

UK National Screening Committee (UK NSC)

Screening for prostate cancer

Consultation responses from stakeholders

Date: 11 May 2026

Note: The names and organisations of submitters have been disclosed only when consent was provided in the submission form. Some personally identifiable information in this document has been redacted; redacted text is indicated by *****.

#	Submitter name	Organisation (if applicable)	Consultation response
S1	Jonathan Miller		Citing the lack of evidence for screening in black men doubles down on the inequality by penalising black men for the inequality of the research. It also seems perverse that the research in Sweden points to benefit in white men, but you conclude that this cannot be used to predict benefit in black men with double the risk of prostate cancer. The confounding issue of normal levels of PSA in black men can be accommodated in any screening program. Finally, using MRI as the initial test following a raised PSA, finds more cancers of concern and fewer indolent cancers. This reduces the harms of overdiagnosis and gives men the choice on how to manage their diagnosis. I think we should commission to evaluate of screening in black men and those with a strong family history of prostate, breast or ovarian cancer, or ensure all such men are eligible and invited to the various research studies in setup.
S2	Pauline Bradshaw		Unfortunately the rational for this decision does not stand up We have a higher population of ethnic minority men than other countries who have adopted a risk based screening approach successfully Staying with our current approach is outdated we are already slipping down the tables of effective healthcare as a country It will cost more upfront to save down the line but it will save significantly on continued care of patients with prostate cancer It feels like finance is taking priority over quality of care
S3			the evidence is unequivocal – early screening saves lives and is immensely more cost effective than treating late stage disease
S4	Takeshi Takahashi		The United Kingdom continues to attract global attention, differing from countries where economic priorities led by the US and EU dominate. Consequently, decisions made by the National Screening Committee (NSC) have global ramifications. I am submitting my comments from the perspective of an international

		observer, and I hope they will be considered for evaluation of evidence. These comments partly overlap with my previous rapid response regarding breast cancer screening in BMJ and summarize my prior publications on the subject. Recently, Dr. Lucassen and colleagues accurately and calmly pointed out that nearly all clinical studies on prostate cancer screening lack proper controls, and overall survival (OS) is not an endpoint in these studies [1]. Therefore, clinical benefits remain unproven, with many studies merely being case series or feasibility/pilot studies. This is not a novel observation but rather a well-established fact found in medical textbooks for medical students. The reason behind this issue is the lack of validation of OS in the natural course of screen-detected prostate cancer, making scientifically valid clinical trials virtually impossible [2]. This observation applies equally to research mentioned in the NSC draft, such as studies on genetic risks like BRCA and Black men, as well as clinical research on MRI, including the Transform trial. In terms of the evidence hierarchy, these studies are at the very bottom or outside the pyramid. The concept of overdiagnosis assumes that the OS of screen-detected cancers is worse than that of the general population. This gap diminishes or disappears when elderly individuals are considered. However, in the case of prostate cancer screening, where the natural history of the disease has not been validated, this concept does not apply. It remains unclear what is meant by the “harm of overdiagnosis.” Among the clinical trials on prostate cancer screening, only three—PLCO, ERSPC, and CAP—have appropriate controls, and all consistently found that screening does not improve OS, providing level 1 evidence. Ideally, evidence evaluation for prostate cancer screening should end here. However, lengthy discussions on cancer-specific mortality continue to appear in articles and guidelines, such as those from the USPSTF, with urology guidelines suggesting that data from ERSPC may imply a reduction in mortality, even though this is not supported by evidence. Cancer-specific mortality is often used in cancer registries and epidemiological surveys, but it is a subjective measure based on the judgment of the physician who certifies the death, and it is not suitable for mathematical or statistical analysis. For it to be a valid endpoint in clinical research, the cause of death must be precisely identified, and cancer-specific mortality must be scientifically defined, both of which are practically impossible. Thus, cancer-specific mortality is not a reliable measure and should not be considered as an endpoint in clinical trials. Neither of the three RCTs reports a scientific definition or measurement method for cancer-specific mortality. Describing aspects of clinical trials beyond the endpoints is not the “result” of the study and falls outside the applicable categories for

			clinical research. Such descriptions would, at best, constitute expert opinion, which lies outside the evidence hierarchy. Level 1 evidence, at the top of this pyramid, cannot be overturned. When OS is used as an endpoint, researchers must observe the progress until death, which requires long-term effort. To alleviate this burden, surrogate endpoints are sometimes used. However, cancer-specific mortality, like OS, requires observation until death, yet it lacks the simplicity and reliability of OS. Thus, there is no reason to focus on cancer-specific mortality. Screening proponents often emphasize cancer-specific mortality due to its measurement challenges, which can lead to errors. These errors may result in apparent reductions in cancer deaths (as in ERSPC), which are then presented as evidence. Strangely, despite being scientifically and EBM-wise unsound, the claim that “screening reduces cancer-specific mortality” is widely believed within the medical community. Recommending an intervention with no benefit to the general population is not medical practice but clinical research. It raises serious ethical and economic concerns. The USPSTF does not recommend organized screening, and most countries, including those in Europe, conduct “opportunistic screening”—screening offered to individuals who present for unrelated reasons. Studies like the Transform trial mentioned in the draft also use materials from such opportunistic screening cases. Additionally, in the UK, NICE allows opportunistic screening, which has led to widespread prostate cancer screening. Regardless of whether it is organized or opportunistic, prostate cancer screening has no OS benefit and remains a clinical trial. Following the Helsinki Declaration, appropriate information, including the lack of benefits, must be provided before PSA testing, and consent must be obtained. As per the USPSTF statement, “clinicians and patients should discuss the benefits and harms of screening before PSA testing,” which suggests that screening should only occur if the individual expresses preference. These clinical trials must have appropriate control groups, including a natural history group, with OS as the endpoint. Without these conditions, the trials will merely accumulate feasibility studies that cannot be scientifically interpreted, as seen in previous clinical practices. If the NSC recommends research like the BRCA-related studies or the Transform study, such conditions must be imposed. Furthermore, interventions with no benefits lead to an infinite cost-effectiveness ratio, meaning public funds should not be allocated to such endeavors. If it is a clinical trial, the funding should come from research grants, not public health insurance. Policy makers must uphold scientific integrity, as failure to do so can cause significant harm to both individuals and society. Case series, feasibility studies, and expert opinions should not be published as original articles in medical journals. Articles on PSA

