Active Surveillance in Early Prostate Cancer

Active Surveillance in Low Risk Disease: Who Doesn't Need Treatment?

Rationale for active surveillance

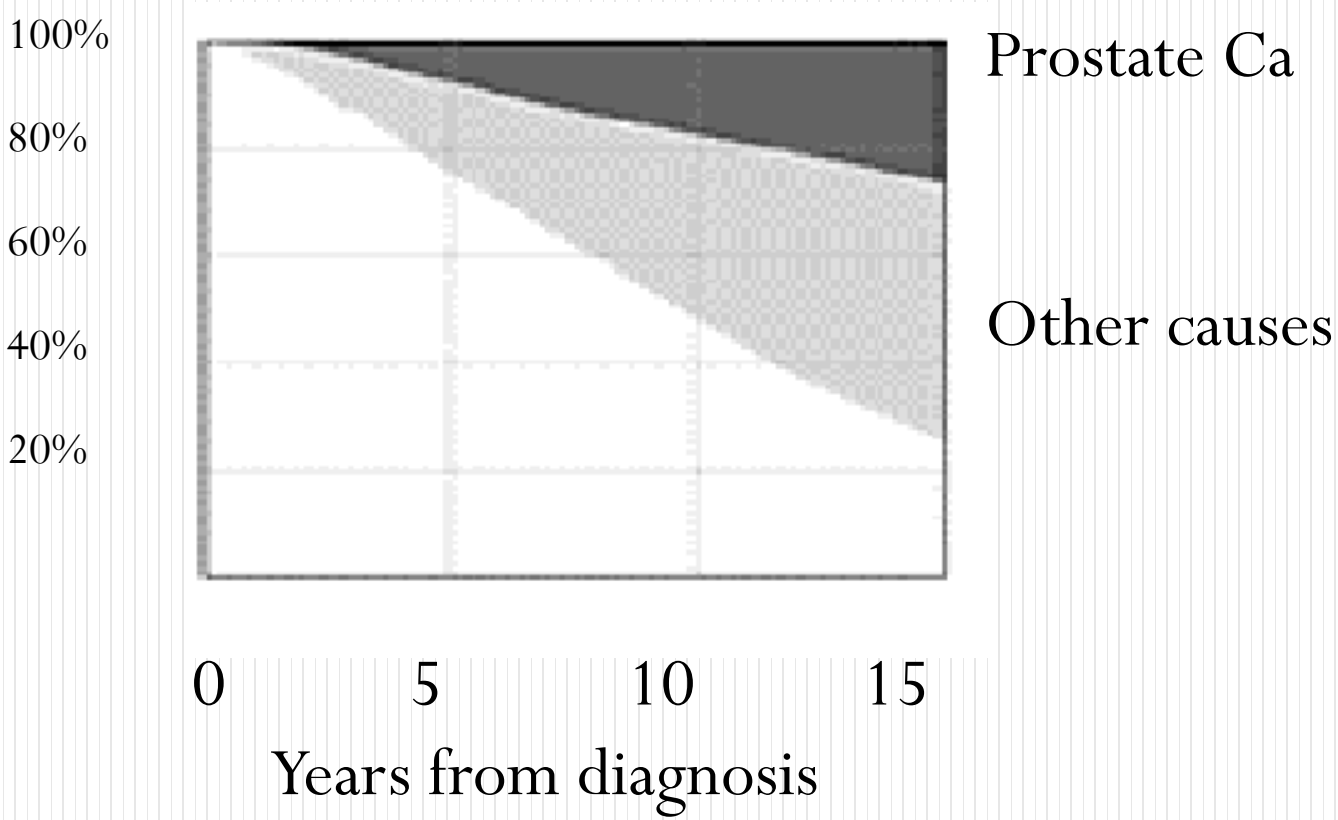
Results of active surveillance

THE ROYAL MARSDEN

The Institute of Cancer Research

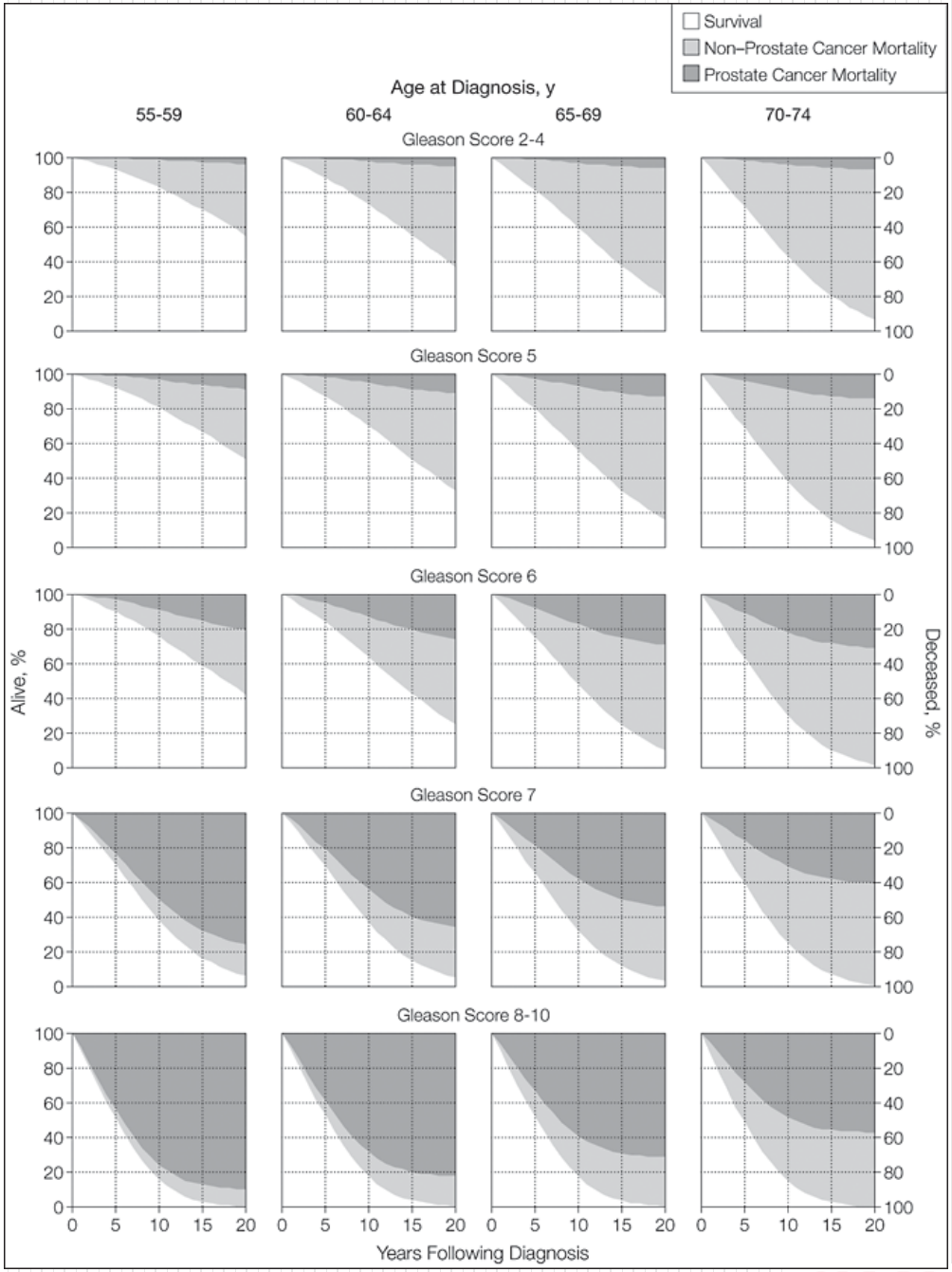
Albertsen study of men with prostate cancer not treated with curative techniques

Cumulative mortality: age 65-69, GS 6



20-Year Outcomes Following Conservative Management of Clinically Localized Prostate Cancer

Albertsen, P. C. et al. JAMA 2005;293



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JAMA

Rationale for active surveillance

- **Some** men with prostate cancer benefit from radical treatment
- Treatment is toxic, and should be given only to those who stand to benefit
- **Most** men with screen detected prostate cancer do not benefit from treatment

