PSA & Prostate Cancer Screening

Dr Jonathan Rees MD MRCS MRCGP

Patient / Physician
Stimulus of Anxiety

Risk Factors for Progression

- Age over 70 with LUTS
- Moderate - severe symptoms i.e. IPSS > 7
- **PSA > 1.4 ng/ml**
- Prostate volume over 30ccs (i.e. feels enlarged on DRE)
- Flow rate <12 ml/sec

PSA can be useful in assessment of men with LUTS-BPH

Take Home Message 1
Should we routinely do a PSA test in a man presenting in primary care with lower urinary tract symptoms?

- Patient is usually worried about prostate cancer
- Partner is usually worried about prostate cancer
  - 71% of partners attending a LUTS clinic (1)
- GP is usually worried about prostate cancer
  - only 11% confident in distinguishing between BPH & Prostate Cancer (2)

2. Prostate of the Nation Report (Prostate Action)

Offer men information, advice and time to decide if they wish to have a PSA test if:

- Their LUTS are suggestive of bladder outflow obstruction due to BPE
- Their prostate feels abnormal on DRE
- They are concerned about prostate cancer

Screening with PSA may be better than you think

Take Home Message 2
**Screening for prostate cancer**

- European Randomised Study on Screening for Prostate Cancer
- Commenced in 1993
- 162,000 men aged between 55 and 69, from 8 countries
- Offered PSA screening at an average of once every 4 years or to a control group

**ERSPC**

- 82% of men accepting at least one offer of a PSA test
- Median follow up 9 years
- Cumulative incidence of prostate cancer was 8.2% (screening group) versus 4.8% (control group)
- Absolute risk difference for death was 0.71 fewer deaths per 1000 men in screening arm – 20% decrease in risk of dying (27% for those actually screened)
- 1410 screened men per CaP life saved.
- 48 treatments per life saved

**‘Gothenburg study’: Cumulative risk of death**

- Schroder FH et al. NEJM 2009; 360: 1320-8
**Prostate cancer mortality**

*Intention to screen analysis*

- Relative risk (RR) of PC death 0.56 (95% CI 0.39-0.82, P=0.002), a 44% relative reduction
- Absolute risk reduction: 34 per 10,000 men screened
- NNS: 293 (95% CI 177-799)
- NNT: 12 (in excess of control group)

**PSA screening in context**

- Number needed to screen to prevent 1 death:
  - ERSPC 1410 (offered) – 1068 (screened)
  - Gothenburg 293
  - Colorectal 1173
  - Breast 2000

**PSA screening in context**

- Reduction in relative risk of death:
  - ERSPC 20%
  - Gothenburg 44%
  - Colorectal 16%
  - Breast 15-20%

**A national screening programme with PSA is not going to happen**

Take Home Message 3
UK National Screening Committee

- Estimated cost of policy of screening men aged 50-74 with PSA 4 yearly:
  - £0.8 billion p.a.

UK NSC Conclusion

- The harms from prostate cancer screening using PSA are likely to outweigh the benefits. Screening cannot be justified on the current evidence:
  - PSA poor test – more sens / spec test needed
  - Unable to identify cancers which will progress vs. those which are indolent
  - Poor data on incidence and treatments

-Published May 2012

- "moderate or high certainty that the service has no benefit or that the harms outweigh the benefits"

- Grade D recommendation – ‘discourage the use of this service’

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BAUS position on screening
- NSC consultation assumes practice unchanged since PLCO/ERSPC commenced
- NICE Prostate Cancer guideline - active surveillance encouraged for low risk disease
- Gothenburg study not considered - early review required
- Not enough evidence for national programme but ‘more finely balanced than NSC report would suggest’
- BAUS concerned by reports that ‘significant numbers of men requesting PSA are refused the test by their GP’
- ‘Men should be aware that prostate cancer can be diagnosed earlier by PSA testing and biopsy, and that this can save lives’

http://www.baus.org.uk/AboutBAUS/publications/prostate-screening

Who gets screening at present?

Association of PSA testing (%) with Age

We currently screen the wrong patients

Take Home Message 4

BMJ review 2013
- Increasing age the most important risk factor for prostate cancer
- Most effective way to reduce incidence of prostate cancer is
  - Reduce PSA testing
  - Raise thresholds that define abnormality
- Screening with PSA results in small reduction in mortality & leads to considerable harms
- Physicians should recommend against PSA screening
- Most men diagnosed via screening have tumours that will not cause health problems (overdiagnosis) but almost all undergo early treatment (overtreatment)

Wilt TJ. Prostate cancer screening & the management of locally advanced disease. BMJ 2013; 346: f325

Williams N et al BJU Int 2011; 108: 1402-1408
Who gets screening at present?

