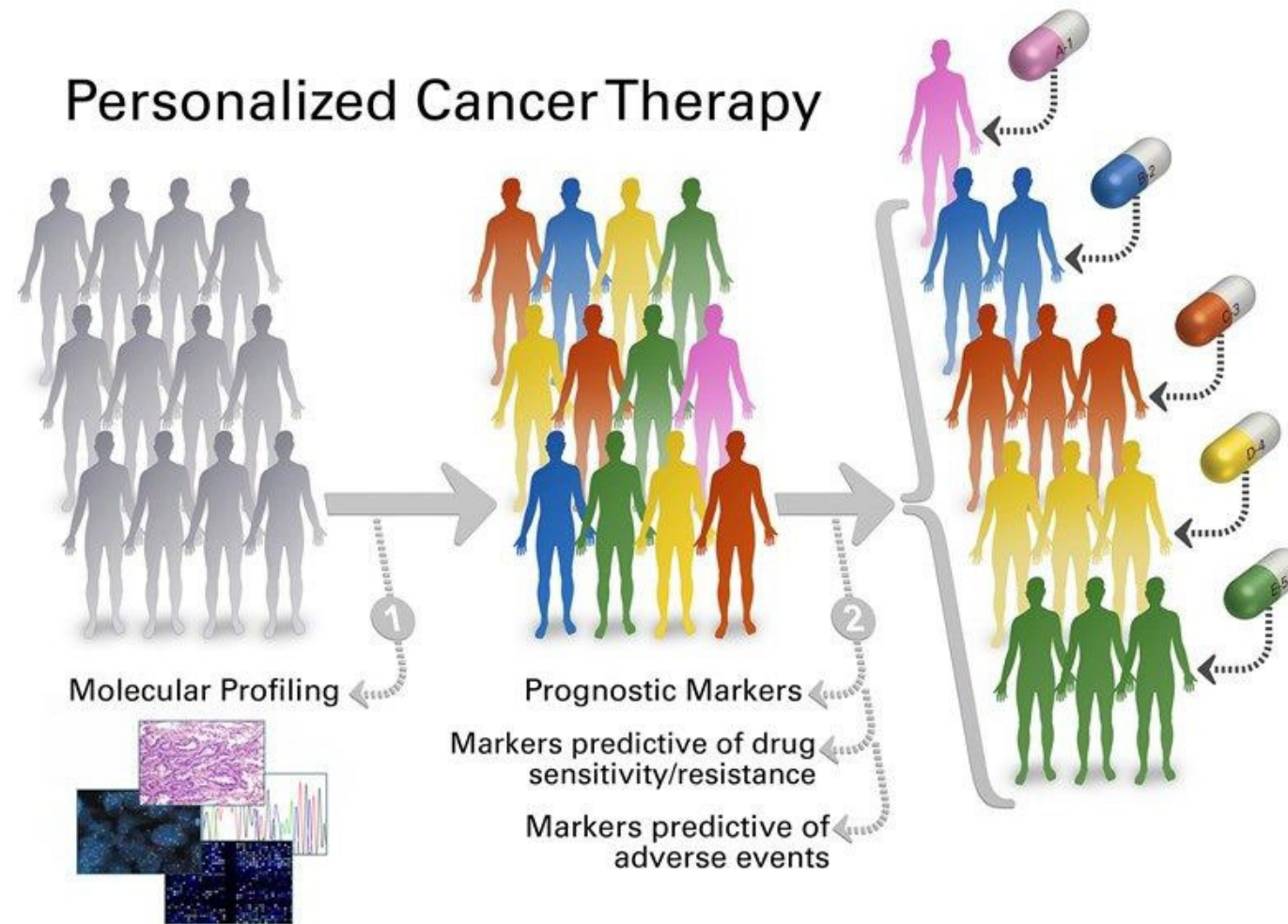
Test	Analyte	Tissue	Outcome	Best evidence
Oncotype Dx	mRNA	Biopsy	TG	Retrospective
Prolaris	mRNA	Biopsy	TA,	Retrospective
ProMark	protein	Biopsy	TA, GS	Retrospective
Decipher	mRNA	Biopsy	TA	SRMA
miR risk	miRNAs	Serum	GS, BCR (RP)	Retrospective
PTEN	protein	Biopsy	GS, stage, DM, BCR (RP)	SRMA
miR Sentinel	sncRNAs	Urine	TG	Case-control

PORTOS	mRNA	RP	Response to RT	Retrospective
Decipher	mRNA	RP	DM, PCSM, BCR (RT), impact of bicalutamide on OS (sRT)	SRMA, prospective registry, post hoc analysis of RCT
Prolaris	mRNA	RP	BCR (RP, RT), PCSM, DM	Retrospective
Oncotype Dx	mRNA	Biopsy	BCR (RP), DM	Retrospective
Ki67	Protein	Biopsy, RP	BCR (RP, RT), DM, OS	SRMA



What is Personalized Treatment?

