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Cancer Center™

Prostate Cancer
Active Surveillance

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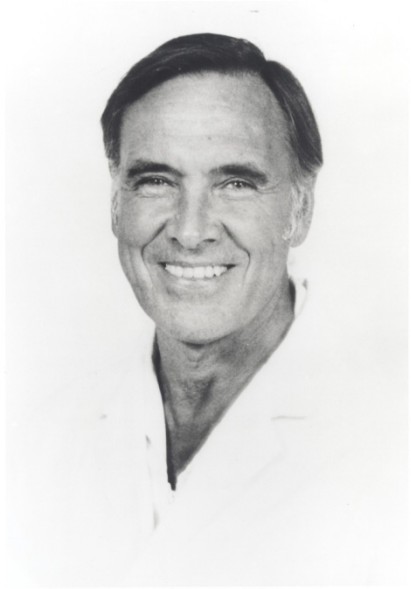

Willet Whitmore, Jr, MD

Chief of the Urology Service 1952 - 1983
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Whitmore's dilemma

"Is cure possible when it is necessary?
Is cure necessary when it is possible?"

- With active surveillance, the goal is to avoid radical therapy when *cure is possible but not necessary*.

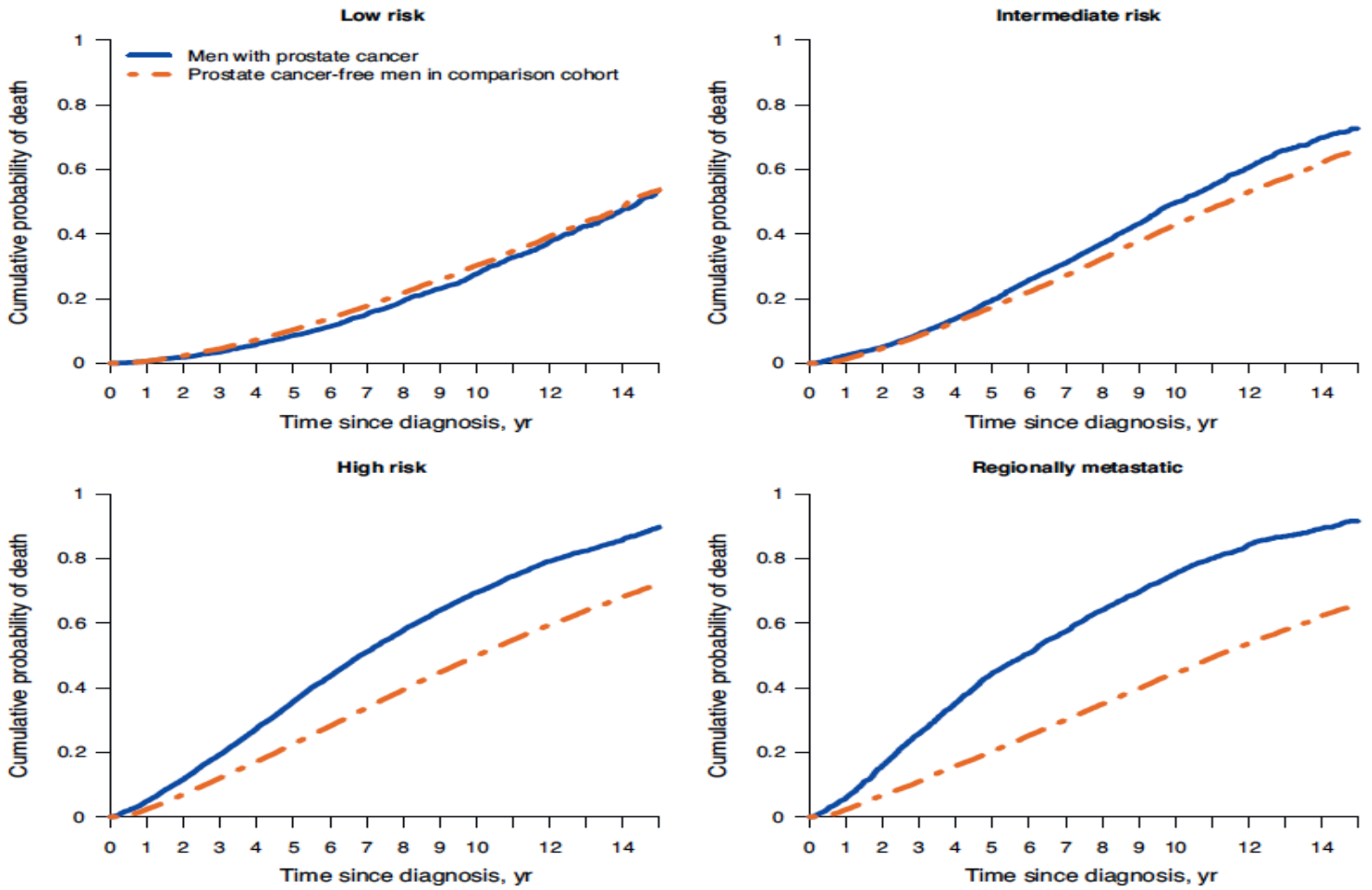
The right treatment for the right cancer
in the right patient at the right time

