Managing Prostate Cancer in General Practice

Tuesday 18th September 2018
Presenters: Prof Jon Emery
Assoc Prof Declan Murphy

The education has been developed in partnership with Cancer Council Victoria, the University of Melbourne and supported by the Victorian Government.

Acknowledgement of Country

We recognise the traditional custodians of the land and sea on which we live and work.

We pay our respects to Elders past and present.
Where is my control panel?

Look in the top right of your screen for a small red arrow. Click on it to open the rest of the control panel.

Listen only mode

You have been placed on "mute" to optimise the learning experience for you and your peers.

Use the question box function to talk to us.
Learning Outcomes

By the end of this online QI & CPD activity you should be able to:

1. Describe the current evidence related to prevention, early detection, presentation, initial investigations and referral for prostate cancer
2. Use evidence-based tools and resources to determine patients risk of prostate cancer and to help asymptomatic patients decide whether to proceed with PSA testing
3. Identify how to access local diagnostic imaging and specialist appointment referral pathways for patients presenting with signs and symptoms of prostate cancer
Polling question

How would you rate your current awareness of the Optimal Care Pathways?

- Excellent
- Very good
- Good
- Fair
- Poor
- None

Optimal Care Pathways

- Facilitate consistent care based on best evidence and practice
- Guides to optimal care across 15 tumour types for health professionals, including quick reference guides for GPs
- Have become recognised as a “standard of care”
- Encourage concept of an integrated pathway of care
- High level overview of what, where and who
- Emphasises the importance of communication across care sectors and at transition points for patients and carers
- Tool to assist health services, clinicians, service planners to map, plan and benchmark services
- Inform quality improvement projects by identifying gaps
Prostate Cancer

Overview

**Key messages**
- Most common cancer diagnosed in men
- Very high 5-year survival rate
- Significant sub-group report poor quality of life post treatment

**GP role**
- Delivering prevention messages
- Being aware of risk factors
- Informing and assisting men with their decision regarding PSA-based testing
- Knowing how to investigate symptoms
- Where to refer
Prostate cancer statistics

Estimated number of new cases of prostate cancer diagnosed in 2018

17,729 males

Estimated % of all new male cancer cases diagnosed in 2018

23.8%

Estimated number of deaths from prostate cancer in 2018

3,500 males

Estimated % of all male deaths from cancer in 2018

12.7%

Prostate cancer statistics

Chance of surviving at least 5 years (2010–2014)

95%

Males living with prostate cancer at the end of 2013 (diagnosed in the 5 year period 2009 to 2013)

93,343
Risk factors: age

![Risk factors graph]

Risk factors

- Age – most important – risk increases from >50 years
- Family history – brother or father, especially if before 60 years old
- Race – African descent
- Possibly diets high in animal fats, dairy products or calcium

Genetic factors

- Known mutations in BRCA1 or BRCA2 genes
- Lynch syndrome
Polling question

In men at average risk of prostate cancer who wish to be tested, you should perform the following:

Options:
- DRE plus PSA with cut off value of 3ng/ml
- DRE plus PSA with cut-off value of 4ng/ml
- PSA alone with cut-off value of 3ng/ml
- PSA alone with cut-off value of 4ng/ml

Testing recommendations

- Australian consensus guidelines 2016
- Key recommendations about PSA testing
- Rationale and evidence
- Implications for practice
US PLCO trial results at 13 years

RR = 0.79 (95% CI = 0.69-0.91 p = 0.001)

European ERSPC trial results at 13 years

RR = 0.79 (95% CI = 0.69-0.91 p = 0.001)

Source: Schroder et al Lancet 2014 (n = 162,388 men randomised)
Summary of ERSPC results: 11 and 13 years follow-up

<table>
<thead>
<tr>
<th>Results</th>
<th>Results up to 11 years of follow-up</th>
<th>Results up to 13 years of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median follow-up (years)</td>
<td>11.0</td>
<td>13.0</td>
</tr>
<tr>
<td>Number of prostate cancer deaths in intervention group</td>
<td>299</td>
<td>355</td>
</tr>
<tr>
<td>Number of prostate cancer deaths in control group</td>
<td>462</td>
<td>545</td>
</tr>
<tr>
<td>Relative risk of death from prostate cancer – intervention group relative to control group</td>
<td>0.79 (95% CI 0.68–0.91)</td>
<td>0.79 (95% CI 0.69–0.91)</td>
</tr>
<tr>
<td>Absolute difference in risk of death from prostate cancer between intervention group and control group</td>
<td>-0.10 per 1,000 person years</td>
<td>-0.11 per 1,000 person years</td>
</tr>
<tr>
<td>Number needed to invite (NNI) to avert one prostate cancer death</td>
<td>1,055</td>
<td>781</td>
</tr>
<tr>
<td>Number needed to detect (NND) to avert one prostate cancer death</td>
<td>37</td>
<td>27</td>
</tr>
</tbody>
</table>


