All-Party Parliamentary Group on Prostate Cancer

Minutes of meeting: Tuesday 22nd April 2025

Committee Room 18

Attendees

- **Iqbal Mohamed MP** *(meeting chair)*
- **Peter Prinsley MP** *(officer)*
- **The Rt Hon Sir Damian Hinds MP**
- **Seamus Logan MP**
- **The Rt Rev. the Lord Bishop of Manchester**
- **Baroness Freeman of Steventon**
- **Lord Bethell**
- **Lord Rogan**
- **The Rt Hon Lord Tyrie**
- **Lord Wigley**

Speakers

- **Natalia Norori** (Senior Data & Evidence Manager, Prostate Cancer UK)
- **Professor Caroline Moore** (Professor of Urology, University College London)
- **Professor Vincent Gnanapragasam** (Professor of Urology, University of Cambridge & Honorary Consultant Urologist, Addenbrooke's Hospital)
- **Maurice Blake** (Patient Advocate, Can-Survive UK)

1. Meeting chair's welcome and introductory remarks

The chair for this meeting in the absence of the officers from its start was Iqbal Mohamed MP, who welcomed attendees to the meeting and provided his reflections on and learnings from February's meeting on identifying men at high risk of prostate cancer, before introducing the speakers for this meeting on 'Understanding the risk of overdiagnosis and overtreatment'.

2. Natalia Norori – Using real world data to bridge the evidence gap left by prostate cancer screening trials

Ms Norori provided an overview of the topic of overdiagnosis and overtreatment through her presentation titled '*What is overdiagnosis and how can real-world data help us understand the harms of the prostate cancer diagnostic pathway?'*

Ms Norori began by defining what is meant by the terms 'over-diagnosis' and 'over-treatment' where overdiagnosis is understood as the diagnosis of cancers that grow so slowly (or not at all), that they don't cause any symptoms or harm if left untreated. These are known as clinically insignificant or indolent cancers. 'Overdiagnosis' happens when these harmless cancers are found through screening or tests and can lead to psychological and physical harms, including unnecessary worry and overtreatment.

'Overtreatment' is a consequence of overdiagnosis and happens when a man receives unnecessary treatment for a prostate cancer (PCa) that would not have caused any harm if left untreated. Some of the physical harms associated with overtreatment including urinary incontinence, erectile dysfunction, fatigue, bowel issues, and higher risk of infection. Men who are overtreated experience the harms from treatment but not the benefits, because their cancer was not harmful to begin with and would be unlikely to develop into cancer that was more serious.

Ms Norori demonstrated how the diagnostic pathway in PCa has shifted from 2019 to present, with the introduction of multiparametric MRI (mpMRI), post a raised PSA and prior to biopsy thanks to the PROMIS trial[1], and the shift from transrectal biopsies to transperineal. These changes have brought with them a reduction of harms experienced by men undergoing diagnosis.

Pre-biopsy mpMRI reduces the number of men who have an unnecessary biopsy, and has reduced the amount of clinically insignificant PCa diagnoses.

Data released in 2021 indicated that 40% of prostate biopsies were now transperineal in England (and is likely to have risen since), which has significantly reduced the risk of sepsis.[2]

Since 2019, the use of a pre-biopsy mpMRI is recommended by NICE, with transperineal biopsies recommended since June 2023. This pathway is used by the NHS, but has not been tested in clinical trials for screening prostate cancer.

To understand the effects of these changes in a real-world setting Ms Norori et al. analysed data from 16 hospitals in London and the South West of England to measure how many men experienced harm after a PSA test under the current prostate cancer pathway. They then compared those rates to older data from the CaP[3] and ProtecT[4] screening trials, which were based on the pre-2019 pathway, to see whether the harms from PSA testing have reduced over time.

This analysis was published in 2024[5] and found that advances in technology have reduced the risk of harm when being tested for PCa by 79% and that through current UK clinical practice 90% fewer men develop sepsis after a PSA blood test.

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[1] Ahmed, Hashim U et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. The Lancet, Volume 389, Issue 10071, 815 - 822

[2] NPCA Annual Report. National Prostate Cancer Audit. 2021. https:// www.npca.org.uk/reports/npca-annual-report-2021/. Accessed February 18, 2024.