Why active surveillance?

Very few men die of low-risk prostate cancer

All-cause mortality in healthy men with prostate cancer on WW in Sweden

Charlson co-morbidity index 0



J Rider et al. Long-term outcomes according to risk category of prostate cancer. Nation-wide, population-based cohort. *Eur Urol* 2012.

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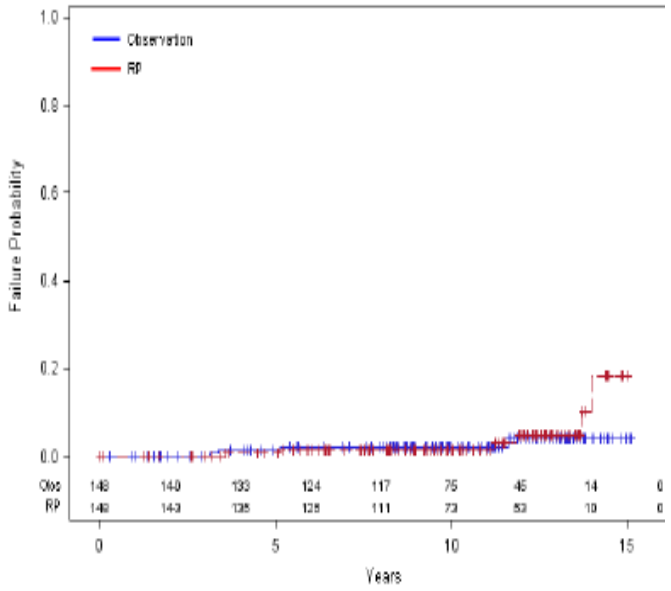
PIVOT randomized trial of RP v. WW

(N = 731, mean age 67)

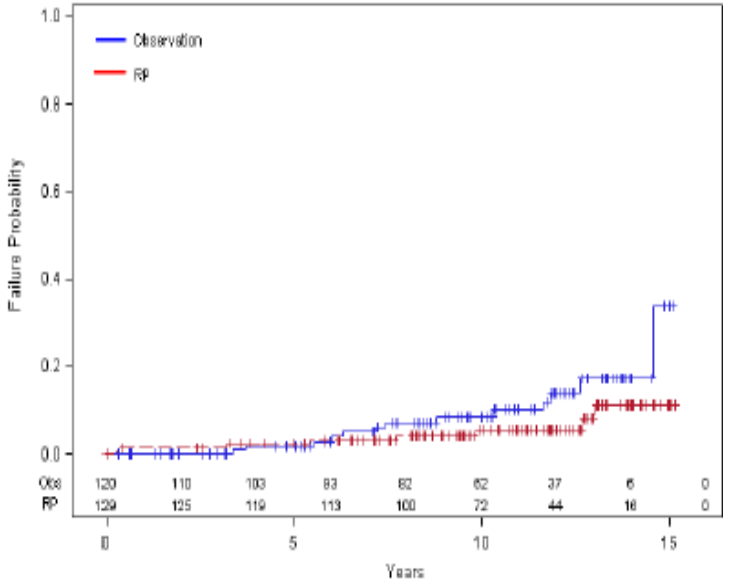
Prostate cancer mortality by risk category

