Prostate Cancer Screening

Stephen Mark
Urologist
Christchurch
Background

- Consultant Urologist 15 yrs
- Clinical lecturer Univ of Otago
- RACS Examiner 10yrs (senior 2 yrs)
- PI multiple Ca Pr clinical studies

- Exercise for Cancer prevention
- Know my own PSA
Objectives

- Prostate cancer overview
- PSA
- Screening studies
- Recommendations
Prostate cancer incidence 2008

Age standardised incidence rates for prostate cancer 2008

- Australia/New Zealand: 104
- Western Europe: 94
- Northern Europe: 86
- North America: 86
- Caribbean: 71
- Southern Africa: 54
- South America: 50
- Southern Europe: 50
- Central America: 35
- Central and Eastern Europe: 29
- Western Africa: 22
- Sub-Saharan Africa: 21
- Middle Africa: 16
- Eastern Africa: 15
- Western Asia: 14
- South-Eastern Asia: 8
- Eastern Asia: 8
- Northern Africa: 8
- South-Central Asia: 4
Prostate cancer

- Commonest solid malignancy diagnosed
- 3rd commonest cause cancer death (600/yr)
- Majority die with not because of Ca Pr
- Long natural Hx, benefit of treatment > 10y
- Screening studies inadequate follow up
- Reduction advanced disease / mortality (40%)
Current data

- PSA > 4 abnormal: 25% PPV for Ca Pr
- Biopsy: 2.5% sepsis, 0.5% retention
- Treatment: 35% Active Surveillance, 45% surgery, 20% radiotherapy

Metastatic disease morbid/expensive
Reduction in mortality
Prof Richard Ablin

Prof Immunology from Arizona

Discovered PSA: Prostate specific not Cancer specific
Normal protein, role to liquify sperm

No PSA level that diagnose Ca Pr

Increase PSA increase Ca Pr diagnosis

**PSA > 4 ng/ml is abnormal**

<table>
<thead>
<tr>
<th>Age Range (years)</th>
<th>Serum PSA Concentration (ug/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 - 49</td>
<td>&lt; 2.5</td>
</tr>
<tr>
<td>50 - 59</td>
<td>&lt; 3.5</td>
</tr>
<tr>
<td>60 - 69</td>
<td>&lt; 4.5</td>
</tr>
<tr>
<td>70 - 79</td>
<td>&lt; 6.5</td>
</tr>
</tbody>
</table>

Source: Oesterling JE et al. *JAMA* 1993; 270:860
Men over 50 yrs : PSA

- Healthy man
- Man with prostate cancer
- Missed cases

PSA suggests cancer where there is none
PSA misses these two cases
PSA finds these three cases
PSA in “younger” male

- Longitudinal population studies
- PSA < 0.6ng/ml 40-45 yrs… reassuring
- PSA > 0.6ng/ml 40-45 yrs… Incr diagnosis and death Ca Pr

- 2.5 - 4 times risk with positive family history
General Practitioners attitudes and practices towards PSA screening in asymptomatic men

Van Rij S**, Dowell T#, Nacey J^*
* Wellington Hospital, # Otago University Department of General practice, ^Otago University Department of Surgery

Percentage of population who had PSA testing by age bracket
(label indicates actual number of men tested)

<table>
<thead>
<tr>
<th>Age Bracket</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 to 44</td>
<td>12555</td>
<td>9%</td>
</tr>
<tr>
<td>45 to 49</td>
<td>23474</td>
<td>16%</td>
</tr>
<tr>
<td>50 to 54</td>
<td>35753</td>
<td>25%</td>
</tr>
<tr>
<td>55 to 59</td>
<td>40064</td>
<td>32%</td>
</tr>
<tr>
<td>60 to 64</td>
<td>45148</td>
<td>40%</td>
</tr>
<tr>
<td>65 to 69</td>
<td>38885</td>
<td>45%</td>
</tr>
<tr>
<td>70 to 74</td>
<td>30907</td>
<td>45%</td>
</tr>
<tr>
<td>75 to 79</td>
<td>20207</td>
<td>42%</td>
</tr>
<tr>
<td>80 and over</td>
<td>20044</td>
<td>25%</td>
</tr>
</tbody>
</table>
1000 survey sent and 280 responded
20% male 40-60yrs have PSA
GP initiates majority assessment
20% GP will not initiate discussion
35% PSA done over 75yrs
Difficulties:
Pre screen PSA, PSA in Control group and

No investigation in active arm with abnormal PSA
Recent update...