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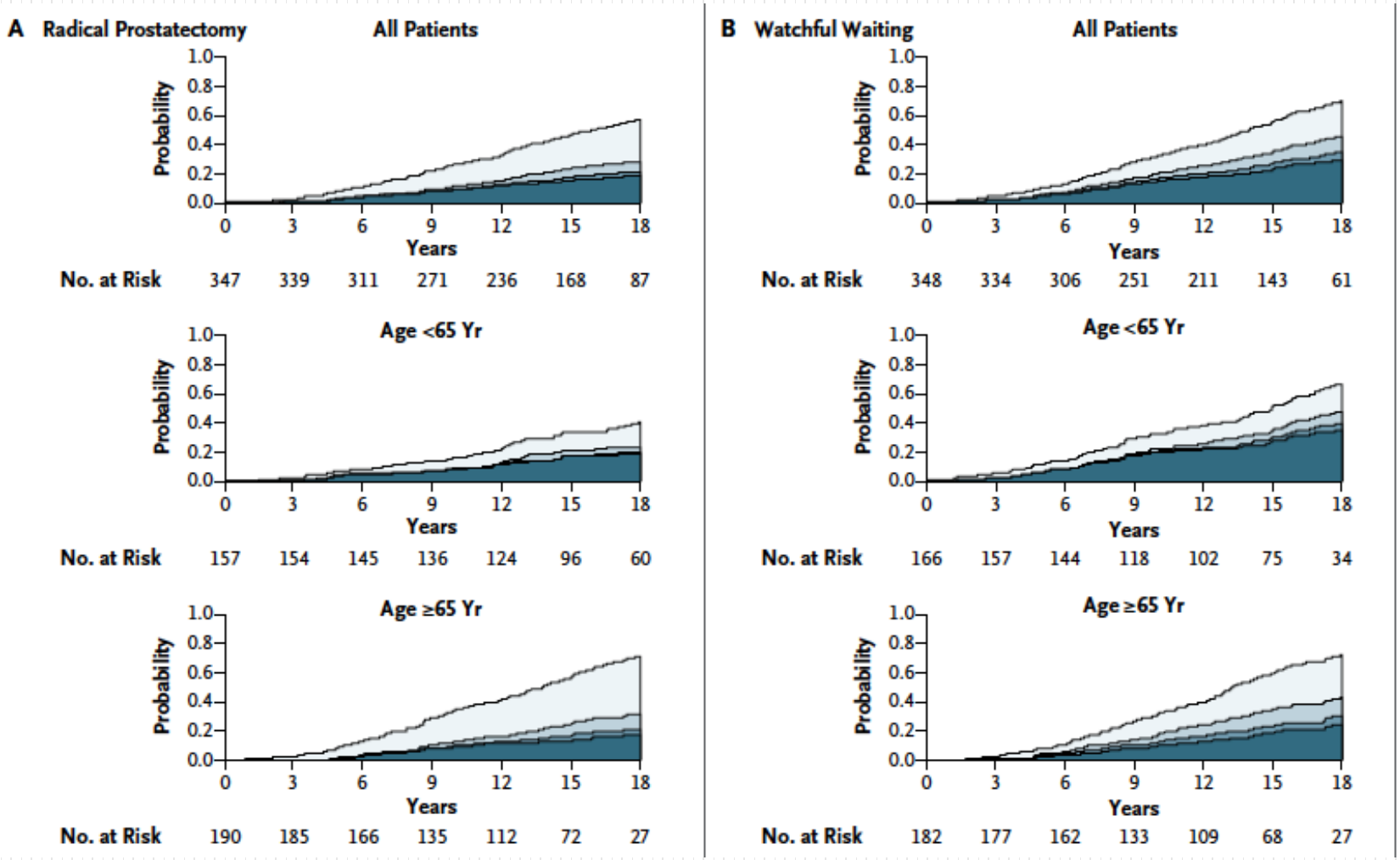
A Randomized Trial Comparing Radical Prostatectomy with Watchful Waiting in Early Prostate Cancer

Scandinavian Prostatic Cancer Group Study NEJM (2005)/(2014)



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A Randomized Trial Comparing Radical Prostatectomy with Watchful Waiting in Early Prostate Cancer

Scandinavian Prostatic Cancer Group Study NEJM (2005)/(2014)

