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
Cumulative mortality: age 65-69, GS 6

Albertsen study of men with prostate cancer not treated with curative techniques
20-Year Outcomes Following Conservative Management of Clinically Localized Prostate Cancer

Albertsen, P. C. et al. JAMA 2005;293
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
A Randomized Trial Comparing Radical Prostatectomy with Watchful Waiting in Early Prostate Cancer

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


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

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

<table>
<thead>
<tr>
<th>End Point</th>
<th>Cumulative Incidence</th>
<th>Absolute Risk Reduction with Radical Prostatectomy</th>
<th>Relative Risk with Radical Prostatectomy (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rad Prostatectomy (N = 347)</td>
<td>Watchful Waiting (N = 348)</td>
<td>percentage points (95% CI)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>no. of events</td>
<td>% (95% CI)</td>
<td>no. of events</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td><strong>Death from prostate cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>63</td>
<td>17.7 (14.0 to 22.4)</td>
<td>99</td>
<td>28.7 (24.2 to 34.2)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 yr</td>
<td>31</td>
<td>18.3 (13.1 to 25.7)</td>
<td>58</td>
<td>34.1 (27.3 to 42.5)</td>
</tr>
<tr>
<td>≥65 yr</td>
<td>32</td>
<td>17.3 (12.5 to 24.0)</td>
<td>41</td>
<td>23.9 (18.2 to 31.5)</td>
</tr>
<tr>
<td>Tumor risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>11</td>
<td>10.2 (5.8 to 18.0)</td>
<td>20</td>
<td>14.0 (9.1 to 21.5)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>24</td>
<td>15.1 (10.2 to 22.2)</td>
<td>50</td>
<td>39.3 (31.3 to 49.3)</td>
</tr>
<tr>
<td>High</td>
<td>28</td>
<td>33.1 (24.0 to 45.7)</td>
<td>29</td>
<td>35.7 (26.3 to 48.5)</td>
</tr>
</tbody>
</table>
A Randomized Trial Comparing Radical Prostatectomy with Watchful Waiting in Early Prostate Cancer

Scandinavian Prostatic Cancer Group Study NEJM (2002)

- Distress from urinary leakage
- Protective aids against leakage
- Distress re sexual dysfunction
- Erectile dysfunction

The bar chart shows the percentage of patients experiencing distress in each category for Watchful Waiting (purple) and Radical Prostatectomy (yellow).
Prostate cancer is not what it used to be!

US prostate cancer incidence
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 \( \leq 3+3 \))

- **How?**
  - Regular PSA/clinical assessment
  - Repeat biopsy
  - MRIs
Results of active surveillance of localised prostate cancer
Active Surveillance: RMH Cohort 2013

Ineligible
- $n = 28$
  - 6 PSA level $\geq 15$
  - 13 GS 3+4 aged $\leq 65$ yr
  - 4 age $< 50$ yr
  - 3 GS 4+3
  - 2 PPC $> 50$

Patients enrolled in study
- $n = 499$

Active surveillance
- $n = 471$

Surveillance
- $n = 323$
  - 263 remain on surveillance
  - 35 now on watchful waiting
  - 17 deaths
  - 8 lost to follow-up

Deferred Treatment
- $n = 148$
  - 91 ADT/radiotherapy
  - 43 radical prostatectomy
  - 10 brachytherapy
  - 1 HIFU
  - 3 ADT alone
  - 10 deaths, 2 from prostate cancer
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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy progression</td>
<td>18</td>
<td>13%</td>
</tr>
<tr>
<td>PSA v &gt;1ng/ml</td>
<td>56</td>
<td>41%</td>
</tr>
<tr>
<td>Both</td>
<td>23</td>
<td>17%</td>
</tr>
<tr>
<td>Patient decision</td>
<td>40</td>
<td>29%</td>
</tr>
</tbody>
</table>
Active Surveillance: RMH Cohort 2013

Time to adverse pathology

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

5-yr rate of adverse histology: 22% (95% CI, 16–29%)

Time to treatment

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

5-yr treatment-free rate: 70% (95% CI, 65–75%)
### RMH prospective study of active surveillance of early prostate cancer

Multivariate analysis of time to treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>P value</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>%free PSA</td>
<td>&lt;0.001</td>
<td>0.93 (0.89-0.97)</td>
</tr>
<tr>
<td>PSAV &gt;1</td>
<td>&lt;0.001</td>
<td>1.5 (1.2-1.9)</td>
</tr>
<tr>
<td>T stage</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>PSAD</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>Gleason 3+4</td>
<td>0.005</td>
<td>3.4 (1.4-8.0)</td>
</tr>
</tbody>
</table>
## Surveillance Studies

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

FFT= Freedom from treatment  
PCM=Prostate cancer mortality
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.