ERSPC
an update

Monique Roobol
Associate professor
Dept. of Urology
Erasmus University Medical Centre
Rotterdam
The Netherlands
Over 180000 enrolled
Design

Randomization

182,160 Men of all ages underwent randomization

162,388 Men in core age group (55–69 yr) underwent randomization

145 Died during randomization process
62 Were in the screening group
83 Were in the control group

72,891 Were assigned to the screening group
89,352 Were assigned to the control group
Results

Incidence

- Follow-up: median 9.0 years
- 126,462 screens, 2.1 screens per subject, PPV 24.1%
- Screening arm: 5,990 PC’s (8.2%)
- Control arm: 4,307 PC’s (4.8%)
- Excess incidence: 34 per 1000 men

- Follow-up: median 11.0 years
- 136,689 screens, (7.5% increase)
- 2.3 screens per subject, PPV 24.2%
- Screening arm: 6,963 PC’s (9.6%) (an increase of 14%)
- Control arm: 5,396 PC’s (6.0%) (an increase of 20%)
- Excess incidence: 35 per 1000 men
Screening outcome

NNI / NND

- NNI = 1410 (1/abs. Risk reduction)
- NND = 48 (1/abs. Risk reduction * excess incidence)

- NNI = 936 and NND = 33
- A 34% reduction caused by an increase of the absolute risk difference of PC mortality

- Data on year 10-11 after randomisation:
  - Rate ratio of 0.62, 38% relative reduction in favor of screening, p=0.003

- Mortality reduction in men actually screened was 0.71, p=0.001, a 29% relative reduction.
Results

Mortality

- Screening arm: 214 PC deaths (3.6%) (0.29%)
- Control arm: 326 PC deaths (7.6%) (0.37%)
- 15.8% of men died
- Rate ratio of PC death: 0.80, a 20% reduction in favor of screening, P=0.04
- Absolute risk reduction 0.71 death per 1000 men

- Screening arm: 299 PC deaths (4.3%) (an increase of 16%) (0.41%)
- Control arm: 462 PC deaths (8.6%) (an increase of 29%) (0.52%)
- 19.2% of men died (an increase of 17.7%)
- Rate ratio of PC death: 0.79, a 21% reduction in favor of screening, P=0.001
- Absolute risk reduction 1.07 death per 1000 men (an increase of 34%)
Conclusions

• Some men can benefit from PSA based screening
• Some men will not benefit, they might be harmed
• PSA based screening needs to be individualised, no population based programs at this point in time

• Currently the situation for men remains unchanged:
• Outcome needs to be balanced against number of screens/biopsies and overdiagnosis
Update

The 2012 data

- Confirmation of 2009 data, screening reduces prostate cancer mortality (p=0.001)
- No single center is responsible for the significant PC mortality reduction
- NNI and NND have reduced
- Only 19% of men randomised have died
- Longer follow-up is needed to assess effect of PSA based screening.
Mission to provide evidence based recommendations

Grade D for PSA (moderate to high certainty of no benefit and some harm)

PSA not accurate
Biopsy process morbid
Treatment morbid
Majority don’t need treatment
Consequences of treatment

Major morbidity: < 2%, Mortality < 0.1%
Contemporary Issues

- Increased length of life
- Increased expectation health service
- Younger male PSA may be more accurate
- Less treatment morbidity when younger
- Increased number on Active Surveillance
- Reduction in advanced disease (25% to 5%)
- Reduction in death rate
Prostate Cancer Taskforce

- Multidisciplinary group (GP, public, specialists)
- MoH directed
- Deliver guidelines on Prostate Cancer
- Not screening review
- Recommendations late 2012
Recommendations on PSA testing

- Not recommend screening
- Understand issues
- Review patient age / morbidities
- Listen to patient issues and respond
- Identify choice and present evidence
- Allow reflection
- Negotiate decision
If PSA abnormal

- Refer if DRE abnormal
- MSU
- Repeat in 4 – 6 weeks
- Understand local referral pathway

Refer if remains abnormal
Conclusion/ What I believe…

- Screening will diagnose and cure more cancer
- Potential harms and benefits need discussion
- Offered to all men with > 10 yr life expectancy
- Initial screen DRE and PSA, then PSA 1 -3 yrly
- Selective treatment offered
- Significant reduction in mortality