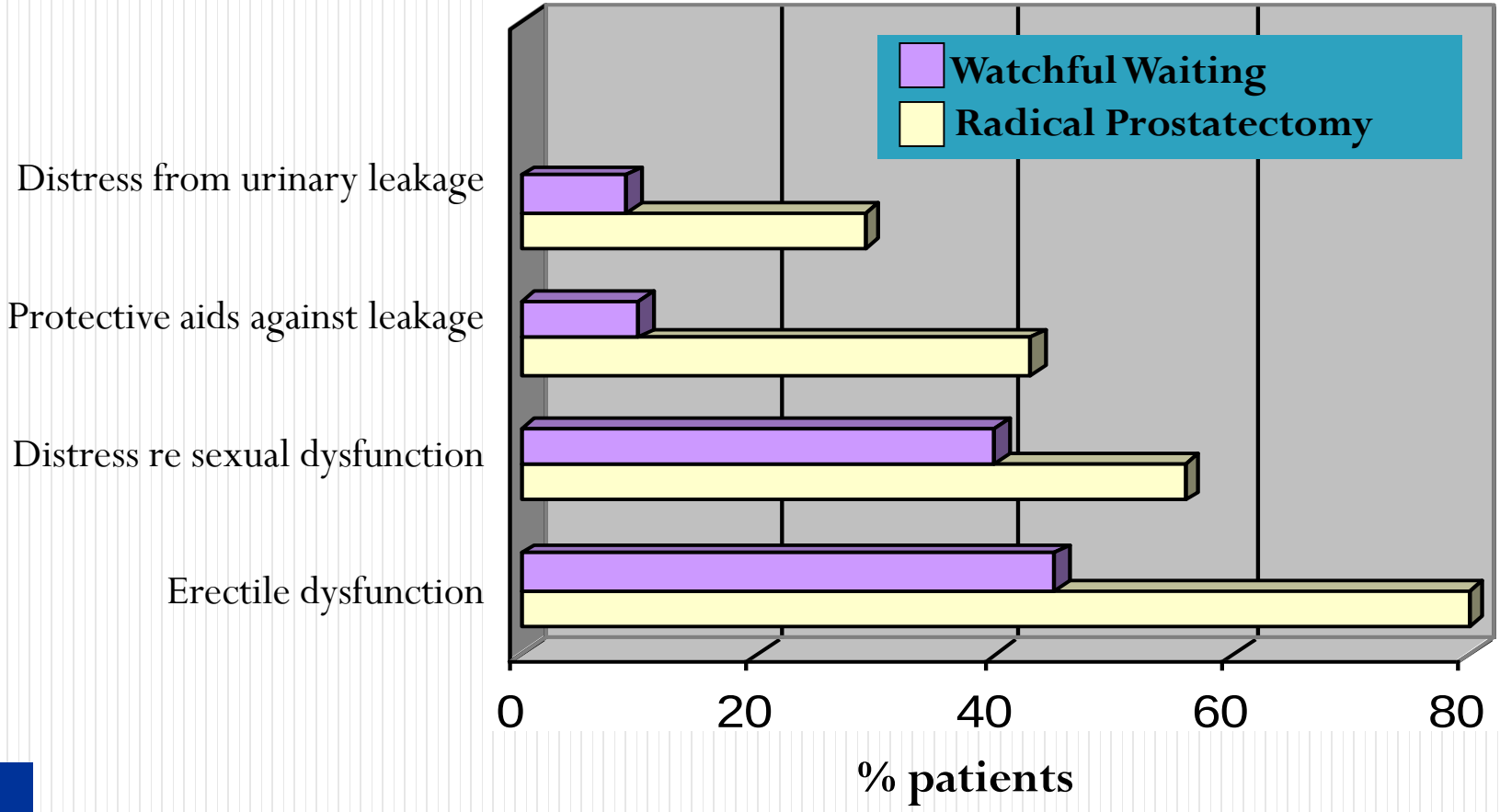
End Point	Cumulative Incidence				Absolute Risk Reduction with Radical Prostatectomy	Relative Risk with Radical Prostatectomy (95% CI)	P Value
	Radical Prostatectomy (N=347)		Watchful Waiting (N=348)				
	no. of events	*% (95% CI)*	*no. of events*	*% (95% CI)*	*percentage points (95% CI)*		
Death from prostate cancer							
All	63	17.7 (14.0 to 22.4)	99	28.7 (24.2 to 34.2)	11.0 (4.5 to 17.5)	0.56 (0.41 to 0.77)	0.001
Age							
<65 yr	31	18.3 (13.1 to 25.7)	58	34.1 (27.3 to 42.5)	15.8 (6.0 to 25.5)	0.45 (0.29 to 0.69)	0.002
≥65 yr	32	17.3 (12.5 to 24.0)	41	23.9 (18.2 to 31.5)	6.6 (−2.1 to 15.2)	0.75 (0.47 to 1.19)	0.19
Tumor risk							
Low	11	10.2 (5.8 to 18.0)	20	14.0 (9.1 to 21.5)	3.8 (−4.6 to 12.2)	0.54 (0.26 to 1.13)	0.17
Intermediate	24	15.1 (10.2 to 22.2)	50	39.3 (31.3 to 49.3)	24.2 (13.6 to 34.9)	0.38 (0.23 to 0.62)	<0.001
High	28	33.1 (24.0 to 45.7)	29	35.7 (26.3 to 48.5)	2.6 (−12.7 to 17.8)	0.87 (0.52 to 1.46)	0.84

THE ROYAL MARSDEN

The Institute of Cancer Research

A Randomized Trial Comparing Radical Prostatectomy with Watchful Waiting in Early Prostate Cancer

Scandinavian Prostatic Cancer Group Study NEJM (2002)



