Prostate cancer screening: have we tipped the seesaw?

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On behalf of the SW Prostate Dashboard Study Group: On behalf of The Rapid Pathway Team

Background

The European Randomized Study of Screening for Prostate Cancer (ERSPC) has demonstrated a 20% reduction in prostate cancer specific mortality but also significant harms.

- Pathway changes since ERSPC have reduced harms. The introduction of pre-biopsy multi-parametric MRI (mpMRI) has allowed targeting of lesions and avoidance of biopsy in MRI-negative patients. In addition, increased use of transperineal biopsy has reduced biopsy harms, including sepsis.
- We sought to understand whether these pathway changes have tipped the seesaw to such an extent that screening would now deliver more benefit than harm
- We did this by evaluating harm from the prostate cancer diagnostic pathway across 3 major harms that are possible outcomes from a decision to have a PSA test
  - A biopsy in a man without prostate cancer
  - A diagnosis of clinically insignificant prostate cancer (Gleason Grade 3+3)
  - Sepsis as a result of biopsy

Conclusions

- Modern diagnostic practice including pre-biopsy mpMRI has reduced risk of harm from prostate cancer testing reducing the total number of men exposed to biopsy and therefore sepsis rates, the number of negative biopsies, and the number of diagnoses of clinically insignificant prostate cancer while maintaining detection of clinically significant cancers.
- This reduction in harm may be underestimated when considering individual trial results separately in evidence reviews.
- Data from UK centres which apply (and audit) up-to-date best practice reinforces this conclusion and suggests that the harm reduction in practice is even greater than that predicted by combined trial data used in creation of the modern pathway model.
- New research should focus on delivering further reduction in harms, improvements in accuracy, and reduction in false negative results at all stages of the pathway to tip the seesaw even further towards benefit.

Methods

- First, we created a model assessing outcomes for 10,000 men undergoing PSA testing based on evidence from multiple prospective clinical trials and current UK practice patterns according to the National Prostate Cancer Audit. This model pathway is represented in the diagram below in the blue box.
- Next, using data from the CaP trial as a benchmark for the diagnostic pathway that was in place before the introduction of mpMRI, we compared our model modern pathway to historical practice to illustrate the predicted reduction in each of these harm outcomes. This historical pathway is represented in the diagram below in brown
- Finally, we compared real world outcome data from 2 multi-hospital NHS prospective registries to investigate if the harm reduction predicted in the model pathway would be seen in actual practice
  - The Rapid Assessment for Prostate Imaging and Diagnosis (RAPID) cancer registry represented in the diagram below in dark blue
  - The SW England Prostate Dashboard Study Group registry represented in the diagram below in dark grey

NB for ease of comparison all results were scaled to 1,610 men entering the pathway with a suspicion of prostate cancer (equivalent to 10,000 men having a PSA test in the modelled pathway)

References:


3. Kassourov P, El-Khoury G, Molavi H, et al. Modern diagnostic practice including pre-biopsy mpMRI reduces risk of harm from prostate cancer testing reducing the total number of men exposed to biopsy and therefore sepsis rates, the number of negative biopsies, and the number of diagnoses of clinically insignificant prostate cancer while maintaining detection of clinically significant cancers.


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Summary of key results

<table>
<thead>
<tr>
<th>Possible harm outcome after a PSA test</th>
<th>Pre-MRI (CaP)</th>
<th>Modern pathway model</th>
<th>Actual practice (London)</th>
<th>Actual practice (SW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of men having a PSA test who have a biopsy showing no cancer</td>
<td>9.46%&lt;sup&gt;1&lt;/sup&gt;</td>
<td>6.46%</td>
<td>2.33%</td>
<td>1.52%</td>
</tr>
<tr>
<td>% of men having a PSA test who have biopsy showing insignificantly significant prostate cancer (≥3+4) prostate cancer</td>
<td>3.83%&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1.10%</td>
<td>0.73%</td>
<td>0.83%</td>
</tr>
<tr>
<td>% of men having a PSA test who suffer sepsis</td>
<td>0.1%&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.07%</td>
<td>0.02%</td>
<td>No data</td>
</tr>
</tbody>
</table>

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