$p = 0.13$



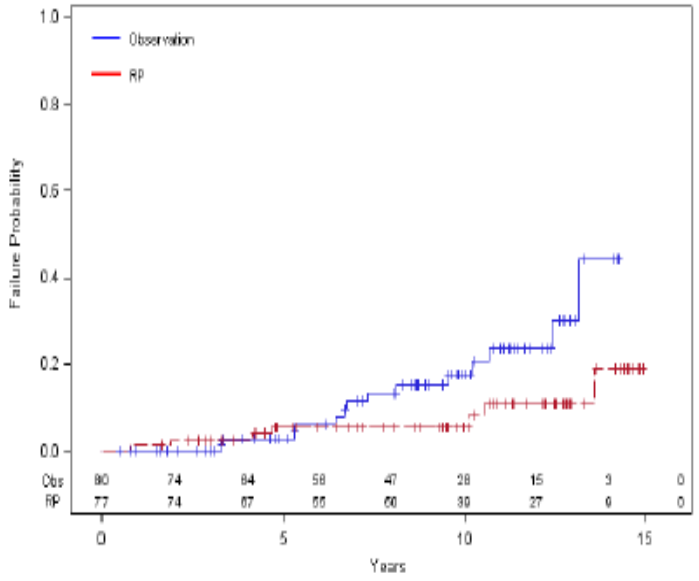
Low Risk
n = 296

$p = 0.84$



Intermediate Risk
n = 249

$p < 0.05$



High Risk
n = 157

From Wilt TJ et al. Radical prostatectomy versus observation for localized prostate cancer. *N Engl J Med* 2012;367:203-13 (Supplementary Appendix, Figure S3c-e).

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Increased use of AS for low-risk cancer after 2009

40% in 2013 (CapSURE) and 55% in 2018 (AQUA registry)

