Abstract #43

Prostate cancer screening: have we tipped the seesaw?

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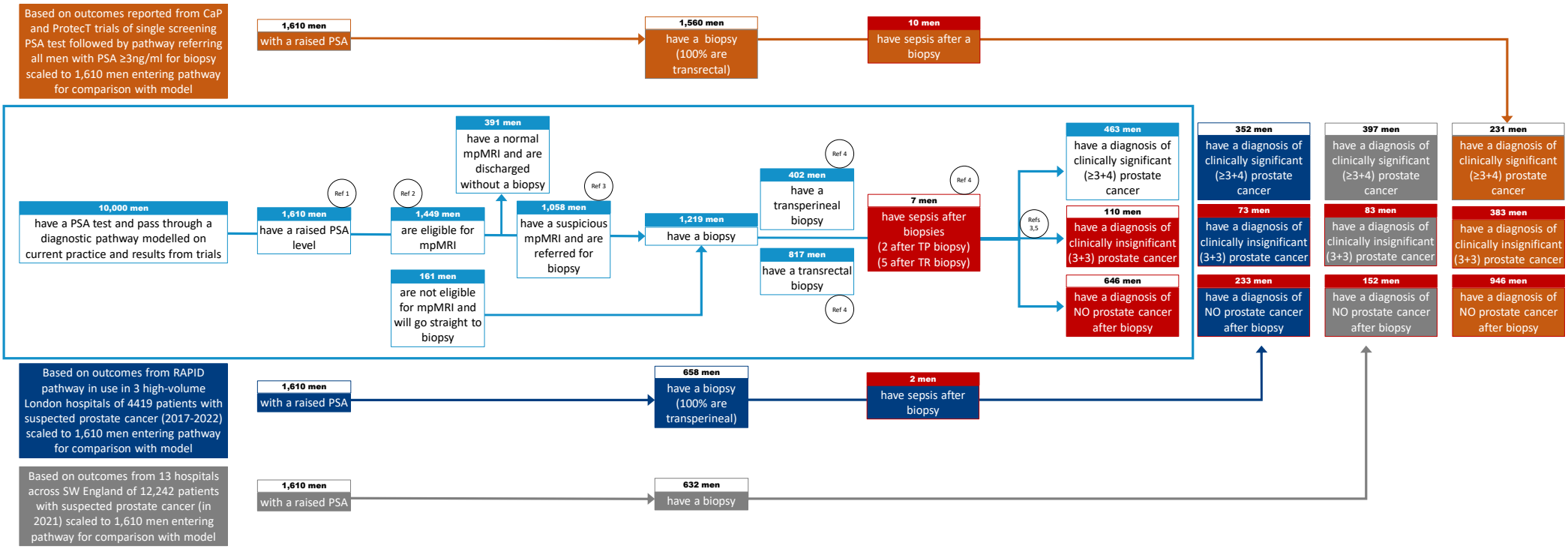
Background

- 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 muti-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

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)



Summary of key results

Possible harm outcome after a PSA test	Pre-MRI (CaP)	Modern pathway model	Actual practice (London)	Actual practice (SW)
% of men having a PSA test who have a biopsy showing no cancer	9.46%[6]	6.46%	2.33%	1.52%
% of men having a PSA test who have a biopsy showing insignificant cancer	3.83%[6]	1.10%	0.73%	0.83%
% of men having a PSA test who suffer sepsis	0.1%[7]	0.07%	0.02%	No data

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.

References:

1. Moss S, Melia J, Sutton J, Mathews C, Kirby M. Prostate-specific antigen testing rates and referral patterns from general practice data in England. Int J Clin Pract. 2016 Apr;70(4):312-8. doi: 10.1111/ijcp.12784. Epub 2016 Mar 14. PMID: 26987766.
2. Prostate Cancer UK - 2018 Freedom Of Information request
In 2018, Prostate Cancer UK submitted a Freedom of Information Request to estimate mpMRI availability and patient eligibility rates. The most frequent eligibility rate stated by mpMRI adopters was 90%. This diagram assumes that 90% of men referred will be eligible for a mpMRI, considering contraindications to mpMRI and other eligibility criteria.
3. Ahmed HU, El-Shater Bosaily A, Brown LC, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): A paired validating confirmatory study. The Lancet. 2017;389(10071):815-822.
4. Tamhankar AS, El-Taji O, Vasdev N, Foley C, Popert R, Adshead J. The clinical and financial implications of a decade of prostate biopsies in the NHS: analysis of Hospital Episode Statistics data 2008-2019. BJU Int. 2020 Jul;126(1):133-141. doi: 10.1111/bju.15062. Epub 2020 Apr 22. PMID: 32232966.
5. Kasivisvanathan V, Emberton M, Moore CM, et al; PRECISION Study Group Collaborators. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N Engl J Med. 2018 May 10;378(19):1767-1777. doi: 10.1056/NEJMoa1801993. Epub 2018 Mar 18. PMID: 29552975; PMCID: PMC9084630.
6. Martin RM, Donovan JL, Turner EL, et al. Effect of a Low-Intensity PSA-Based Screening Intervention on Prostate Cancer Mortality: The CAP Randomized Clinical Trial. JAMA. 2018;319(9):883–895. doi:10.1001/jama.2018.0154
7. Rosario DJ, Lane JA, Metcalfe C, Donovan JL, Doble A, Goodwin L, Davis M, Catto JW, Avery K, Neal DE, Hamdy FC. Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen: prospective evaluation within ProtecT study. BMJ. 2012 Jan 9;344:d7894. doi: 10.1136/bmj.d7894

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