		screening or the results of ERSPC should have undergone rigorous scientific evaluation during the peer-review process. Once published in a top-tier medical journal, such articles become difficult to criticize by young or non-specialized medical professionals. If such policies are endorsed by governments, the public and healthcare professionals alike stop questioning them. Safeguards for scientific integrity lie first with the journal's editorial board and then with policy makers, who have a responsibility not to let their financial interests lead to harmful outcomes. Prostate and breast cancer screening highlight the weight of this responsibility. *****. After gaining significant experience, I could no longer recommend PSA tests and subsequent procedures to my patients *****. ***** my perspective on this issue is shaped by both personal and professional experience. I will never undergo a PSA test myself, nor would I review any erroneous results [3]. I understand that PSA is a tissue-specific marker with no proven link to cancer, biopsy pathology is unreliable, and there is no evidence it extends life. ***** Since 1990, numerous prominent urologists worldwide have pushed for prostate cancer screening. These individuals, now between their late 50s and early 80s, likely underwent prostate cancer screening during their appropriate age range. While I often hear that they still undergo PSA tests, I have never heard of them undergoing biopsies or surgeries. Perhaps the NSC should consider interviewing these prominent British urologists and former experts. REFERENCE 1. Lucassen A, McCartney M, Sullivan R. Prostate cancer: polygenic risk scores have not shown clinical benefit. BMJ. 2025 Jun 10;389:r1179. doi: 10.1136/bmj.r1179. 2. Takahashi T. Prostate cancer screening and Gleason score: empirical clinical practice. Virchows Arch. 2024 Aug 20. doi: 10.1007/s00428-024-03900-x. 3. Takahashi T. Prostate cancer screening and the golden rule of humanity. BMJ. 2023 Jun 26;381:1390. doi: 10.1136/bmj.p1390. Below is the manuscript currently submitted to a certain medical journal. I would appreciate it if you could refer to it as well. Title: Prostate Cancer Screening: Evidence, Endpoints, and Ethical Implications Prostate cancer screening expanded rapidly with the advent of prostate-specific antigen (PSA) testing in the 1990s, transforming what had been a relatively uncommon cancer into the most

		frequently diagnosed malignancy among men.^{1,2}In 2012, the U.S. Preventive Services Task Force (USPSTF)—composed primarily of general internists and public health physicians—issued a Grade D recommendation against PSA-based screening, concluding that harms outweigh benefits.³ In 2018, citing new randomized trial results, the USPSTF changed its recommendation to Grade C, stating that the balance of benefits and harms remains uncertain and that decisions about PSA testing should be individualized after clinician–patient discussion of potential benefits and harms.⁴ Urologists, pathologists, radiologists, and other proponents of screening opposed the 2012 Grade D recommendation and developed their own guidelines.^{1,5-7} Although they viewed the 2018 shift from Grade D to Grade C as an “upgrade,” they did not revise their own guidance, which continues to diverge from the USPSTF position. Their guidelines assert that screening reduces cancer mortality and that “prebiopsy risk stratification” with MRI or polygenic risk scores can mitigate overdiagnosis, thereby improving the balance of benefits and harms. Top-tier journals, including the New England Journal of Medicine (NEJM), BMJ, and JAMA, have repeatedly published the views of screening proponents in recent years.⁸⁻²⁵ NEJM recently presented long-term follow-up from the ERSPC (European Randomized Study of Screening for Prostate Cancer) trial and an accompanying editorial echoing pro-screening arguments;⁸ nearly all NEJM articles on prostate cancer screening since 2018 have advanced similar claims.⁸⁻¹⁷ Notably, the initial studies that laid the foundation for using PSA as a screening tool were also published in NEJM.^{1,26} Dr. Lucassen and colleagues have offered a thoughtful and appropriate critique:²⁷ clinical studies of prostate cancer screening often lack proper controls and fail to use overall survival (OS) as the primary endpoint. Such studies may demonstrate feasibility but not clinical benefit. These observations are not novel. Foundational principles—“clinical trials require controls” and “OS is among the few available and scientifically valid endpoints”—are taught in basic medical texts. Similar cautions from public health physicians have been raised frequently but, regrettably, have been largely ignored.²⁸⁻³² Most clinical reports on prostate cancer screening are, in terms of study design, case series or feasibility/pilot studies. The natural history of screen-detected prostate cancer has not been rigorously established; specifically, we lack data showing that untreated OS among screen-detected cases is inferior to OS in the general healthy population.³³⁻³⁶ In that context, conducting the kind of “scientifically valid” clinical trials advocated by Lucassen and colleagues²⁷ is, in practice, extremely challenging. Although such studies would normally not qualify as original research, a vast