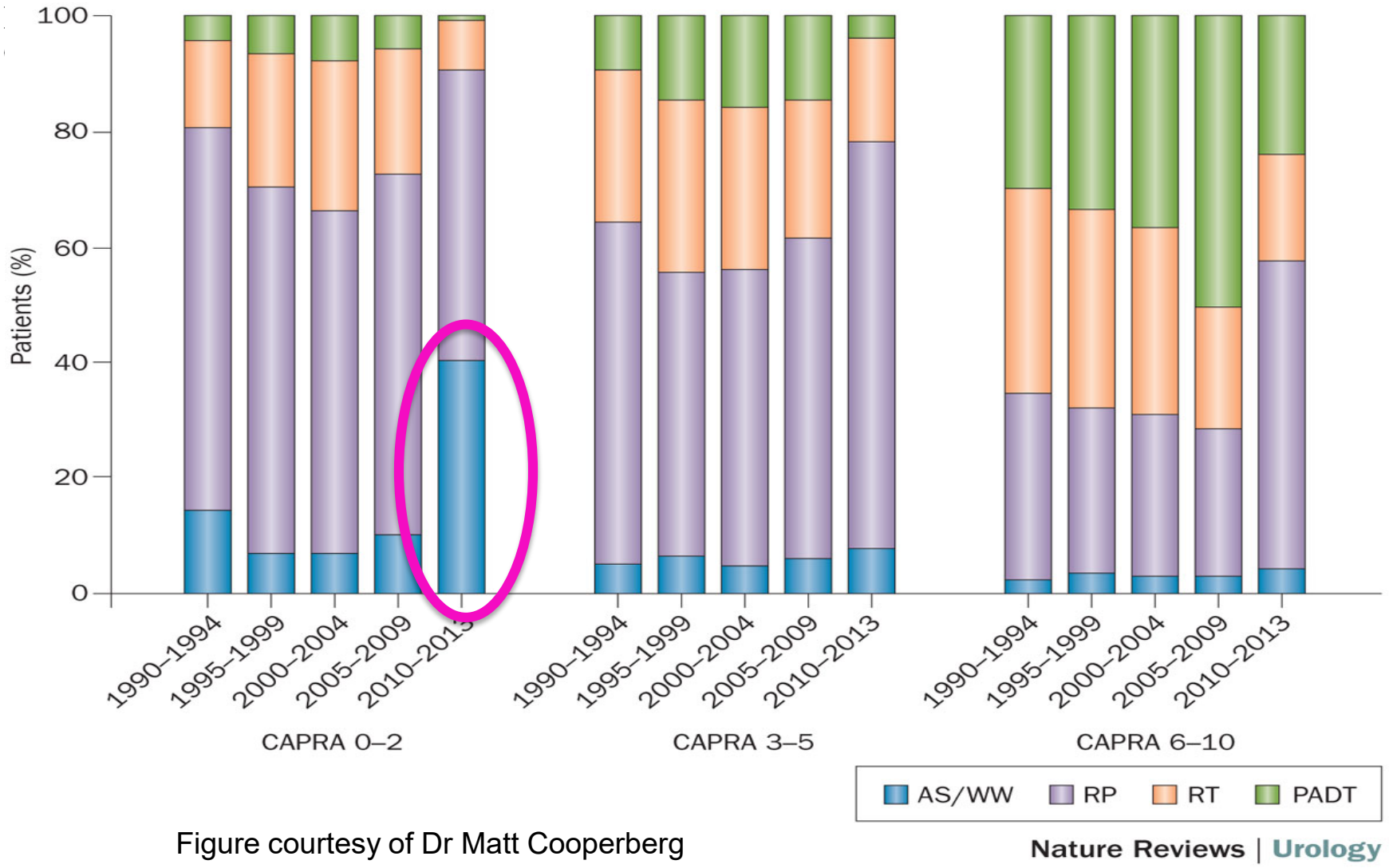

Figure courtesy of Dr Matt Cooperberg

Murphy, D. G. & Loeb, S. (2015) Growth of AS in the USA signals reduction in overtreatment. *Nat. Rev. Urol.* doi:10.1038/nrurol.2015.236

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Why Active Surveillance?

Not all prostate cancers need immediate treatment.

All treatments have potential side effects.

If men are observed carefully, the cancer can still be treated within the window of opportunity for cure.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

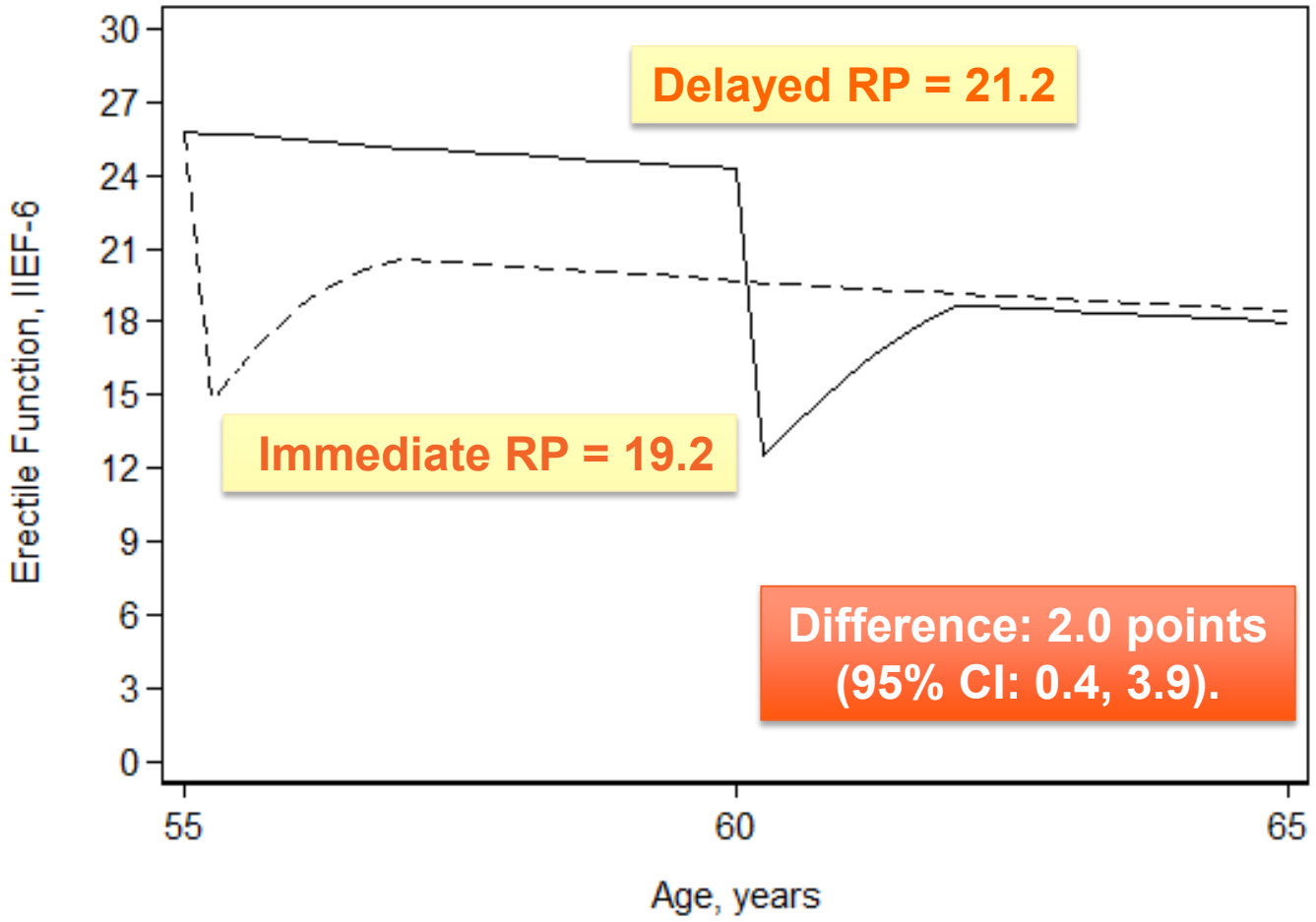
Quality of Life and Satisfaction with Outcome among Prostate-Cancer Survivors