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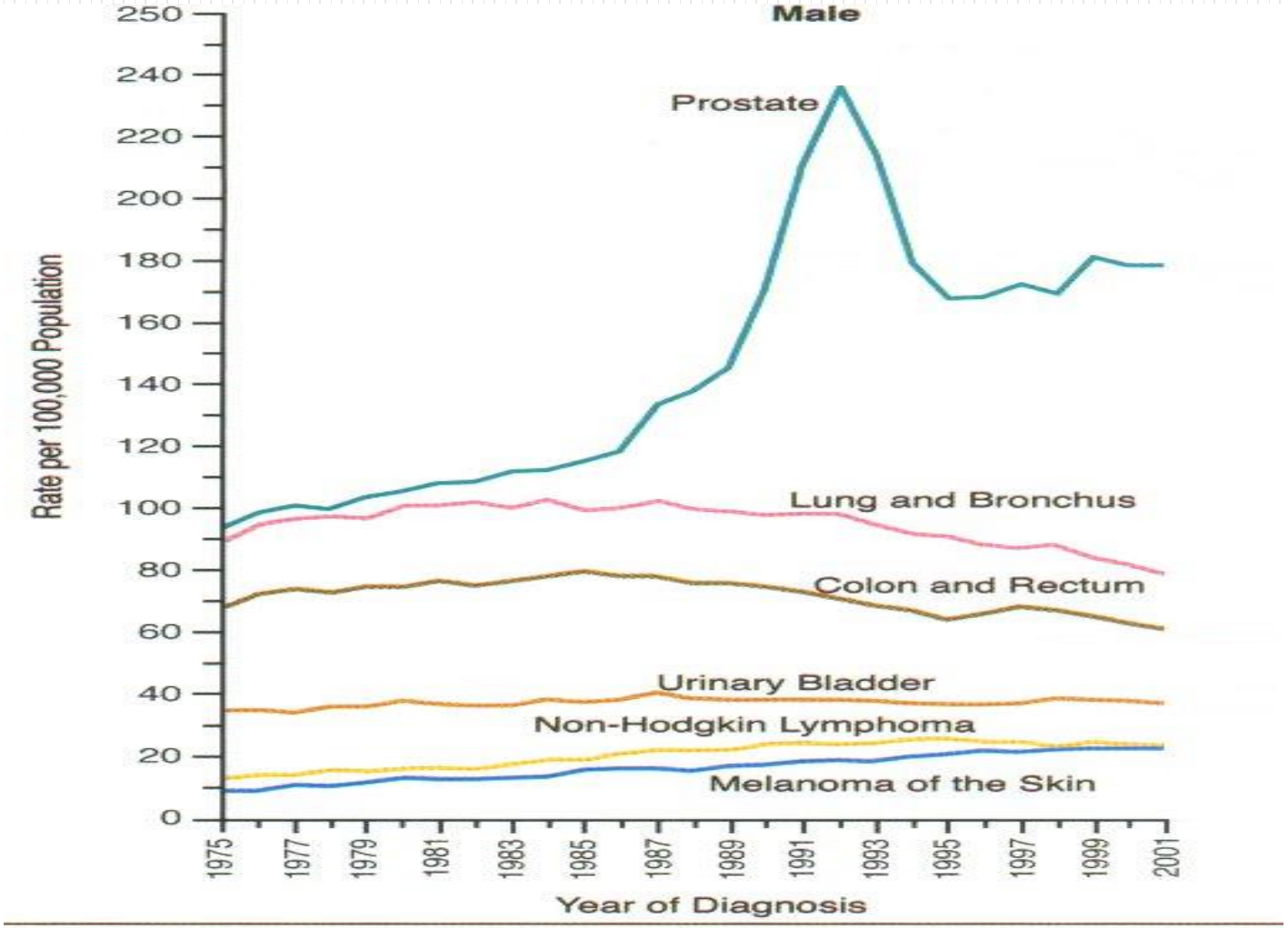
Prostate cancer is not what it used to be!

