Do you think we should have a national screening programme for Prostate Cancer using PSA?

- YES – it’s an outrage, women have breast cancer screening etc
- NO – a complete waste of time, PSA is useless, overdiagnosis...
- Maybe.....
- Don’t know.....
• PSA testing is not usually recommended for asymptomatic men with < 10 years life expectancy
• Before having a PSA test men should not have:
  • had a DRE in the previous week
  • an active UI (PSA may remain raised for many months)
  • ejaculated in previous 48 hours
  • exercised vigorously in previous 48 hours
  • had a prostate biopsy in previous 6 weeks

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

TAKE HOME MESSAGE 1

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

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

The man with LUTS

- 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)

PSA testing in men with LUTS

- 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

2. Prostate of the Nation Report (Prostate Action)
Screening with PSA may be better than you think

TAKE HOME MESSAGE 2

ERSPC

- 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

Screening and prostate cancer mortality in a randomised European study. Schroder FH et al. NEJM 2009; 360: 1320-8

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

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

TAKING 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’
BMJ review 2013

- Increasing age the most important risk factor for prostate cancer
- New risk that has not yet reached incidence of prostate cancer
- Reduced by testing
- Undesired side effects of testing unnecessary
- 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)

TAKE HOME MESSAGE 4

Who gets screening at present?

Association of PSA testing (%) with Age

- PSA tests need to be targeted at the high risk patients

TAKE HOME MESSAGE 5

We currently screen the wrong 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

Odds of prostate cancer diagnosis by plasma total PSA levels at baseline venepuncture.

<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>66</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>
</tr>
<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>38.8</td>
<td>60</td>
</tr>
</tbody>
</table>

MPP continued

- 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.
  - 82% 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 2-4 yrs</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>
</tr>
</tbody>
</table>

Conclusion: A baseline serum PSA should be offered to all men 40-45 yr of age to initiate a risk-adapted follow-up approach with the purpose of reducing PCa mortality and the incidence of advanced and metastatic PCa. In the future, the development and
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%

Risk based approach to screening

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

TAKE HOME MESSAGE 6

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

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

Melbourne Consensus Statement

1. For men aged 50–69, level 1 evidence demonstrates that PSA testing reduces prostate cancer-specific mortality and the incidence of metastatic prostate cancer.

2. Prostate cancer diagnosis must be uncoupled from prostate cancer intervention.

3. PSA testing should not be considered on its own, but rather as part of a multivariable approach to early prostate cancer detection.

4. Baseline PSA testing for men in their 40s is useful for predicting the future risk of prostate cancer.

5. Older men in good health with over ten year life expectancy should not be denied PSA testing on the basis of their age.

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

PSA

- Pretty
- Straightforward
- Actually??