Personalized Therapy to the Oncologist



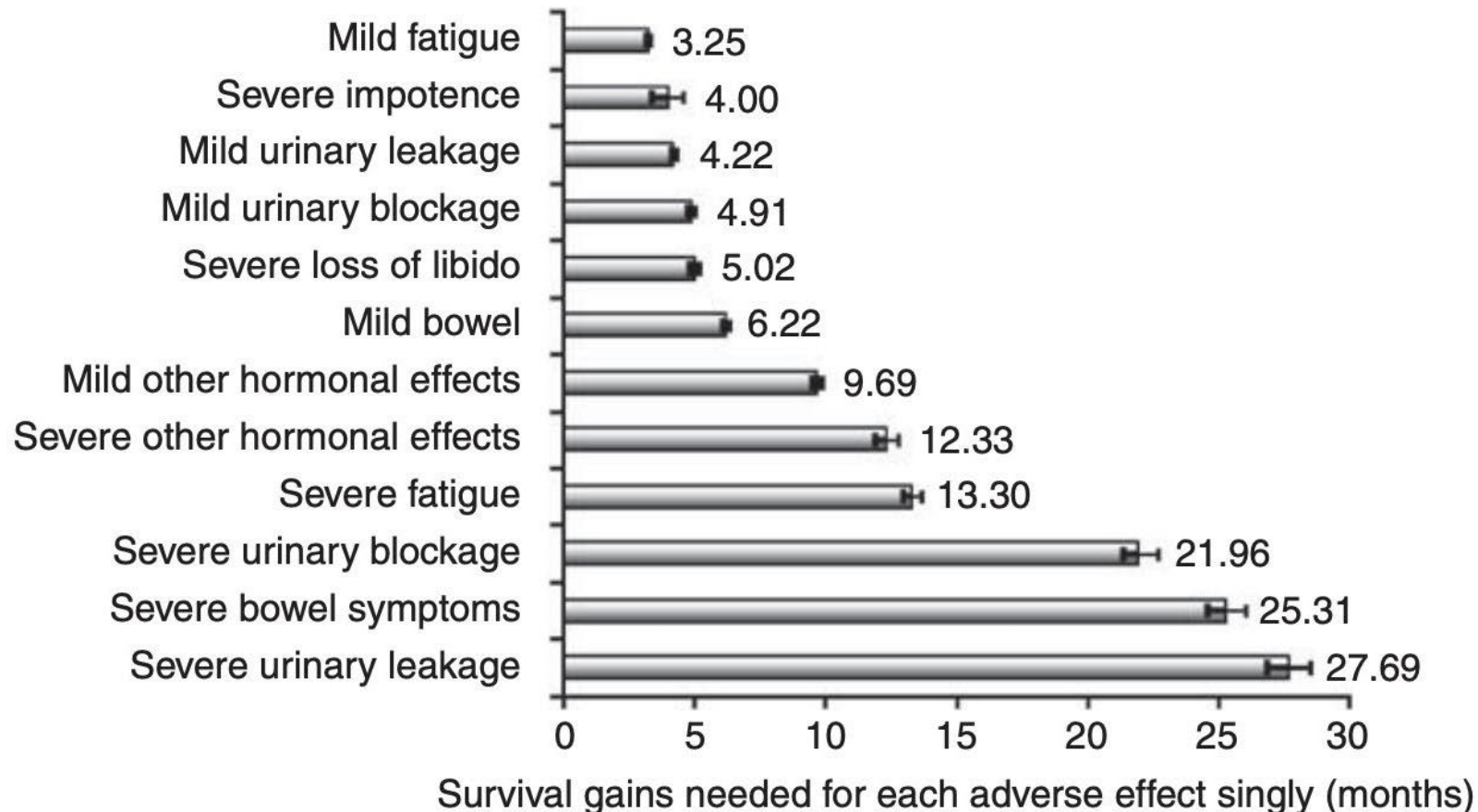
Personalized Therapy to the Patient



"C'mon c'mon - it's either one or the other".