US prostate cancer incidence



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PIVOT Trial

Wilt et al NEJM July 2012 367; 203-13

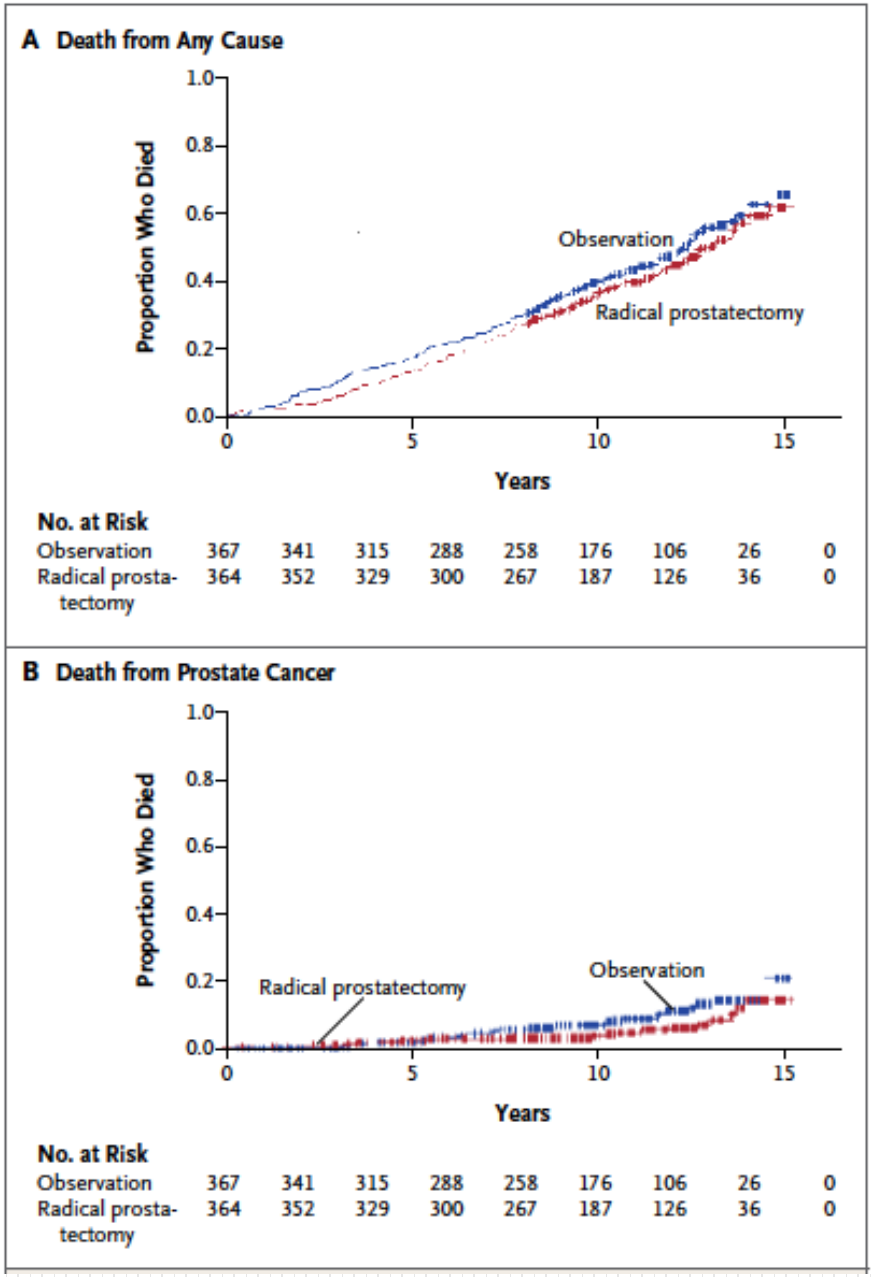
731 man 1994-2002
T1-T2 M0, PSA<50, age<75
Randomised to prostatectomy or observation.
Median FU 10 years.

No difference in primary endpoint of overall survival

Cause-specific mortality 5.8% vs 8.4% p=0.09

For high risk tumours cause specific mortality 9.1% vs 17.5% P=0.02. No significant benefit for intermediate or low risk.

Conclusions
Overall RP did NOT reduce all-cause or prostate-cancer-specific mortality



Active surveillance as a treatment option

- Aim
  - To select patients that will benefit from treatment.
- Who?
  - Suitable for radical treatment
  - Low volume cancer
  - Low grade (usually Gleason score ≤3+3)
- How?
  - Regular PSA/clinical assessment
  - Repeat biopsy
  - MRIs