[3] Martin RM, Turner EL, Young GJ, et al. Prostate-Specific Antigen Screening and 15-Year Prostate Cancer Mortality: A Secondary Analysis of the CAP Randomized Clinical Trial. *JAMA*. 2024;331(17):1460–1470. doi:10.1001/jama.2024.4011

[4] Freddie C. Hamdy, Jenny L. Donovan et al. Fifteen-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer. March 11, 2023. N Engl J Med 2023;388: 1547-1558. VOL. 388 NO. 17. DOI: 10.1056/NEJMoa2214122

[5] Norori N et al. Using real world data to bridge the evidence gap left by prostate cancer screening trials. ESMO Real World Data and Digital Oncology, Volume 6, 100073

The conclusion from Ms Norori's presentation outlined that her study provided the first quantitative estimates of reduction in harm after a PSA test. In so doing they were able to confirm that the current UK PCa diagnostic pathway is safer and more accurate.

The consequence of that confirmation entails the conclusion that NHS guidelines for diagnosing asymptomatic men are out of date. With this new evidence, Ms Norori outlined that men at highest risk should be proactively informed of their risk and given the choice of a PSA test while the outcome of the UK NSC's review is awaited.

3. Professor Caroline Moore – The role of MRI in reducing over-diagnosis

Professor Moore began by adding to Ms Norori's description of physical harms associated with overtreatment, by highlighting a recent study she was involved in showing that even with robotic surgery, urine leakage and sexual function are a problem for many patients – at 12 months after surgery, one in ten men reported a moderate or big problem with urine leakage and one in five men reported sufficient erections.[6] With this as the baseline, she stressed that it was vital to get the balance right on the risks of prostate cancer with the risks of diagnosis and treatment.

The traditional prostate cancer pathway before MRI became routine was highlighted as contributing to both overdiagnosis of indolent disease (often leading to overtreatment), while also resulting in an underdiagnosis of areas missed by standard biopsy, or with a low PSA. Professor Moore described how MRI currently allows us to risk stratify men who have been referred with a high PSA, and how MRI has the potential to transform the whole pathway – improving screening, diagnosis, active surveillance and treatment decision support.

Professor Moore highlighted the multi-centre UK NHS PROMIS trial that has shown the value of newer forms of MRI to reduce overdiagnosis in those with a high PSA. In a comparison to a transrectal ultrasound scan (TRUS) biopsy in this trial, MRI performed with twice the sensitivity for clinically significant disease.[7] TRUS detected 111 significant cancers, but missed 119, whereas MRI detected 213 significant cancers and missed only 17 (a sensitivity rate of 93% compared to 48% for TRUS). MRI also performed favourably compared to TRUS in the PRECISION trial that Professor Moore was involved in, looking at which could detect more clinically significant cancer (Gleason 3 + 4), less clinically insignificant cancer, and which used fewer biopsies in fewer men.[8]

Overall, Professor Moore summarised the impact that MRI has had on the diagnostic pathway as meaning that 1 in 3 men avoid a biopsy, more significant prostate cancer is now found than

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[6] Bridge J, Labban M, Cole AP et al. TrueNTH Post Surgery UK Investigators. Urinary and Sexual Impact of Robotic Radical Prostatectomy: Reporting of Patient-reported Outcome Measures in the First Year after Radical Prostatectomy in a Contemporary Multicentre Cohort in the United Kingdom. Eur Urol Open Sci. 2024 May 21;64:11-21. doi: 10.1016/j.euros.2024.05.003.

[7] 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. Lancet. 2017 Feb 25;389(10071):815-822. doi: 10.1016/S0140-6736(16)32401-1.

[8] Kasivisvanathan V, Rannikko AS, Borghi M 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.

through a standard biopsy, and it has effectively halved the number of men that are over-diagnosed with a low risk prostate cancer – which is why it has become part of routine care across the NHS.