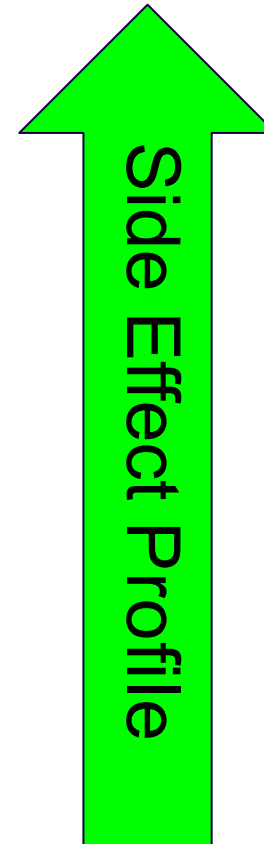
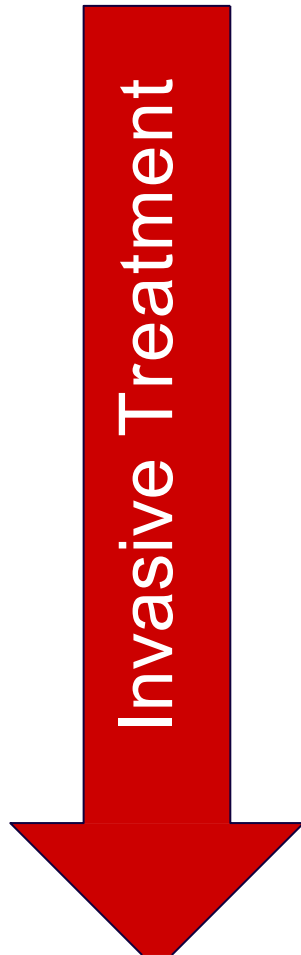
What are Patients Willing to Give Up?

King et al



Personalized Therapy

Weighing individualized risks associated with each treatment



Functional Outcomes for Focal Ablation

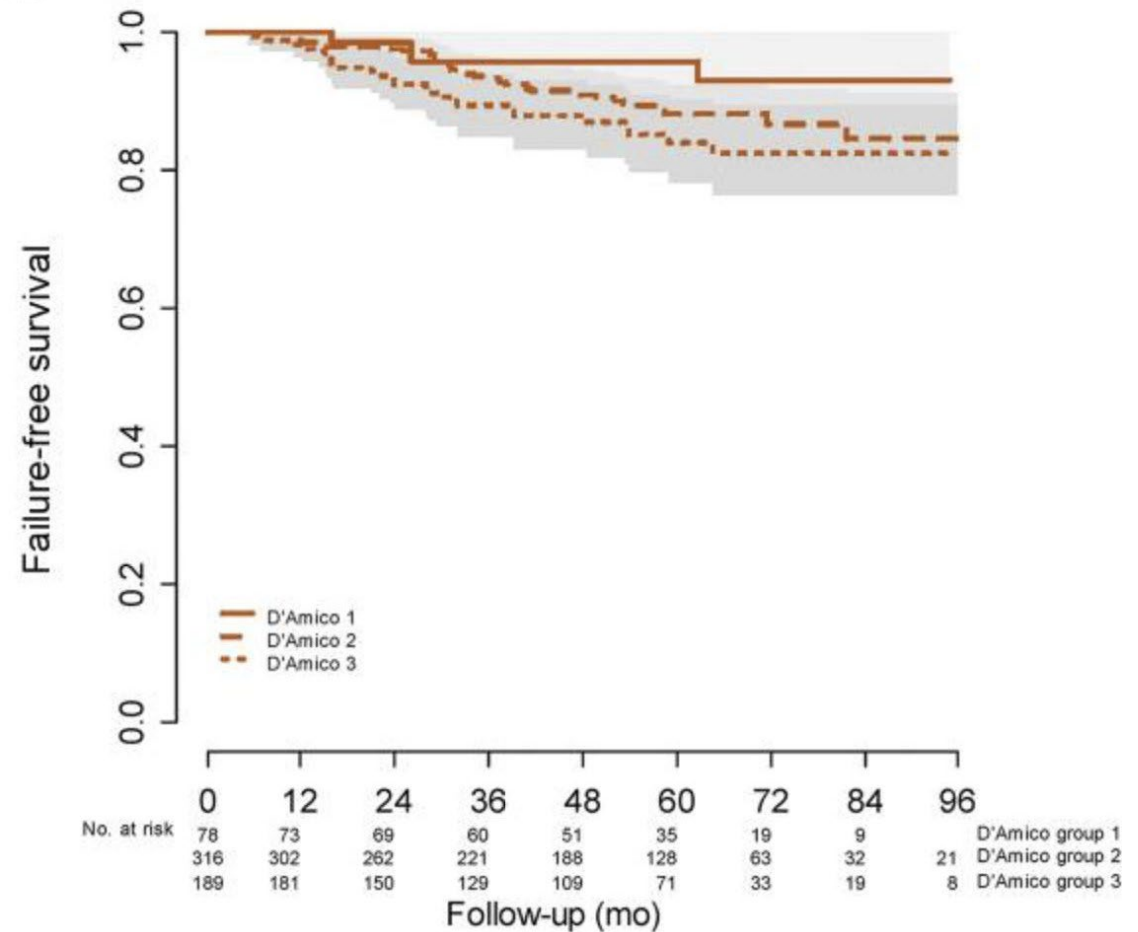
Patient-reported urinary incontinence	Patients, <i>n</i> (%)	
	1–2 yr FU	2–3 yr FU
0 pads	304/313 (97)	241/247 (98)
0–1 pads	313/313 (100)	247/247 (100)
No leakage at all	208/250 (83)	156/195 (80)