Martin G. Sanda, M.D., Rodney L. Dunn, M.S., Jeff Michalski, M.D.,

NEJM2008;358:1250-61

- **Sexual function caused moderate or severe distress after 2 years in 43% of men after RP, 37% after XRT and 30% after brachy;**
- **Urinary function led to moderate or severe distress after 1 yr in 7% of patients after RP, 11% after XRT and 18% after brachy**
- **GI symptoms caused moderate or severe distress in 9% of patients 1 year after radiation (XRT or brachy)**

Delayed radical prostatectomy has greater average 10-year erectile function



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[Lee, AUA 2016]

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The NEW ENGLAND JOURNAL of MEDICINE

September 14, 2016

ORIGINAL ARTICLE

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

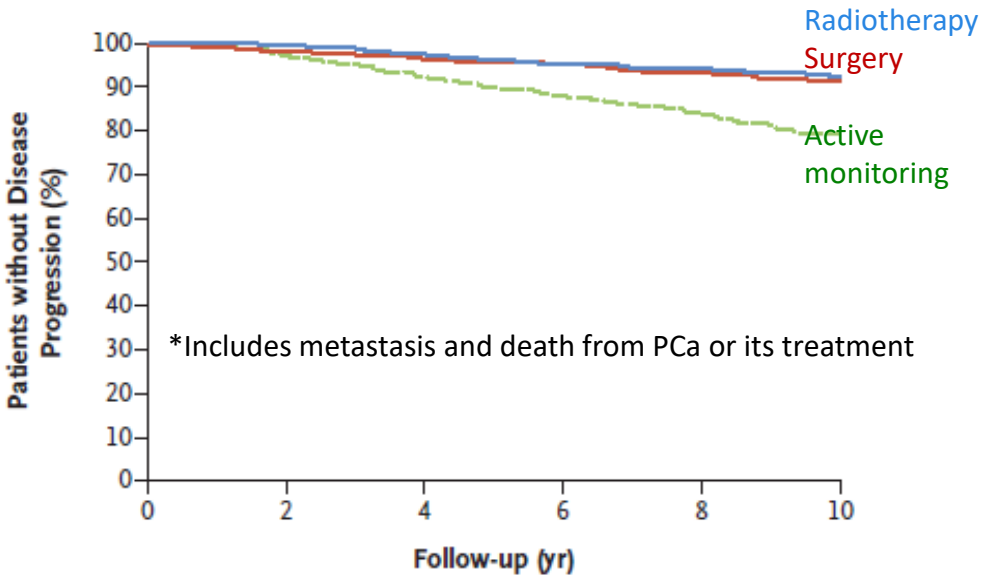
F.C. Hamdy, J.L. Donovan, J.A. Lane, M. Mason, C. Metcalfe, P. Holding, M. Davis, T.J. Peters, E.L. Turner, R.M. Martin, J. Oxley, M. Robinson, J. Staffurth, E. Walsh, P. Bollina, J. Catto, A. Doble, A. Doherty, D. Gillatt, R. Kockelbergh, H. Kynaston, A. Paul, P. Powell, S. Prescott, D.J. Rosario, E. Rowe, and D.E. Neal, for the ProtecT Study Group*

CAUTION ABOUT A.S.!