		number of them have been published over the past 30 years. Their results do not constitute evidence. The conceptual origin of “screen-detected prostate cancer” traces to pathology criteria proposed by a single physician in support of the Bowery series in the 1950s.³³⁻³⁵ Those criteria were based on knowledge of latent carcinoma at the time and lacked scientific validation. Arthur Stout, a pathologist, and Perry Hudson, a urologist, who led the Bowery series, acknowledged that whether such lesions were biologically malignant could only be determined through clinical follow-up, yet used these criteria to justify prostatectomy.^{34,35} The Bowery series ended after a few years amid concerns about litigation risk, but the pathology standard persisted. In the 1980s, before PSA testing was widespread, Dr. Chodak reviewed contemporary screening practices and concluded that prostate cancer screening should be considered experimental until decisive evidence became available.²⁸ When PSA testing became clinically available in the 1990s, thresholds for biopsy were set by comparing PSA values with histopathological findings, and “PSA screening” began.^{1,26} These thresholds were determined largely by expert opinion rather than empirical validation. Such studies lacked controls and did not use OS as an endpoint; they were descriptive and do not constitute evidence. PSA is organ-specific but not a tumor marker. Very high levels may indicate advanced cancer, but the clinical meaning of values within physiological ranges remains unclear, and the relationship between PSA levels and cancer incidence or progression is unresolved. Thus, there is no robust theoretical rationale for using PSA in screening. Due to its simplicity (a blood test) and the appeal of numerical results in clinical conversations, PSA screening spread rapidly, accompanied by development of related tools and practices: Gleason scoring, TNM T1 categorization, ultrasound, CT, MRI, surgical treatment, radiation therapy, active surveillance, and biochemical recurrence monitoring.¹ Yet the clinical studies supporting these developments are also predominantly case series or feasibility/pilot studies and therefore lack evidentiary weight. Prostate cancer screening should be regarded as experimental until decisive evidence is obtained.²⁸ Only a small number of scientifically rigorous trials exist: PLCO (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial), ERSPC, and CAP (Cluster Randomized Trial of PSA Testing for Prostate Cancer).⁴ These randomized controlled trials (RCTs) consistently show that screening does not improve OS—Level 1 evidence—indicating that screening does not prolong life and confers no survival benefit.

			A systematic review of prostate cancer screening could reasonably end at this point. Nonetheless, USPSTF4 and Ilic et al.³⁷ report the OS findings but do not emphasize them as decisive evidence, devoting substantial space instead to cancer-specific mortality. Proponents cite ERSPC's reports of cancer-specific mortality to claim that screening reduces cancer deaths.⁵⁻²⁵ However, such descriptions address a secondary aspect that was not the primary endpoint of the RCTs and are essentially narrative rather than data suitable for formal mathematical or statistical analysis. At best, they amount to expert opinion. In the hierarchy of evidence, concordant OS results from multiple RCTs occupy the apex; expert opinion sits at the bottom.³⁸ Cancer-specific mortality is commonly reported in epidemiologic studies and registries, but it is based on the certifying physician's subjective attribution and is fundamentally descriptive.³⁹ To use it as a trial endpoint would require precise determination of cause of death and a scientifically rigorous definition of cancer-specific death—requirements that are, in practice, rarely met. Systematic reviews and trial reports do not provide a scientific basis for its validity as an endpoint.^{4,37} It is not reliably measurable and, therefore, not suitable for statistical analysis. In oncology drug trials, surrogate endpoints (e.g., pathologic complete response, recurrence-free survival) may be accepted when OS requires prolonged follow-up; cancer-specific mortality, like OS, still requires observation until death. Given that OS is measurable, scientifically valid, and available in these trials, there is no justification for substituting a less reliable endpoint such as cancer-specific mortality. Proponents' preference for cancer-specific mortality likely reflects its measurement difficulty and susceptibility to error; ERSPC's figures are cited selectively in a favorable direction.⁵⁻²⁵ Even proponents' reviews and guidelines tend to imply—rather than state—that “evidence exists,” while largely ignoring OS. The USPSTF's 2018 statement, noting insufficient certainty regarding benefits, implicitly acknowledges the absence of benefit.⁴ If benefits are absent, the net balance necessarily favors harm regardless of its magnitude, rendering the Grade C designation internally inconsistent; the recommendation should have remained Grade D. A second line of argument advanced by proponents—now supported by numerous publications—is that MRI or polygenic risk scores can reduce the harms of overdiagnosis.⁵⁻²⁵ However, if screening yields no OS benefit, then even if harms are reduced, the net balance remains unfavorable. Moreover, these studies are case series or feasibility/pilot studies and do not constitute evidence. The evidentiary basis for “overdiagnosis” in prostate cancer screening is itself unclear.⁴⁰ If overdiagnosis were demonstrable, one would expect, under the premise that the natural-history OS of screen-detected cancers is worse than that of healthy individuals, that restricting cohorts to older age groups would diminish or eliminate any observed difference. Because this

		premise has not been verified, the presence or extent of overdiagnosis cannot be determined. The term has been used without adequate justification, creating the impression of clarity while resting on an unstable conceptual foundation. It is often said that prostate cancer screening has been debated for decades.^{1,12} In practice, proponents have amplified their aspirations or expert opinions derived from case series to shore up an established practice. In contrast, Drs. Chodak and Lucassen, along with public health colleagues, have reiterated basic scientific and medical principles,²⁷⁻³² yet their guidance has rarely been seriously heeded—even by leading journals. In real-world clinical practice, urologists—who directly manage prostate cancer—exert substantial influence. Screening continues to increase and is likely to do so. Although the USPSTF’s 2018 statement advised against “organized” screening, rates have risen because “opportunistic” screening—offering PSA testing to patients presenting for unrelated reasons—has been permitted or recommended by NICE in the United Kingdom and by national urological societies across Europe, Canada, Australia, Japan, and elsewhere.^{5-25,41} Whether organized or opportunistic, the absence of benefit remains. Administering a non-beneficial intervention to healthy individuals raises ethical concerns and should be considered research. Under the Declaration of Helsinki, participants must be provided appropriate information—including the fact that no benefit has been demonstrated—and must give informed consent. The USPSTF’s call for clinician–patient discussion of the benefits and harms before PSA testing and for refraining from screening individuals who do not express a preference is, albeit indirect, consistent with adherence to Helsinki.⁴ Such research would require a natural-history control arm and OS as the primary endpoint. Without these features, as in current practice, the literature will continue to accumulate noninterpretable case series and feasibility/pilot studies. Additionally, the costs of such research should not be borne by participants or public insurance but should be supported by dedicated research funding. REFERENCE 1. Catalona WJ. Prostate Cancer Screening. <i>Med Clin North Am</i>. 2018 Mar;102(2):199-214. doi: 10.1016/j.mcna.2017.11.001. 2. Harris E. Prostate Cancer Cases Might Rise to 3 Million Globally by 2040. <i>JAMA</i>. 2024 May 28;331(20):1698. doi: 10.1001/jama.2024.6729. 3. Moyer VA; U.S. Preventive Services Task Force. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. <i>Ann Intern Med</i>. 2012 Jul 17;157(2):120-34. doi: 10.7326/0003-4819-157-2-201207170-00459. 4. US Preventive Services Task Force; Grossman DC, Curry SJ, Owens DK, et al. Screening for Prostate Cancer: US Preventive Services Task Force Recommendation Statement. <i>JAMA</i>. 2018 May 8;319(18):1901-1913. doi:

		10.1001/jama.2018.3710. 5. Wei JT, Barocas D, Carlsson S et al. Early Detection of Prostate Cancer: AUA/SUO Guideline Part I: Prostate Cancer Screening. J Urol. 2023 Jul;210(1):46-53. doi: 10.1097/JU.0000000000003491. 6. Cornford P, van den Bergh RCN, Briers E et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on Prostate Cancer-2024 Update. Part I: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol. 2024 Aug;86(2):148-163. doi: 10.1016/j.eururo.2024.03.027. 7. Schaeffer E, Srinivas S, Antonarakis ES et al. NCCN Guidelines Insights: Prostate Cancer, Version 1.2021. J Natl Compr Canc Netw. 2021 Feb 2;19(2):134-143. doi: 10.6004/jnccn.2021.0008. 8. Roobol MJ, de Vos II, Månsson M et al; ECRPC Investigators. European Study of Prostate Cancer Screening – 23-Year Follow-up. N Engl J Med. 2025 Oct 30;393(17):1669-1680. doi: 10.1056/NEJMoa2503223. 9. McHugh JK, Bancroft EK, Saunders E et al.; BARCODE1 Steering Committee and Collaborators. Assessment of a Polygenic Risk Score in Screening for Prostate Cancer. N Engl J Med. 2025 Apr 10;392(14):1406-1417. doi: 10.1056/NEJMoa2407934. 10. van As N, Griffin C, Tree A et al. Phase 3 Trial of Stereotactic Body Radiotherapy in Localized Prostate Cancer. N Engl J Med. 2024 Oct 17;391(15):1413-1425. doi: 10.1056/NEJMoa2403365. 11. Hugosson J, Godtman RA, Wallstrom J et al. Results after Four Years of Screening for Prostate Cancer with PSA and MRI. N Engl J Med. 2024 Sep 26;391(12):1083-1095. doi: 10.1056/NEJMoa2406050. 12. Pinsky PF, Parnes H. Screening for Prostate Cancer. N Engl J Med. 2023 Apr 13;388(15):1405-1414. doi: 10.1056/NEJMcp2209151. 13. Hugosson J, Månsson M, Wallström J et al.; GÖTEBORG-2 Trial Investigators. Prostate Cancer Screening with PSA and MRI Followed by Targeted Biopsy Only. N Engl J Med. 2022 Dec 8;387(23):2126-2137. doi: 10.1056/NEJMoa2209454. 14. Eklund M, Jäderling F, Discacciati A et al; STHLM3 consortium. MRI-Targeted or Standard Biopsy in Prostate Cancer Screening. N Engl J Med. 2021 Sep 2;385(10):908-920. doi: 10.1056/NEJMoa2100852. 15. Shoag JE, Nyame YA, Gulati R, Etzioni R, Hu JC. Reconsidering the Trade-offs of Prostate Cancer Screening. N Engl J Med. 2020 Jun 18;382(25):2465-2468. doi: 10.1056/NEJMSb2000250. 16. Ahdoot M, Wilbur AR, Reese SE et al. MRI-Targeted, Systematic, and Combined Biopsy for Prostate Cancer Diagnosis. N Engl J Med. 2020 Mar 5;382(10):917-928. doi: 10.1056/NEJMoa1910038. 17. 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. 18. Ng ABCD, Asif A, Agarwal R et al.; PRIME Study Group Collaborators. Biparametric vs Multiparametric MRI for Prostate Cancer Diagnosis: The PRIME Diagnostic Clinical Trial. JAMA. 2025 Oct 7;334(13):1170-1179. doi: 10.1001/jama.2025.13722. 19. Kinnaird A, Luger F, Cash H et al.; OPTIMUM Investigators. Microultrasound-Guided vs MRI-Guided Biopsy for Prostate Cancer Diagnosis: The OPTIMUM Randomized Clinical Trial. JAMA. 2025 May 20;333(19):1679-