Testing recommendations

- Offer men opportunity to discuss benefits and harms of PSA testing before making a decision
- Harms of PSA testing may outweigh benefits particularly in men 70+ years
- Men at average risk who decide to have regular testing
  - Should be offered PSA every 2 years from 50 – 69 years
  - Offer further investigation if PSA >3.0ng/mL
Testing recommendations

• Follow-up of raised PSA
  • If initial PSA 3-5.5 ng/ml, measure free-to-total when repeat PSA
  • If repeat total PSA >5.5 ng/ml, refer to urologist
  • If repeat total PSA 3-5.5 ng/ml and free-to-total PSA is <25%, refer to urologist
Polling question

Your patient, Barry, mentions his brother had prostate cancer diagnosed at 58. From what age should you offer PSA testing?

Options:
40
45
50
55
PSA testing in men with a family history of prostate cancer

<table>
<thead>
<tr>
<th>Relative risk of prostate cancer</th>
<th>Mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age 40</td>
</tr>
<tr>
<td></td>
<td>(mortality at age 50 minus mortality at age 40)</td>
</tr>
<tr>
<td>1.0 (average risk)</td>
<td>2.3</td>
</tr>
<tr>
<td>2.0</td>
<td>4.7</td>
</tr>
<tr>
<td>2.5</td>
<td>5.8</td>
</tr>
<tr>
<td>3.0</td>
<td>7.0</td>
</tr>
<tr>
<td>3.5</td>
<td>8.2</td>
</tr>
<tr>
<td>4.0</td>
<td>9.3</td>
</tr>
<tr>
<td>5.0</td>
<td>11.7</td>
</tr>
<tr>
<td>6.0</td>
<td>14.0</td>
</tr>
<tr>
<td>7.0</td>
<td>16.4</td>
</tr>
<tr>
<td>8.0</td>
<td>18.7</td>
</tr>
<tr>
<td>9.0</td>
<td>21.1</td>
</tr>
<tr>
<td>10.0</td>
<td>23.6</td>
</tr>
</tbody>
</table>

Testing recommendations

Men at increased risk to their family history

- Father or one brother diagnosed with prostate cancer should be offered PSA testing every 2 years from 45 – 69 years
- Father and 2 or more brothers diagnosed with prostate cancer should be offered PSA testing every 2 years from 40 – 69 years
Signs & Symptoms

- Most men with prostate cancer do not have symptoms
- Individual symptoms are weak predictors of prostate cancer diagnosis
- Most important predictor on its own is abnormal DRE so important in assessment of symptomatic men

Supportive care resources

- Cancer Council
  - Phone 13 11 20
- OCP - quick reference guide & full version
- What to expect: only if a positive diagnosis
- LiveLighter program
  - Resources for HPs and Patients
- Quitline
  - [www.quit.org.au](http://www.quit.org.au) for HP referral
  - GP software link
  - 13 78 48
Localised Prostate cancer:  
Active surveillance | Management choices

Associate Professor Declan Murphy  
Consultant Urologist & Director of GU Oncology  
Peter MacCallum Cancer Centre | Melbourne

Disclosures

None relevant
Outline

Active surveillance
- Background
- Utilisation
- How we do it
- Some concerns

Decision-making in active management
- Surgery or Radiotherapy
- NAVIGATE study

Principles of active surveillance
Avoidance of intervention (and side-effects of intervention) for localized prostate cancer, without compromising likelihood of metastases and death from prostate cancer
Outline

Active surveillance
- Background
- Utilisation
- How we do it
- Some concerns

Utilisation is increasing
AS for low-risk has surged from 6.7% to 40.4%
AS for intermediate-risk in 7.6% of cases
(RP in high-risk has increased from 25.3% to 53.3%)
Updated 2018

Population registry
- Victoria, Australia
2009-2013
N=980 on active surveillance
- 37% of all low-risk
- 8.9% of all intermediate-risk
At one year, 17% convert to intervention

n= 3129 on active surveillance
- 55.9% of all low-risk
- 15.3% of all intermediate-risk

Weerakoon et al. BJUI 2015;115(s5):50-6

Long-term safety data is good
(for low-risk)
• At 15 years:
  • 62% overall survival
  • 94% cancer-specific survival
• 28 (2.5%) patients have developed metastatic disease, including 7 “very low risk” patients
• There have been 15 prostate cancer deaths (1.5% of total cohort)

Take home messages 1

• AS now widely accepted for low-risk localised prostate cancer
  – Even in the USA
• Utilisation increasing in Australia
  • Among the best in the world
• Long-term safety data is good
• This has mitigated the “harms” of over-diagnosis due to PSA testing


Active surveillance: *Easy decision*

68 year old, very low risk
PSA 4.1
PSA density 0.15
T1c
No family history
Normal MRI
Transperineal biopsy 2/20 cores
positive Gleason 3+3
  – 2mm & 1mm max core length

Outline

**Active surveillance**

• Background
• Utilisation
  • *How we do it*
• Some concerns
Active surveillance in prostate cancer: a critical review

Many protocols to choose from

Table 1.—Eligibility criteria for selected AS series.