On overtreatment, Professor Moore went on to offer some thoughts on active surveillance in the current pathway, highlighting that uptake varies internationally and locally, and that many men will still opt for radical treatment despite being eligible for active surveillance. Professor Moore compared the risk of being on active surveillance to other health concerns, with men on active surveillance said to be ten times as likely to die from heart disease than prostate cancer. On acceptance of active surveillance, Professor Moore highlighted that where this is MRI-led menwere far less likely to choose active treatment due to anxiety, with this reducing from 20% to 2%.

On additional approaches that have reduced harms to patients, Professor Moore mentioned the promising impact that focal therapy has had from use in the NHS based on UK registry data over 15 years. An analysis of over 1300 patients that had high-intensity focal ultrasound showed that this can provide an alternative to treating the whole prostate and minimising side effects, showing survival without radical treatment as 73% at 7 years, with two-thirds of patients not needing tablets for erections and less than 1% requiring pads for incontinence.[9]

In her final section, Professor Moore presented her hopes on screening in the future, highlighting that the UK has higher prostate cancer death rates than Italy, Spain, France, USA, with the UK's informed choice approach meaning that many men don't ask, and that while existing risk checkers can increase uptake they do not reach all that could benefit. However, recent evidence looking at long-term mortality impact suggests that population screening with a single PSA test is not adequate for prostate cancer screening.[10] Regular PSA testing combined with TRUS biopsy has been shown in European research (pre use of MRI) to reduce mortality by 20%, but with 3 in 4 biopsies considered unnecessary.[11]

In contrast, when tested separate of PSA in the ReIMAGINE prostate cancer screening study led by Professor Moore, 1 in 6 men screened with MRI had a lesion, and over half of the men with significant cancer on biopsy had a PSA <3 ng/mL – with less than 1% over-diagnosed with low-risk disease.[12] While this was promising, Professor Moore highlighted that more data was needed to develop this further – and also to address the low response rate in Black men (only

[9] Reddy D, Peters M, Shah TT et al. Cancer Control Outcomes Following Focal Therapy Using High-intensity Focused Ultrasound in 1379 Men with Nonmetastatic Prostate Cancer: A Multi-institute 15-year Experience. Eur Urol. 2022 Apr;81(4):407-413. doi: 10.1016/j.eururo.2022.01.005.
[10] Martin RM, Turner EL, Young GJ et al; CAP Trial Group. Prostate-Specific Antigen Screening and 15-Year Prostate Cancer Mortality: A Secondary Analysis of the CAP Randomized Clinical Trial. JAMA. 2024 May 7;331(17):1460-1470. doi: 10.1001/jama.2024.4011.
[11] Hugosson J, Roobol MJ, Månsson M et al; ERSPC investigators. A 16-yr Follow-up of the European Randomized study of Screening for Prostate Cancer. Eur Urol. 2019 Jul;76(1):43-51. doi: 10.1016/j.eururo.2019.02.009. Epub 2019 Feb 26.
[12] Moore CM, Frangou E, McCartan N et al. Prevalence of MRI lesions in men responding to a GP-led invitation for a prostate health check: a prospective cohort study. BMJ Oncol. 2023 Aug 21;2(1):e000057. doi: 10.1136/bmjonc-2023-000057.

20% responded to invitations), which will be built into the various arms of the TRANSFORM trial.

4. **Professor Vincent J Gnanapragasam – The role of active surveillance in reducing over-treatment**

Professor Gnanapragasam began his presentation 'The critical importance of understanding prognosis from prostate cancer in increasing uptake of active surveillance' by highlighting the contradictions of recent media coverage of PCa where headlines about the high mortality of PCa are published as well as headlines about the potentially unnecessary treatment of many PCa cases.

This led [him] to an appeal to the facts concerning the disease's lethality, where the lifetime risk of PCa for all men regardless of ethnicity is 13.4% and the lifetime risk of PCa death is 4.3%.[13]

Professor Gnanapragasam went on to highlight a study by Popiolek et al.[14] 'Natural history of early, localized prostate cancer: a final report from three decades of follow-up' which demonstrated that from 223 patients with untreated, localized PCa after 32 years of follow-up, all but 3 of the 223 men had died, 38 (17%) of whom had died of PCa.