Results of active surveillance of localised prostate cancer

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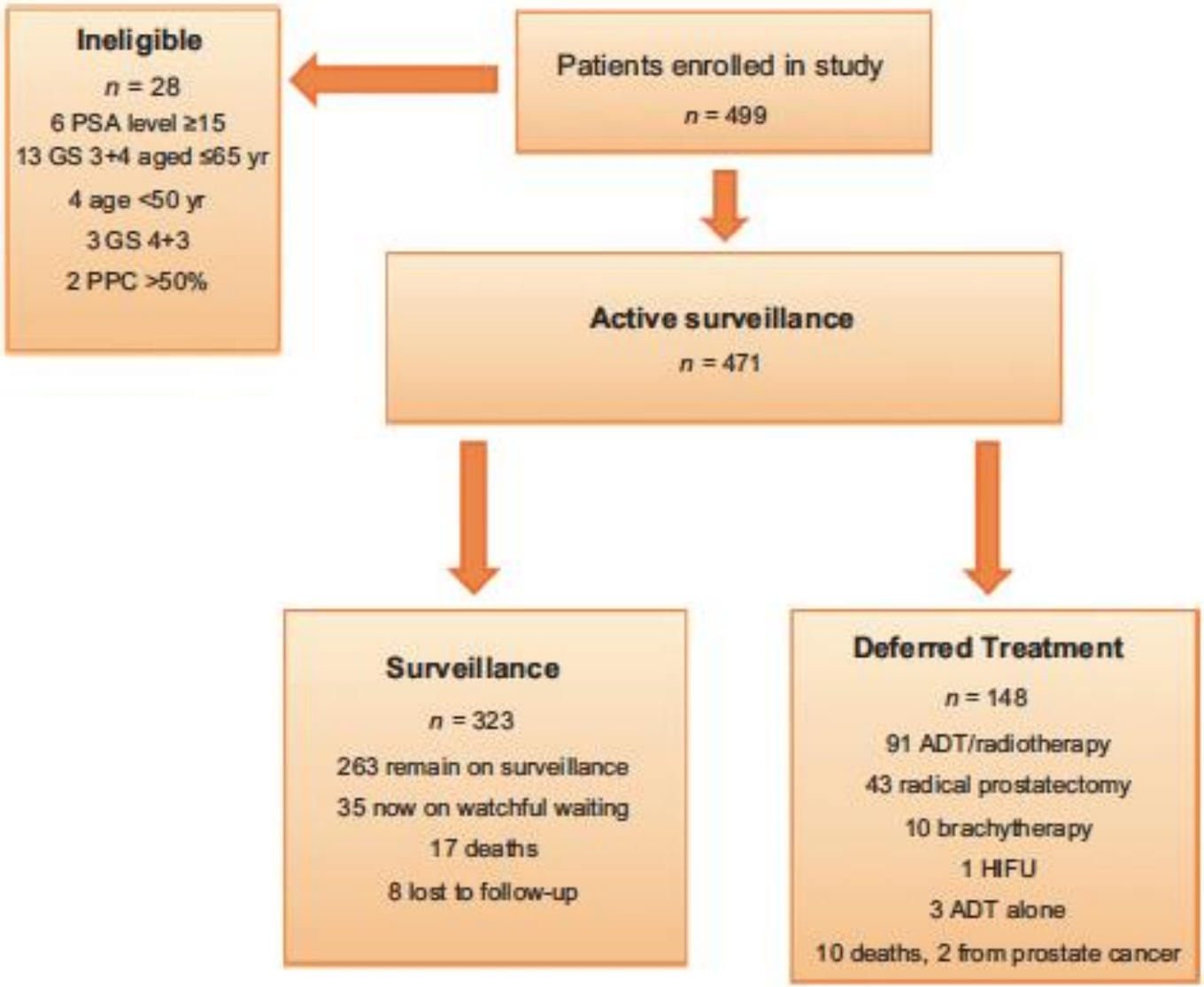
Active Surveillance: RMH Cohort 2013



Active Surveillance for Prostate Cancer

Royal Marsden Series : Selvadurai et al Eur Urol 2013

Eligibility: age 50-80; T1/T2; PSA<15; Gleason <3+3 (3+4 if aged >65); <50% cores +. <50% of any core involved.

Method: PSA and DRE q 3 monthly year 1, q4 monthly year 2 then 6 monthly
Re-biopsy every 2 years.

Treat if: PSAv > 1ng/ml/yr or if biopsy volume or grade progression

Results: 471 patients 2002- 2011 median FU 5.7 years
93% Gleason 3+3
median initial PSA 6.4

5 yr biopsy progression 22% (95% CI 16-29%)
Treatment-free at 5 years 70% (95% CI 65-75%)

155 patients treated; PSA failure post treatment 16% at 5 years
2 prostate cancer deaths. 25 unrelated deaths.

RMH prospective study of active surveillance of early prostate cancer

Indications for treatment

	Number	%
Biopsy progression	18	13%
PSA v >1ng/ml	56	41%
Both	23	17%
Patient decision	40	29%