		1687. doi: 10.1001/jama.2025.3579. 20. Newcomb LF, Schenk JM, Zheng Y et al. Long-Term Outcomes in Patients Using Protocol-Directed Active Surveillance for Prostate Cancer. JAMA. 2024 Jun 25;331(24):2084-2093. doi: 10.1001/jama.2024.6695. 21. Auvinen A, Tammela TLJ, Mirtti T et al.; ProScreen Trial Investigators. Prostate Cancer Screening With PSA, Kallikrein Panel, and MRI: The ProScreen Randomized Trial. JAMA. 2024 May 7;331(17):1452-1459. doi: 10.1001/jama.2024.3841. 22. 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. 23. Kotecha P, Rajan P, Figiel S, Lamb AD. Screening for prostate cancer. BMJ. 2025 May 27;389:r1031. doi: 10.1136/bmj.r1031. 24. Vaccarella S, Li M, Bray F, Kvale R et al. Prostate cancer incidence and mortality in Europe and implications for screening activities: population based study. BMJ. 2024 Sep 4;386:e077738. doi: 10.1136/bmj-2023-077738. 25. Vickers A, O'Brien F, Montorsi F et al. Current policies on early detection of prostate cancer create overdiagnosis and inequity with minimal benefit. BMJ. 2023 May 17;381:e071082. doi: 10.1136/bmj-2022-071082. 26. Catalona WJ, Smith DS, Ratliff TL et al. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. N Engl J Med. 1991 Apr 25;324(17):1156-61. doi: 10.1056/NEJM199104253241702. 27. Lucassen A, McCartney M, Sullivan R. Prostate cancer: polygenic risk scores have not shown clinical benefit. BMJ. 2025 Jun 10;389:r1179. doi: 10.1136/bmj.r1179. 28. Chodak GW, Schoenberg HW. Progress and problems in screening for carcinoma of the prostate. World J Surg. 1989 Jan-Feb;13(1):60-4. 29. Adami HO, Baron JA, Rothman KJ. Ethics of a prostate cancer screening trial. Lancet. 1994 Apr 16;343(8903):958-60. doi: 10.1016/s0140-6736(94)90071-x. 30. Woolf SH. Screening for prostate cancer with prostate-specific antigen. An examination of the evidence. N Engl J Med. 1995 Nov 23;333(21):1401-5. doi: 10.1056/NEJM199511233332107. 31. Swanson G. Survival and conservative treatment for localized prostate cancer. JAMA. 1996 Jan 3;275(1):31; author reply 32. 32. Chodak GW. Comparing treatments for localized prostate cancer--persisting uncertainty. JAMA. 1998 Sep 16;280(11):1008-10. doi: 10.1001/jama.280.11.1008. 33. Young RH, Eble JN. The history of urologic pathology: an overview. Histopathology. 2019 Jan;74(1):184-212. doi: 10.1111/his.13753. 34. TOTTEN RS. Some experiences with latent carcinoma of the prostate. Bull N Y Acad Med. 1953 Jul;29(7):579-82. 35. Aronowitz R. "Screening" for prostate cancer in New York's skid row: history and implications. Am J Public Health. 2014 Jan;104(1):70-6. doi: 10.2105/AJPH.2013.301446. 36. Albertsen PC. Observational studies and the natural history of screen-detected prostate cancer. Curr Opin Urol. 2015 May;25(3):232-7. doi: 10.1097/MOU.0000000000000157. 37. Ilic D, Djulbegovic M, Jung JH et al. Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. BMJ. 2018 Sep

		5;362:k3519. doi: 10.1136/bmj.k3519. 38. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ. 1996 Jan 13;312(7023):71-2. doi: 10.1136/bmj.312.7023.71. 39. Penston J. Should we use total mortality rather than cancer specific mortality to judge cancer screening programmes? Yes. BMJ. 2011 Oct 13;343:d6395. doi: 10.1136/bmj.d6395. 40. Walter LC, Covinsky KE. Cancer screening in elderly patients: a framework for individualized decision making. JAMA. 2001 Jun 6;285(21):2750-6. doi: 10.1001/jama.285.21.2750. 41. Jackson SD, de la Rue MR, Greenslade TP, et al. Screening asymptomatic men for prostate cancer: A comparison of international guidelines on prostate-specific antigen testing. J Med Screen. 2022 Dec;29(4):268-271. Doi: 10.1177/09691413221119238. RECENT PUBLICATIONS Takahashi T. Evidence-Based Prostate Cancer Screening. Ann Surg Oncol. 2025 Sep 2. doi: 10.1245/s10434-025-18262-0. Takahashi T. Organized prostate cancer screening and the declaration of Helsinki. Scand J Urol. 2025 Aug 8;60:149-150. doi: 10.2340/sju.v60.44242. Takahashi T. Evidence and Rationale for Prostate Cancer Screening. Prostate. 2025 Sep;85(13):1245-1247. doi: 10.1002/pros.70002. Takahashi T. MRI in Prostate Cancer Screening: Clinical Trial Requirements. Acad Radiol. 2025 Jul;32(7):4340-4341. doi: 10.1016/j.acra.2025.05.045. Takahashi T. Technical comment on: Würnschimmel C, et al. Prostate cancer screening in Switzerland: a literature review and consensus statement from the Swiss Society of Urology. Swiss Med Wkly. 2025 Apr 30;155:4069. doi: 10.57187/s.4069. Takahashi T. The Natural History of Screen-Detected Prostate and Breast Cancer. AJR Am J Roentgenol. 2025 May 28. doi: 10.2214/AJR.25.33170. Takahashi T. Benefits of Prostate Cancer Screening for Black Men. J Cancer Educ. 2025 Mar 19. doi: 10.1007/s13187-025-02607-0. Takahashi T. Urologists and pathologists in prostate cancer screening. Virchows Arch. 2024 Sep 21. doi: 10.1007/s00428-024-03929-y. Takahashi T. Observational study on screen-detected prostate cancer: case series of empirical clinical practice. BJU Int. 2025 Jan;135(1):177-178. doi: 10.1111/bju.16525.