Prostate cancer-specific survival

No. at Risk	1643	1628	1605	1575	1286	746

Freedom from disease progression*



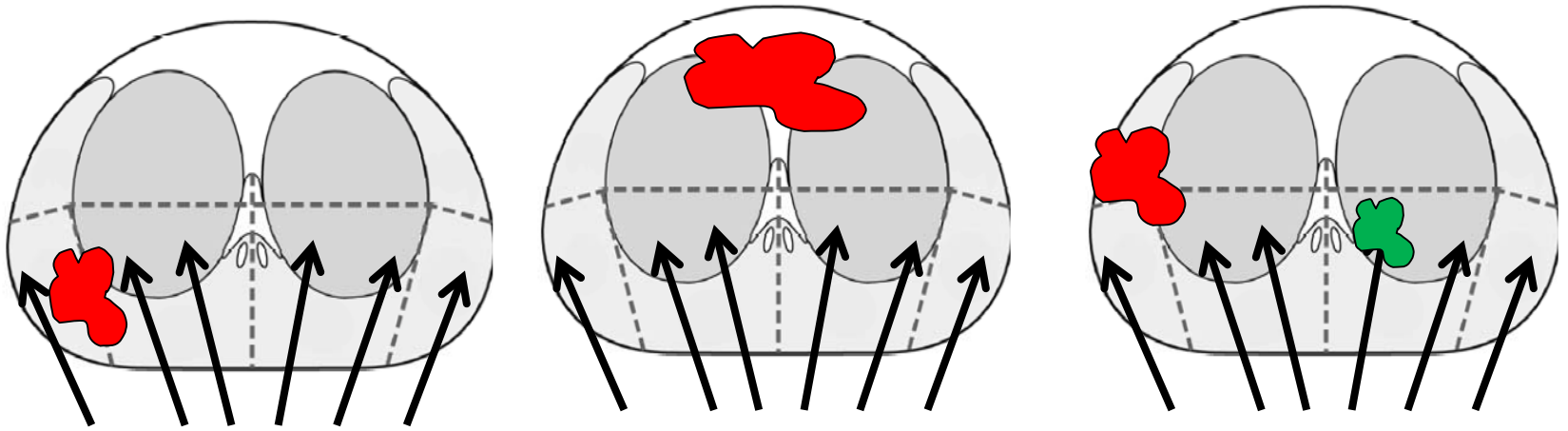
*Includes metastasis and death from PCa or its treatment

No. at Risk	1643	1601	1533	1467	1175	666

Active Surveillance - Who, How, When

- **Who:** low-risk prostate cancer patients based on clinical and pathological factors
- **How:** regular visits to include PSA , clinical examinations, imaging, and follow-up biopsies
- **When to treat:** based on reclassification of prostate cancer risk

Some clinically significant cancers are missed because of sampling error of the biopsy, and many men are diagnosed with clinically insignificant disease.



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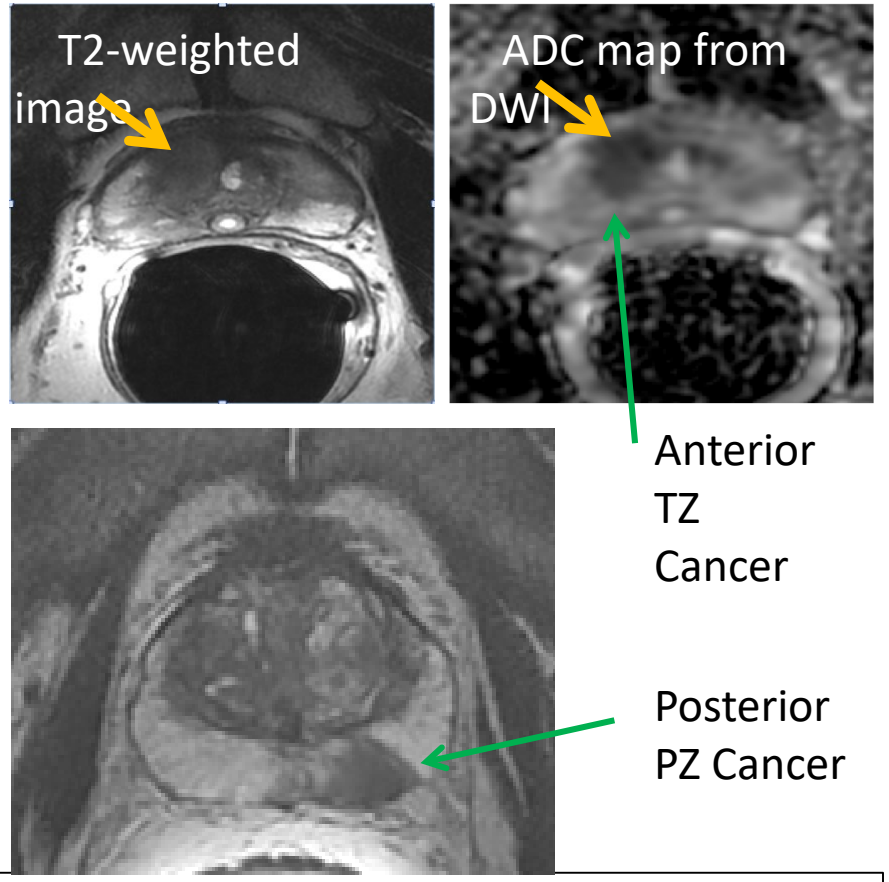
Restaging low-risk cancer with confirmatory biopsy and prostate MRI