With that understanding of PCa mortality Professor Gnanapragasam showed the results from the ProtecT trial which compared outcomes after fifteen years for PCa patients with localised disease who were randomly assigned treatment of either active surveillance, surgery [prostatectomy], or radiotherapy.

After 15 years of follow-up, prostate cancer–specific mortality was low regardless of the treatment assigned. Because of these facts PCa is best understood as a balance between risk and benefit led by personalised choice.

NICE stratifies prostate cancer into five Cambridge Prognostic Groups (CPG 1 to 5) to link management of PCa to the risk of the disease causing death/mortality. CPG1 and CPG2 account for 40% of all new cancer diagnoses in the UK each year. The mortality rates within these groups is very low.

Current NICE guidelines (NG131) either recommends active surveillance (AS) or suggests it should be considered for all CPG1 and 2 PCa patients and recommends considering AS for CPG3.

Professor Gnanapragasam then outlined the 'Predict Prostate' tool he developed as a personalised prognostic tool to balance the risk from prostate cancer versus other competing risks to inform the need for treatment. Predict Prostate is one of the few validated and NICE-endorsed tools in this space tested across >350,000 men, with multiple ethnicities and age groups.

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[13] Lloyd T, Hounsome L, Mehay A, Mee S, Verne J, Cooper A. Lifetime risk of being diagnosed with, or dying from, prostate cancer by major ethnic group in England 2008-2010. BMC Med. 2015 Jul 30;13:171. doi: 10.1186/s12916-015-0405-5. PMID: 26224061; PMCID: PMC4520076.

[14] Popiolek M, Rider JR, Andrén O, Andersson SO, Holmberg L, Adami HO, Johansson JE. Natural history of early, localized prostate cancer: a final report from three decades of follow-up. Eur Urol. 2013 Mar;63(3):428-35. doi: 10.1016/j.eururo.2012.10.002. Epub 2012 Oct 13. PMID: 23084329.

Despite the guidelines and tools available there are huge variations in NHS treatment rates for men diagnosed at CPG1 or 2, and significant over-treatment depending on where, which hospital or trust and by whom a man is seen. This was demonstrated in the data available through the National Prostate Cancer Audit.[15]

Through his 2019 study 'Understanding of prognosis in non-metastatic prostate cancer: a randomised comparative study of clinician estimates measured against the PREDICT prostate prognostic model.' Professor Gnanapragasam showed a 51% reduction in overtreatment from men diagnosed with CPG1, a 34.6% reduction in over-treatment for men diagnosed with CPG2 and 21% increase in treatment for men diagnosed with CPG 4 & 5.[16]

Professor Ganapragasm's recommendations for reducing over-treatment and national variation were, adherence and compliance with NICE recommendations and tools, a standardized method to provide information and counselling, a national program of clinician re-education, and patient empowerment to access national guidance without the arbitrary knowledge base of which doctors they may see and where.

Currently, there are a large number of differing AS protocols across Cancer Alliances, trusts and ICBs – referred to by Professor Gnanapragasam as 'the Wild West of prostate cancer management'.

This is because AS does not have a quality benchmark which means there is no well evidenced standard, no set protocol or quality control, no measurable outcome no agreed budget/resources, no investment or dedicated team/staff and it is not a priority for cancer targets.

In order to have good AS practice Professor Gnanapragasam outlined that we need a national standardized way to do AS with clear guidelines and outcome measures. Men need to be empowered to be aware of their management and what to look out for. There needs to be a clear evidence-based protocol with end points and triggers for better management. And finally, assurance that men are supported while on AS and can be made aware early of disease progression that needs treatment.

In order to reduce over-treatment of PCa there needs to be, educated doctors and nurses to understand prognosis and use national guidance and tools, along with, robust, standardized and well-resourced AS programmes in the NHS.