<table>
<thead>
<tr>
<th>Cohort (Alphabetical order)</th>
<th>PSAa</th>
<th>PSADb</th>
<th>GS</th>
<th>% PCa / Core(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australian series 15</td>
<td>≤10</td>
<td>—</td>
<td>≥2</td>
<td>—</td>
</tr>
<tr>
<td>Danish series 15</td>
<td>≥10</td>
<td>—</td>
<td>≤6</td>
<td>—</td>
</tr>
<tr>
<td>Goteborg cohort 14</td>
<td>≤10</td>
<td>—</td>
<td>≤6</td>
<td>&lt;50% / core</td>
</tr>
<tr>
<td>John Hopkins 14</td>
<td>≤10</td>
<td>&lt;0.15</td>
<td>≥3</td>
<td>≤50% / core</td>
</tr>
<tr>
<td>MSKCC 8</td>
<td>≤10</td>
<td>—</td>
<td>≥3</td>
<td>≤50% / core</td>
</tr>
<tr>
<td>PRIAS 19</td>
<td>≤10</td>
<td>&lt;0.2</td>
<td>≤6</td>
<td>≤50% / all cores</td>
</tr>
<tr>
<td>Royal Marsden 9</td>
<td>≤15</td>
<td>—</td>
<td>≤6</td>
<td>≤50% / core</td>
</tr>
<tr>
<td>UCSF 20</td>
<td>≤10</td>
<td>—</td>
<td>≤6</td>
<td>≤20% / core</td>
</tr>
<tr>
<td>University of Miami 32</td>
<td>≤10</td>
<td>—</td>
<td>≤6</td>
<td>—</td>
</tr>
<tr>
<td>University of Toronto 29</td>
<td>≤10</td>
<td>—</td>
<td>≤6</td>
<td>—</td>
</tr>
<tr>
<td>Canary PASS 35, 55</td>
<td>—</td>
<td>—</td>
<td>≤2</td>
<td>—</td>
</tr>
</tbody>
</table>

*ng/ml; 1PSAD PSA density ng/ml/cc; two pattern 4 or 5; GS 3-4 was permitted in patients aged >65 yrs; prior to 2000 men >70 yrs and PSAD<15 ng/ml and/or ≤6.5 was permitted, if MRI targeted biopsy there is no limit in the no positive cores and and no limit in the % PCa in the cores, if saturation biopsy (transperineal or transrectal) 13% of the cores can be +ve with a maximum of 4. GS clinical stage; GC: Gleason Score; PCa: prostate cancer; Pos.: positive.
### Table II. — Progression criteria for selected AS series.

<table>
<thead>
<tr>
<th>Cohort (Alphabetical order)</th>
<th>Progression criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PSA&lt;</td>
</tr>
<tr>
<td>Australian series 13</td>
<td>↑ PSA4</td>
</tr>
<tr>
<td>Danish series 15</td>
<td>PSA&lt;≤3 &amp; 4</td>
</tr>
<tr>
<td>Goteborg cohort 14</td>
<td>↑ PSA4</td>
</tr>
<tr>
<td>John Hopkins 0</td>
<td>—</td>
</tr>
<tr>
<td>MSKCC 3</td>
<td>—</td>
</tr>
<tr>
<td>PRIAS 19</td>
<td>PSA&lt;≤3 &amp; 4</td>
</tr>
<tr>
<td>Royal Marsden 1</td>
<td>PSA&lt;≤3 &amp; 4</td>
</tr>
<tr>
<td>UGIF 20</td>
<td>PSA&lt;≤0.75 &amp; 3</td>
</tr>
<tr>
<td>University of Miami 22</td>
<td>—</td>
</tr>
<tr>
<td>University of Toronto 28</td>
<td>PSA&lt;≤3 &amp; 4</td>
</tr>
<tr>
<td>Canary PASS 5</td>
<td>↑ PSA4</td>
</tr>
</tbody>
</table>

*PSA derivatives; Significant established progression; *for men with PSA doubling between 3-5 yrs, treatment options were discussed, if bilateral PCa; PSA<≤3 PSA doubling time (years), only after a minimum of four follow-up visits; PSA<≤3 PSA velocity (ng/mL/year); *for the first 4 yrs PSA<≤2 yrs; CS: clinical stage; GS: Gleason Score; PCa: prostate cancer; Pos.: positive.