Repeat ("confirmatory") systematic biopsy

In 104 men with low-risk cancer* on diagnostic bx (mean 10 cores, range 2-27)

Results: 26% negative
47% positive, unchanged
27% positive, more extensive/higher grade

*cT1-T2a, Gleason ≤ 3+3, PSA ≤ 10, ≤ 3 cores, ≤50% any core



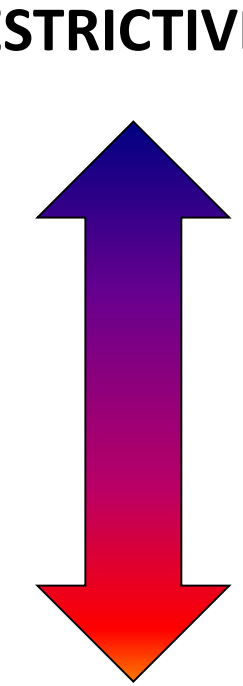
Berglund R et al *J Urol* 2008; 180:1964

- Multiparametric MRI with targeted (MR-Ultrasound fusion and visual) + systematic biopsies
- DRE with finger–guided biopsy of palpable nodule

Who are the right patients? - Eligibility

- Epstein criteria for low risk disease (most restrictive)
  - Gleason score ≤ 3 + 3
  - ≤ 2 cores positive and ≤ 50% of any core
  - Stage T1c
  - Ideal PSA density ≤ 0.15

- Royal Marsden (most permissive)
  - Gleason ≤3 + 4
  - PSA ≤ 15 ng/mL
  - Stage ≤ cT2a
  - ≤ 50% cores positive



Active Surveillance Entry Criteria - MSKCC

- Gleason score = 3 + 3, or low volume 3 + 4
- PSA ≤ 10 ng/mL
- ≤ 3 cores positive and ≤ 50% of any core (14 core biopsy)
- Stage ≤ T2a
- Re-staging – “confirmatory” biopsy
- 3T prostate MRI
- Genomic Profiling

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Active Surveillance Monitoring - MSKCC Protocol

- **Every 6 months – Clinical assessment and PSA**
- **Every 18 months - MRI**
- **Every 36 months - Prostate Biopsy**

Although significant variation exists in identifying patients eligible for active surveillance, detecting disease progression is equally challenging