			Takahashi T. Optimising the use of the prostate-specific antigen blood test in asymptomatic men for early prostate cancer detection in primary care: report from a UK clinical consensus. Br J Gen Pract. 2024 Aug 29;74(746):397. doi: 10.3399/bjgp24X739197. Takahashi T. Prostate-Specific Antigen Screening Should Not Be Covered by Publicly Funded Health Insurance. JAMA Oncol. 2023 Jun 1;9(6):867-868. doi: 10.1001/jamaoncol.2023.0254. Takahashi T. Would You Play a Russian Roulette-type Game of Prostate-specific Antigen Screening on Yourself? Eur Urol. 2022 Jan;81(1):e22. doi: 10.1016/j.eururo.2021.10.003.
S5			I am a ***** retired GP with a strong family history of prostate cancer, with a special interest in men's health and who is currently in remission from prostate cancer after a radical prostatectomy. I support the screening committee's preliminary decision not to advise either a universal or targetted screening programme but have several constructive suggestions. When as a GP I counselled patients about whether to have a PSA or not, it took at least 40 minutes. Whilst there are many complex uncertainties, one of the most difficult issues to articulate was the contrast between a personalised medical service and a population focused service. In the case of my own prostate cancer care, I personally found that decisions made in a personalised model mostly had to be based upon emotional perspectives rather than robust scientific data. I FEEL IT IS CRITICAL THAT IN THEIR FINAL RECOMMENDATION THE SCREENING COMMITTEE ARTICULATES THAT THEIR ROLE IS POPULATION FOCUSED. IF PROSTATE SCREENING IS NOT RIGHT FOR THE WHOLE POPULATION, THIS DOES NOT PRECLUDE A PERSONALISED APPROACH AS FOLLOWS: The 40 minute consultations I used to provide for men requesting a PSA are clearly not widely available from most GPs. Even then, much critical information was not shared due to constraints of time resource. Most men between the ages of fifty and seventy five are IT literate. The entry point for a man requesting asymptomatic prostate screening should be a charity supported web tool. Such a webtool would navigate a patient through the complexities and anxieties of PSA testing, PSA density calculation and PSA velocity determination as the prelude to deciding upon transrectal or template biopsy. It was only as a patient that I understood that with any PSA above 3.0 with a prostate volume of 20cc the psa density is greater than

		0.15 so high risk. By contrast high prostatic volume reduces the concern if it delivers a low PSA density and can allow deferment of referral if the patient so chooses. TRANSRECTAL ULTRASOUND or MRI FOR PROSTATE VOLUME ASSESSMENT SHOULD BE WIDELY AVAILABLE IN THE COMMUNITY As a receptive GP, my patients frequently described the disproportionate, pervasive and destructive anxiety that PSA testing and particularly repeat PSA testing caused them. IATROGENIC HARM TO MENTAL HEALTH BY PSA TESTING DOES NOT SEEM TO HAVE BEEN ADEQUATELY ARTICULATED BY THE SCREENING COMMITTEE. When deciding whether to have a biopsy information on PSA and MRI is critical. No one told me as a man with a strong family history of Ca prostate that when I had a hip replacement ***** that this could obscure my prostate on an MRI. So when my prostate could not be clearly visualised on MRI this precipitated me into biopsy. MEN WITH HIGHER RISK OF PROSTATE CANCER SHOULD BE ADVISED TO CONSIDER ENGAGING WITH PSA TESTING BEFORE HIP REPLACEMENT After biopsy difficult decisions need to be made. THE GRANULARITY OF DATA IN NICE GUIDELINES FOR THE MANAGEMENT OF EARLY PROSTATE CANCER IS SUBOPTIMAL. NICE 10YR OUTCOMES ARE NOT ADEQUATE FOR A 50 YR OLD TO MAKE LIFE CHANGING DECISIONS THAT WILL HOPEFULLY IMPACT ON 30 OR MORE YEARS OF LIFE My personal experience was that my ***** histology and stage was amalgamated with older men with more advanced disease when predicting future outcomes, thereby biasing my decision making to be more interventional. CLINICAL DECISION MAKING SHOULD BE BASED UPON 10, 15 AND 20 YEAR OUTCOME DATA FOR BOTH COMPLICATIONS, SIDE EFFECTS AND MORTALITY/MORBIDITY THAT IS GRANULAR FOR 5YR AGE BANDS AND THE PRECISE GLEESON SCORE FOR EACH OF THE STAGES OF DISEASE. For many patients, as myself, there simply is no scientifically correct choice between active surveillance, radiotherapy or radical prostatectomy. It is impossible for patients to have surgeon specific outcome data which includes doctors in training. WHEN DISCUSSING A PERSONALISED APPROACH TO PROSTATE CANCER CARE IT IS IMPERATIVE FOR THE NHS

		TO BE TRANSPARENT ABOUT DIFFERING OUTCOMES FROM SURGEONS OF DIFFERENT CAREER GRADES. As a patient, due to my relatives' complications from radiotherapy and my own anxieties about active surveillance ***** I chose radical prostatectomy but only because I also chose to commit to funding a private operation by a specific robotic specialist. IF THE NHS LACKS THE CAPACITY TO PROVIDE PATIENTS WITH SURGEON SPECIFIC OUTCOME DATA AND TO PROVIDE SURGERY BY THAT SPECIFIC SURGEON THEN THIS SHOULD BE ARTICULATED IN THE CLINICAL DECISION PROCESS THAT THE PATIENT IS USING. Planar sectioning of an excised prostate leads to many more false positive margins than conical sectioning. Most advanced health economies now use conical sectioning, reducing false positive histology margins and post operative anxiety. THE NHS SHOULD MANDATE CONICAL SECTIONING OF THE PROSTATE. So how does this scattering of observations about the prostate cancer pathway impact upon the very first step of the pathway : educating society, politicians and men themselves about the possible role of prostate screening? The screening committee has to report as scientists following best practice in decision making, which I believe it has. However in the political and media context of high profile expectations, the screening committee needs expertly to communicate the complexities of a population focused system as opposed to a personalised system. In a personalised system of prostate cancer care there is no right path to follow and decisions are usually made with considerable emotional preference between diagnostic and therapeutic options. Therefore, therapeutic options need to be well understood to empower good decision making about diagnostic tools, biopsy, mri, transrectal ultrasound, psa, psa density and psa velocity. Only when all components of a diagnostic and therapeutic pathway for prostate cancer have been fully articulated along with complications, mental health and mortality outcomes can a man robustly engage with having a PSA test. I believe that only a web tool can provide wide access this function and thereby deliver choice and a compromise between population and personalised health care. Thank you for considering my observations.
S6	Robert Beardsell	My name is Dr Robert Beardsell. I am a GP and a prostate cancer survivor. I am in a fairly unique position to assess prostate care in