<table>
<thead>
<tr>
<th>Association of PSA testing with study area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cambridge</td>
</tr>
<tr>
<td>Bristol</td>
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<tr>
<td>Leicester</td>
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<tr>
<td>Leeds</td>
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<tr>
<td>Bristol</td>
</tr>
<tr>
<td>Newcastle</td>
</tr>
</tbody>
</table>

[Williams N et al; BJU Int 2011; 108: 1402-1408]

PSA tests need to be targeted at the high risk patients

Take Home Message 5

Who is at high risk of prostate cancer?

- 'Baseline PSA test' – PSA at 40
- Race
- Family history

'PSA at 40'

Why might 40 be a good place to start?

- No Benign Prostatic Hyperplasia – 'background noise'
- Less prostatitis
- Early stage of disease if found
- Excellent results of treatment
- BUT ... Unnecessary anxiety, biopsy, treatment
Malmö Prevention Project

- PSA testing very low in Sweden, stable population
- 1974-1986, >21,000 men <50 years provided blood within a cardiovascular study
- Prostate cancers were identified in 1999 using the Swedish cancer registry.
- Archived blood samples retrieved

Ulfert D, Cronin AM, Björk T et al. Prostate-specific antigen at or before age 50 as a predictor of advanced prostate cancer diagnosed up to 25 years later: a case-control study. BMC Med 2008; 6: 6

<table>
<thead>
<tr>
<th>Total PSA (ng/mL)</th>
<th>Controls</th>
<th>Cases</th>
<th>Odds Ratio</th>
<th>Probability of Prostate Cancer (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00-0.50</td>
<td>543</td>
<td>68</td>
<td>reference</td>
<td>4</td>
</tr>
<tr>
<td>0.51-1.00</td>
<td>474</td>
<td>147</td>
<td>2.51</td>
<td>8</td>
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<tr>
<td>1.01-2.00</td>
<td>173</td>
<td>146</td>
<td>7.02</td>
<td>20</td>
</tr>
<tr>
<td>2.01-3.00</td>
<td>23</td>
<td>55</td>
<td>19.1</td>
<td>41</td>
</tr>
<tr>
<td>≥ 3.01</td>
<td>9</td>
<td>46</td>
<td>35.8</td>
<td>60</td>
</tr>
</tbody>
</table>

PSA was a very strong predictor of prostate cancer up to 25 yrs subsequently.

Levels of 2–3 ng/mL, (within normal range), associated with increase in odds for subsequent prostate cancer of more than 19-fold.

80% of advanced cancers occurred in men with PSA levels above the median at age 44–50 years.

A national recommendation?

- Single PSA test as predictor for the long-term risk of prostate cancer at 40-45 yrs.
- PSA >0.65 ng/mL (median) → further PSA testing should be considered.

<table>
<thead>
<tr>
<th>PSA Level</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.65-1ng/ml</td>
<td>PSA test every 3-4 years</td>
</tr>
<tr>
<td>&gt;1ng/ml</td>
<td>Annual PSA tests</td>
</tr>
<tr>
<td>&lt;0.65ng/ml</td>
<td>Low risk, further testing 55-60 years</td>
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</tbody>
</table>
**Family history**

- Risk increases with:
  - Increasing number of affected relatives
  - Degree of relatedness
  - Younger age at diagnosis

- Lifetime absolute risk of prostate cancer:
  - Man with no FHx: 8%
  - Man with father affected >60: 12% (worse if brother)
  - Man with 3 or more affected relatives: 35-45%

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**Race**

- Higher incidence of prostate cancer in Afro-Caribbean men
- UK age-adjusted incidence of 166 / 100,000 black men vs. 56.4 / 100,000 white men; Relative risk approx 3
- No difference African vs. Caribbean ethnic origin
- World highest – Kingston 304 / 100,000

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**We need better tools in primary care to aid interpretation of PSA results**

Take Home Message 6
Risk based approach to screening

We need to avoid overtreatment of men with low risk prostate cancer

Take Home Message 7

Overtreatment

- Should low grade disease (Gleason 6) be reclassified as benign / pre-malignant / non-lethal?

- NICE guideline recommending increased role for active surveillance

Conclusion

- Potential for impacting on prostate cancer mortality whilst reducing harm from overtreatment of low risk patients if:
  - PSA tests were targeted at higher risk patients
  - Referral +/- biopsy were carried out on a more sophisticated risk based model
  - Treatment was reliably reserved for those with high risk disease

Pretty
Straightforward
Actually??