### Table III. — Surveillance protocols for selected AS series.

<table>
<thead>
<tr>
<th>Cohort (Alphabetical order)</th>
<th>Surveillance protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DRE (mo.)</td>
</tr>
<tr>
<td>Australian series 13</td>
<td>6</td>
</tr>
<tr>
<td>Danish series 15</td>
<td>3</td>
</tr>
<tr>
<td>Goteborg cohort 14</td>
<td>3-6</td>
</tr>
<tr>
<td>John Hopkins 0</td>
<td>6</td>
</tr>
<tr>
<td>MSKCC 3</td>
<td>6</td>
</tr>
<tr>
<td>PRIAS 19</td>
<td>6</td>
</tr>
<tr>
<td>Royal Marsden 1</td>
<td>6-9</td>
</tr>
<tr>
<td>UGIF 20</td>
<td>6</td>
</tr>
<tr>
<td>University of Miami 22</td>
<td>3-6</td>
</tr>
<tr>
<td>University of Toronto 28</td>
<td>3-6</td>
</tr>
<tr>
<td>Canary PASS 5</td>
<td>6</td>
</tr>
</tbody>
</table>

* Frequency of mpMRI not stated; 2-6 monthly PSA and annual DRE after 2 years; 1 DRE/2 yrs after 2 years; 1 DRE/6 months after 2 years; 6 monthly PSA after 2 years; 6 monthly PSA after 2 years; 6 monthly biopsy; DDR: digital rectal examination; Rx: diagnosis; PCa: prostate specific antigen; PSAd: PSA doubling time; TRUS: transrectal ultrasonography; T-zone: transition zone.

**Overall....**

All protocols restrict to Gleason 6 (ISUP grade group 1), PSA <10, limited core involvement

All protocols list Gleason upgrading and increased core volume as triggers for intervention

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**MRI in AS protocols?**

Yes, but data is lacking

MRI now reimbursed for AS patients every three years in Australia

We use it to avoid biopsy – but patient and clinician need to accept some risk of missing re-classification
Transperineal prostate biopsy

From Kuru et al, BJUI 2013
Overall, TP biopsy is very safe
– Almost zero sepsis
Diagnostic accuracy very good
29% of Gleason 6 (ISUP grade group 1) upgraded on immediate repeat biopsy

TP biopsy should be considered as an inclusion criteria for patients considering AS

50% of prostate biopsies in Victoria are performed using TP approach

Take home messages 2

Protocols provide safe pathway for AS
MRI and TP biopsy improve risk stratification
Outline

Active surveillance
• Background
• Utilisation
• How we do it
• Some concerns

N=1635 men on AS

“Adequate” surveillance defined as at least:
• three PSAs over the two year period following diagnosis
• At least one additional biopsy

75% of men did not have adequate surveillance
Take home messages 3

Adherence to AS protocols are very low
Patients and clinicians need to be aware and vigilant
Perhaps a shared-care model would work better?

Polling question

Would you be comfortable managing active surveillance patients as part of a shared care pathway?

1. Yes, provided there was an agreed protocol
2. No, this should happen in secondary care
Outline

Active surveillance
• Background
• Utilisation
• How we do it
• Some concerns

Decision-making in active management
• Surgery or Radiotherapy
• NAVIGATE study

Vs
A second opinion always adds value
Polling question

I routinely recommend that men with localized prostate cancer seek a second opinion

1. Yes
2. No
Final messages

Active surveillance is highly utilised and outcomes are good
This mitigates the over-diagnosis effect of PSA testing
However, compliance with AS protocols is poor

Surgery vs Radiotherapy – get a second opinion
Decision aids such as NAVIGATE may help

Thank you

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e: declan.murphy@petermac.org
@declangmurphy
Learning Outcomes

By the end of this online QI & CPD activity you should be able to:

1. Describe the current evidence related to prevention, early detection, presentation, initial investigations and referral for prostate cancer
2. Use evidence-based tools and resources to determine patients risk of prostate cancer and to help asymptomatic patients decide whether to proceed with PSA testing
3. Identify how to access local diagnostic imaging and specialist appointment referral pathways for patients presenting with signs and symptoms of prostate cancer

Webinar: Managing Oesophagogastric Cancer in General Practice

This webinar supports general practice to:

- Increase awareness of risk factors
- Improve knowledge of signs & symptoms to investigate further
- Improve understanding of management options and meeting supportive care needs

Date: Wednesday 17th October 2018
Time: 7:00-8:30pm
Location: Your computer or mobile device
Presenters: Prof Jon Emery
           Prof Alex Boussioutas
Thank you