		this country and in particular the way the committee has arrived at its recommendations. It is interesting that the National Screening Committee is basing its recommendations on an obviously flawed model. There are three very significant assumptions at the start that fatally skew the model. The first is the focus on statistics which look at the benefit of a single PSA screening test. The medical profession would all agree that a single test is impossible to read and make clear "next step" medical recommendations. However, having a previous or sequence of PSA test results is a leap forward in accuracy and specificity. If there has been a significant increase since the last test, I can safely say that prostate cancer needs to be excluded with further investigation with a high enough cancer diagnosis rate to justify the cost. A screening program gives GPs that sequence of results. The committee should look to obtain statistics about the benefits of a screening program which is up and running more than 2 yrs to get a proper picture. To find evidence to back this POV up, simply look at the study which the UKNSC already purports to take note of, namely European Randomised Study of Screening for Prostate Cancer. This study in fact shows a screening program with follow up, ie repeat PSAs demonstrates a 20% reduction in mortality. This would be a huge saving of men's lives. The second flaw is using the statistics of only 1000 screenings offered. This means the UKNSC recommendations talk about 1 life saved. In fact, taking the UKNSCs own figures, because there are 8.4 million men in the UK aged 45yrs up to 60 yrs, the actually number of men's lives which would be saved by one PSA test screening across this age group is 8,400 lives saved. It is much harder to argue that it is not worth saving 8400 working men's lives! (This limit suggests to me that the committee's hidden task is to keep spending down and try to justify this mean fisted approach by the government) The third flaw is the assumption that men do not want to be given the chance of cure from cancer simply because there is a risk of incontinence or impotence. I personally took that risk with the hope of a cure and hence no further worry about the cancer coming back. And even though for me it was all in vain, the cancer is still there, I would not have wanted to change any of this. I now have side effects from my surgery and radiotherapy, but to not have been given my chance of cure would have been unthinkable. I urge the committee to correct the model taking into account the above. I am confident this will result in a different recommendation to the Secretary of State for Health regarding screening for Prostate cancer.

		I have considerably more to say on these issues, please feel free to contact me. Tel no *****. Yours Faithfully Dr Robert Beardsell *****
S7	Susan Bewley	I am in agreement with not recommending general population screening. You must continue to resist calls for screening that doesn't 'work'. Please review the infographic – its appalling as it suggests all men should pass through some kind of 'filter'. It is misleading as to the nature of screening – which is ALWAYS harmful (thanks to labels, anxiety, further testing, overdiagnosis and harmful treatments) and only SOMETIMES beneficial (clinically and cost effective, fulfilling W&J criteria). Please review all the information you give for screening. I continue to receive deceitful phone calls and leaflets which do not present it as a properly informed decision. There should be a standard (whether for heel pricks, aneurysms or cancer), along the lines of the Harding Centre Fact Boxes. Always presenting 'Doing Nothing' first, as it is always an acceptable choice, and then the 'Doing Something' without using manipulative colours, words, numbers etc. Until you share things like the prostate cancer icon-array with the general public, they (and all the men who get prostate cancer, whether Chris Hoy, Stephen Fry, or Prof Mike Richards) are able to whip up fervour unreasonably. Please also set up a system for reviewing decisions properly with a built-in mechanism for STOPPING screening systems when they no longer pass the test – this might be because treatments have improved (eg Breast Cancer which NEVER passed the criteria when introduced, and has never been properly investigated), or because the disease has changed in nature (eg cervical precancer in vaccinated girls). If the NHS does not have proper mechanisms for approving, and closing, screening programmes and explaining it properly to the general public, then we will eventually all be at risk of overdiagnosis. I don't want the general public to be terrorised into constant invasive surveillance, which will bankrupt the NHS, such that the well (who will be made ill) are prioritised over the actually sick (who end on waiting lists and trolleys). I have not seen an aggressive communication programme to explain the dangers of screening, nor taking the kind-hearted but wrong-headed men aside. All I see its bloated cancer charities working with CR_UK and its vested interests to 'sell' the dream.

			Please stick to your guns. And put fair information (like what symptoms matter if you dont get screened) decision aids into the public domain. The bowel cancer leaflet is a disgrace – using three different forms of numbers in first paragraphs which knowingly confused and frighten. I cannot trust the NSC and screening programmes because you do not inform me properly.
S8	David Dixon		I have been running a men's health and wellness clinic *****. This is a project that I have initiated after identifying male health inequalities both nationally and within my locality ***** which has a large diverse population and levels of deprivation. The clinics are essentially like an MOT for men, they are designed to promote healthy living, prevention of chronic diseases, cancers and early mental health interventions. It's an opportunity to have a health check that includes BP reading, a routine blood discuss their lifestyle, discuss healthy eating exercise, prevention of cardiovascular disease, diabetes, mental health wellness and male specific cancer's testicular and of course Prostrate cancer. In regards to Prostrate cancer, I discuss the most common related symptoms and identify the high risk groups and as like my father and Sir Chris Hoy many men do not have any symptoms. I then explain about the PSA test informing them very clearly that the test is not a diagnosis and there can be false positives as well as false negatives; out of approximately 500+ men that I have seen in my clinics I have have only 1 patient decline to include the PSA blood test, all the others where very keen to have them as a result I have identified and referred 6 patients to a urologist for further investigation 2 had no concerns and was discharged, 1 patient was identified with an enlarged prostrate 3 had a diagnosis of prostrate cancer and 1 of which his cancer has metastasised, none these cancer would not have been found with out screening. I myself are a high risk patient ***** and I have my PSA blood test taken regularly. It is clearly documented in the first Men's Health Strategy plan released on 19th November 2025 it wants to target cancer, so surely this includes early detection of cancer such as prostrate. I fully support the need of a national screening programme, and I will continue offering PSA testing for my patients irrespective of your final decision.
S9	Dr Kasturi Warnakula suriya		1. If the UK National Screening Committee finds that PSA is an unreliable test for screening it is important to undertake a national pilot studies to develop biomarkers that are more reliable for the early detection of prostate cancer.

