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
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 attempted curative treatment
A Randomized Trial Comparing Radical Prostatectomy with Watchful Waiting in Early Prostate Cancer
Scandinavian Prostatic Cancer Group Study NEJM (2005)/(2014)

56% vs 69%
mortality HR .71
p<0.001

70% vs 72% p0.52
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>no. of events</td>
<td>% (95% CI)</td>
<td>no. of events</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>Death from prostate cancer</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>
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</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

% patients

Watchful Waiting
Radical Prostatectomy
Prostate cancer is not what it used to be!

US prostate cancer incidence

[Graph showing prostate cancer incidence compared to other cancers such as lung and bronchus, colon and rectum, urinary bladder, non-Hodgkin lymphoma, and melanoma of the skin.]
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-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

- Klotz et al 2014
- 993 men median FU 6.4 years
- treat if DT<3 years or Clinical $\uparrow$ or Gleason$\uparrow$
- Median FU 6.4 years
- 2.8% developed metastases
- 1.5% died of prostate cancer (CSS at 10 yrs 98%)
Active Surveillance for Prostate Cancer

Royal Marsden Series (Dr Chris Parker):

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

Results: 471 patients 2002-2011 median FU 5 years
  93% Gleason 3+3
  median PSA 6.4
  5 yr biopsy progression 22%
  Treatment-free at 5 years 70% (95% CI 86-92%)

Selvadurai et al 2013 Eur Urol
### RMH prospective study of active surveillance of early prostate cancer

**Indications for treatment**

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>%</th>
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<tbody>
<tr>
<td>Biopsy progression</td>
<td>18</td>
<td>13%</td>
</tr>
<tr>
<td>PSA ( v &gt;1 \text{ng/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>
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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>
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<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>
AS Trials

- PRIAS- International database with 4000 registered men on AS recruited between 2006-2013

- ProtecT—UK prospective RC phase 3 trial. Men from 337 primary care centres in 9 cities.
  
  230,000 men invited for PSA and counseled.
  100,000 attended and 82k had PSA.
  11% (8.5k) had PSA >3.0 of whom 87% had Bx.
  39% of Bx positive (mainly Gleason 6 T1C).
  2664 eligible for 3 arm trial of which 62% consented:
  Radical Px versus RT vs Active Surveillance.
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.