Digital rectal exam

Serum PSA changes

Adverse findings on MRI

Serial prostate biopsy

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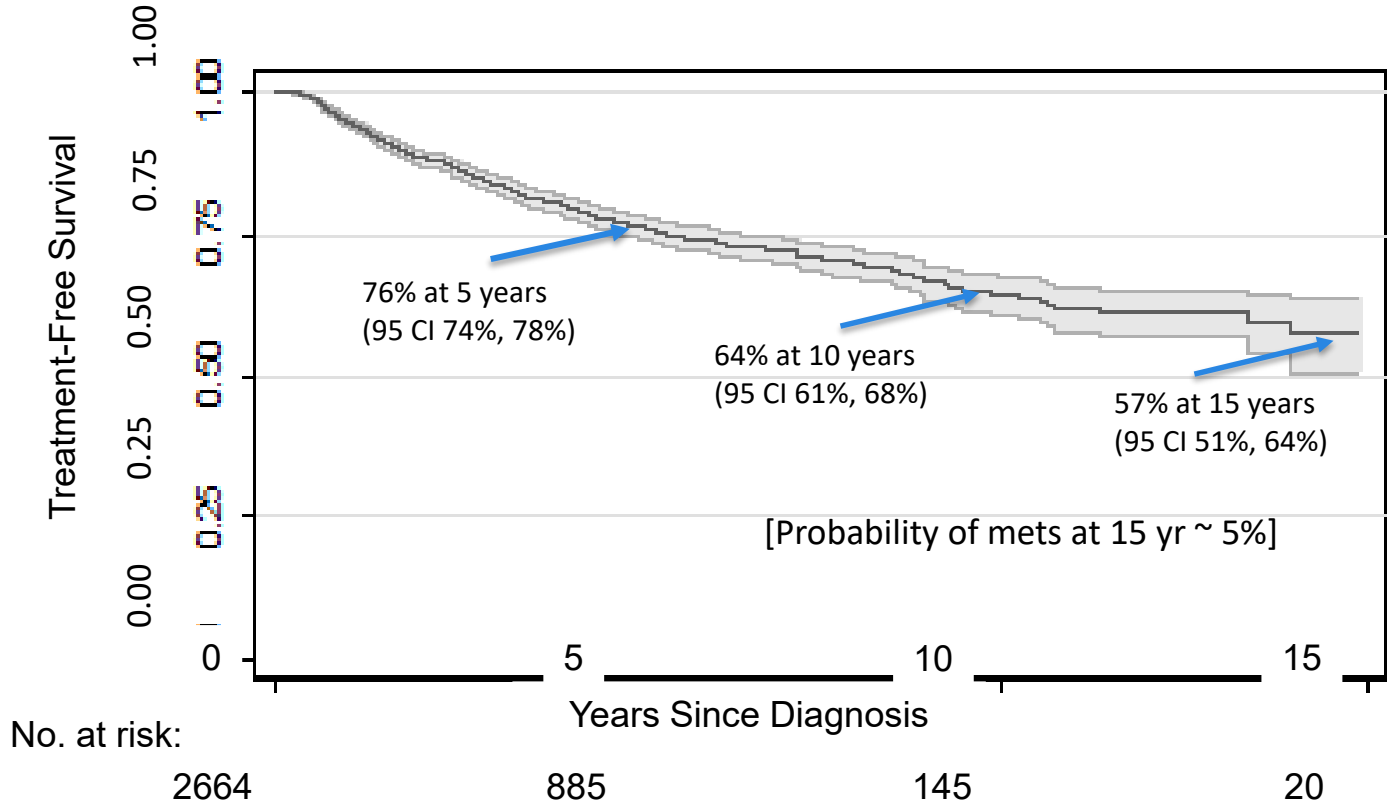
AS for Low-Risk Patients at MSK

Probability of Remaining on AS (N=2,664)



Adapted from Carlsson S, Ehdaie B, Touijer K, et al. 19th Annual Meeting of the Society of Urologic Oncology, November 28–30, 2018. Phoenix, AZ. Podium Abstract. Submitted to J Urol 2019.

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Reasons for Ceasing Active Surveillance

	No. (%)
Gleason 7 or greater on surveillance biopsy	15 (35)
Surveillance biopsy with more than 3 cores or more than 50% in single core	7 (16)
Change in pt preference	6 (14)
Increasing PSA without worsening biopsy features	2 (5)
MRI findings	2 (5)
Voiding symptoms	1 (2)
Bone metastases	1 (2)
Up staging via digital rectal examination	1 (2)
Unknown	12 (28)

Overall greater than 100% as some patients had multiple reasons.

[1]Eggener et al. J Urol 2013

Long-term follow-up of a Large Active Surveillance Cohort of Patients with Prostate Cancer –

Klotz L,. J Clin Oncol 33:272-277

- 993 patients – followed from 0.2-19.8 years
- 27% of patients went on to treatment,
  - 45% by 20 years
- 2.8% patients developed metastasis, follow up 9.6 years
  - Although only 13% of all patients had 3+4 disease, they accounted for 44% of patients who developed metastasis.
- 1.5% died of disease

Active Surveillance - In Conclusion

Immediate treatment in men with low risk disease does not confer a survival advantage.

Active Surveillance is an appropriate treatment option for some men, even men with a long life expectancy.

For many men, active surveillance becomes deferred treatment.

Careful patient selection and close monitoring is necessary.