Oncologic Outcomes of Ablative Treatment for Prostate Cancer

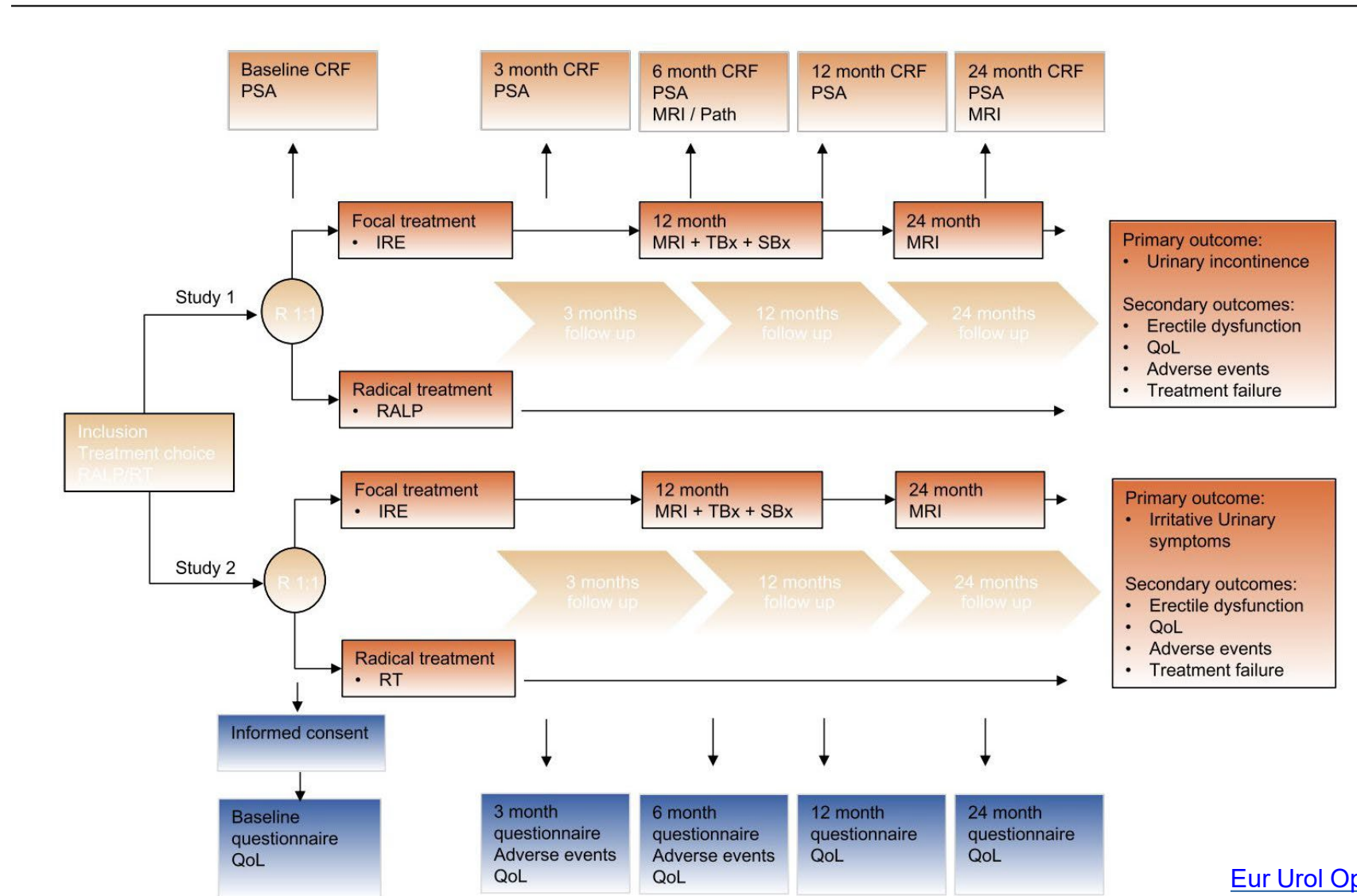
695 men

Treated with focal HIFU at imperial college London

(B)



Future of Prostate Cancer Treatment



Summary

Personalized care in intermediate risk disease requires a shared decision making effort with the patient

Several options, all with their risks and benefits of therapy.