Active Surveillance: RMH Cohort 2013

Time to adverse pathology

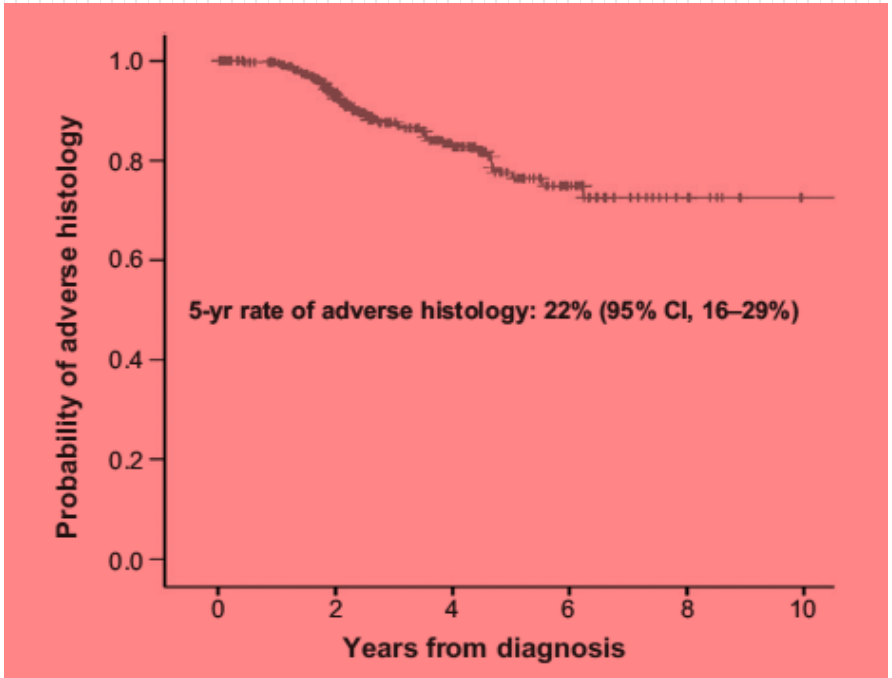


Fig. 2 – Time from diagnosis to adverse histology. CI = confidence interval.

Time to treatment

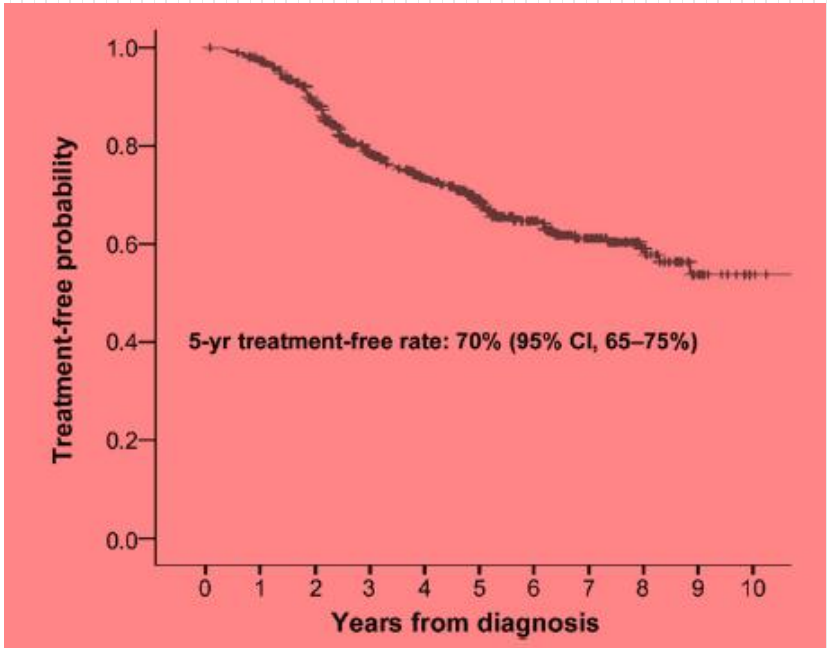


Fig. 3 – Time from diagnosis to deferred radical treatment. CI = confidence interval.

RMH prospective study of active surveillance of early prostate cancer

Multivariate analysis of time to treatment

Variable	P value	HR (95% CI)
%free PSA	<0.001	0.93 (0.89-0.97)
PSAV >1	<0.001	1.5 (1.2-1.9)
T stage	0.3	
PSAD	0.89	
Gleason 3+4	0.005	3.4 (1.4-8.0)

Surveillance Studies

	n	FU (med yr)	FFT (%@ yr)	PCM%
UCSF	321	3.8	67%@5yr	0
Toronto	450	6.8	70%@5yr	3%@10yr
PRIAS	2494	1.6	77%@2yr	0
Johns Hopkins	769	2.7	59%@5yr	0
RMH	471	5.7	70%@5yr	2%@8yr

FFT= Freedom from treatment
PCM=Prostate cancer mortality

ESMO Clinical Practice Guidelines for Prostate Cancer 2013

Management of local/loco-regional disease

•In men with low-risk disease, no benefit for active treatment has been demonstrated in overall survival. Observation should be discussed and should be an option for these patients.

• Options for patients with intermediate-risk prostate cancer include radical prostatectomy, external beam RT plus androgen deprivation therapy (ADT) or high-dose rate brachytherapy.

•Watchful waiting with delayed hormone therapy is an option for men who are not suitable for radical treatment [I, A].

National Institute for Health and Clinical Excellence (*NICE*) *guidelines*

3. Men with low-risk localised prostate cancer who are considered suitable for radical treatment should first be offered active surveillance.