5. Maurice Blake – patient perspective

Maurice Blake, a patient advocate representing Can-Survive UK, shared his personal experience of living with prostate cancer. Diagnosed at the age of 48 following a PSA test and subsequent

[15] https://www.nPCa.org.uk/

[16] Thurtle DR, Jenkins V, Pharoah PD, Gnanapragasam VJ. Understanding of prognosis in non-metastatic prostate cancer: a randomised comparative study of clinician estimates measured against the PREDICT prostate prognostic model. Br J Cancer. 2019 Oct;121(8):715-718. doi: 10.1038/s41416-019-0569-4. Epub 2019 Sep 16. PMID: 31523057; PMCID: PMC6889281.

MRI scan, Mr Blake was initially classified as low-risk with a Gleason score of 6(3+3) and opted for AS as his treatment pathway.

For the following 12 months Mr Blake remained on AS, but unfortunately during this period, his cancer progressed. He was subsequently reclassified as high-risk with a Gleason score of 8(4+4). Thanks to timely intervention, he was able to receive treatment quickly, and his PSA levels are now low and stable.

However, Mr Blake highlighted concerns about the coordination and oversight of his care while under AS. He described significant difficulties in ensuring that his GP was consistently managing the required testing, monitoring, and potential adjustments to his care. Much of the responsibility to track appointments and follow-up fell on him and his family, which added considerable stress to an already challenging situation.

Mr Blake concluded by emphasising that while AS can be an excellent and appropriate option for many patients, it must be delivered in a proactive, consistent, and coordinated manner. He stressed that communication between clinical teams is vital, and the burden of managing care should not fall solely on the patient or their loved ones.

6. Questions

Iqbal Mohammad MP thanked Mr Blake for his contribution and openness. The session was then opened to questions from the attendees.

Lord Tyrie asked as to the reasons why MRI is so expensive, and for the panel's opinions of home PSA testing kits. Caroline Moore explained that through the TRANSFORM trial they will be gathering evidence on bi-parametric (bpMRI) as opposed to the current standard mpMRI, for use in the context of screening. These are cheaper than mpMRI as they don't require a radioactive contrast to be administered by a radiologist thus speeding up the pathway and saving time and money.

The Lord Bishop of Manchester shared his personal perspective on the matters discussed through his own diagnoses and expressed concerns about the future options for treatment if he was older and become unfit for treatment. Professor Gnanapragasam replied that had the Lord Bishop been treated by his team in Cambridge, he would have likely had a very different experience and information provision. He would likely have had comprehensive counselling and evidence on the value of treatment for a man now and in future bearing in mind that if there is a worry about being too unfit in future for treatment then at that time there probably is no actual value in prostate cancer treatment anyway. He said in many circumstances the worry about prostate cancer and ageing is not balanced by the corresponding reduced gain in treatment benefit as a man gets older and has competing morbidity.

Professor Colin Cooper, Professor of Cancer Genetics at the University of East Anglia, asked why in today's discussion there had been no mention about the genetics of PCa and the alternative tests coming through research and onto market. Caroline Moore responded to this question by highlighting that Professor Ros Eeles (Professor of Oncogenetics at the Institute of Cancer Research) spoke on genetics at the February APPG meeting and is developing work in this area through the TRANSFORM trial.

Seamus Logan MP asked why doctors even propose radical treatment for low-risk cancer, and why the UK NSC are not listening to the meeting attendees on screening. In response the panel agreed that patients have to be able to make an informed decision, and said that the UK NSC engages with evidence and data as well as expert perspectives.

In response to some of the mortality figures mentioned by the speakers, Chris Booth (urologist and founder of the CHAPS men's health charity) suggested that there were other European studies where the impact of PSA testing on prostate cancer mortality was much higher, and that one benefit that he believed has been shown in the experience of breast cancer screening was that it has raised the overall standard of care – and that a prostate cancer screening programme may address the AS variability described.

Baroness Freeman asked the final question of the panel, are we ready for screening? Professor Caroline Moore answered that were she the UK NSC and had to implement screening tomorrow she is not sure we are quite there yet. Professor Gnanapragasam said that we have moved far from the concept of 'screening' and suggested looking at the work of the EU's PRAISE-U[17] project, which he described as conducting fantastic work tied to every step of the diagnostic pathway.

Iqbal Mohamed MP thanked everyone for their contributions and concluded the meeting.

Secretariat provided by:

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[17] https://uroweb.org/praise-u