			2. Men's cancers have been overlooked for over decades resulting in significantly more deaths among men due to cancer. 3. PSA testing for men in combination with additional magnetic resonance imaging (MRI) scanning as a follow-up test (before surgery) may decrease over diagnosis which concerns NSC.
S10			You should specifically add a comment about screening in mutation carriers for other susceptibility genes – such as MSH2
S11	Dr Anthony G OSullivan		Thank you for seeking opinions on this. I have had prostate cancer. I understand the importance of weighing up false positives and false negatives against positive identification of cancer cases. Knowing the largely number of men with prostate cancer, and far too many dying after late diagnosis; and knowing that the bad outcomes are loaded against Black men, I urge that the decision taken be reconsidered urgently. And this in the light of: 1. Best practice using the PSA test and MRI scans to justify the next stage – as used in Scandinavian health systems. 2. The great risk to Blackf men from postponing a screening programme targeting those at greatest risk; 3. The loss of confidence of the Black community in our NHS if it is seen to make a discriminatory decision; 4. The significant gains made in Scandinavian countries which, if reproduced in England, would save many lives and much funding spent on late care and palliative care.
S12			Black men are twice as likely to contract prostate cancer – a targeted screening programme supported by AI could save lives and avoid unnecessary late stage treatments. This is both an ethical and economic imperative in line with the 10 year plan. Also the argument that a screening programme would lead to an unnecessary use of resource and false positives ignores the advances made in diagnostics.
S13			As a healthcare professional with training in population health this decision appears to be incorrect and will worsen existing health inequalities in certain populations. I'm sure you know the statistics but let me reiterate them: This is the most common type of cancer for men and will affect up to 1 in 5 men during their lifetime and will kill 11,600 men per year. The risk of being diagnosed with and dying from prostate cancer as a black man is DOUBLE that of a white man. This health inequity requires addressing and a national screening programme is warranted

S14			My GP referred my ***** PSA reading for investigation because of a family history. MRI conducted + Biopsy established I had grade ***** aggressive cancer cells within prostate. NHS refused to operate because I was ***** , so I elected to pay ***** from my pocket for a ***** prostatectomy *****. Follow up NHS appointments have all been deferred for more than 2 years. ***** hospital are still unable to provide any date for a Post op follow up appointment. My private actions to pay have definitely saved my life. I am no longer needing any medication. Shame on the negligent responses I've received from the NHS The testing of all males with a family history of prostate problems is fundamentally necessary to save many lives. STOP WASTING MONEY ELSEWHERE AND GET ON WITH THE JOB at least to the PSA test (+ MRI scan stage where necessary).
S15	Donald MacDonald		The committee are to be congratulated on the thoroughness of their work and their commitment to evidence based medicine in the face of considerable media attention. Thank you for thinking of the majority of men in the UK who would have been harmed by a PSA screening programme but who do not have a charity to represent them. Thank you for trying to help us spend precious funds usefully. Shocking that PPE and time spent leading the country do not equip one with the basic skill of recognising when one is 'off-piste'. Shame we have gone past QI Series S (but very much looking forward to Lady Bracknell)
S16			You don't say how or what physically is involved with the prostate screening of men with a BRCA variant. this is extremely important when communicating with men so that they are not put off by imagining terrible probing tests. perhaps use men and also those born biologically as male, to be inclusive. its not clear to me how this testing relates to the PSA if they have already had one of those or have a raised value of PSA. what would be lovely and clear would be to have a pathway mapped out for these males showing that if they are experiencing

		any of the comprehensive list of symptoms you shared, that they should visit their GP and expect A, B, C It would be so good if those presenting with symptoms could access the Blood test and gene test say R208 and then go onto having the cancer screening... whatever that entails? surely that would be a good patient pathway. also to screen those men with BRCA positive genetic results anyway. but i would like to see a more generic offer to those men with symptoms and a raised PSA getting offered the genetic test and the cancer screening. Surely that fits in better with the 10 year NHS plan to pick up more cancers earlier too
S17	Richard von ABENDO RFF	I have been through the prostate cancer pathway. A chance gardening injury led to repeat of my PSA, showed significant increase in 18 months. Safe MRI and safe biopsy led to Gleason 3 plus 4 diagnosis of cancer in both lobes. Unlike ***** radical prostatectomy was best option. (nerves spared, brilliant outcome despite your reports misleading commentary). Other options available for those concerned about risks. I wanted prostate just removed. I had choice enabled by fortuitous test. Otherwise I may have got diagnosis too late. PSA test is just one aspect of safe, science based prostate cancer treatment pathway. Hospital very informative on this with lots of advice and support. 12000 deaths a year. Many of which could be avoided with proper prostate monitoring pathway. Your conclusions are out of date, conservative and dangerous. Worse still they are misleading in how summarised, putting men off psa tests saying it leads to avoidable impotence and incontinence. Shocking response. As a patient safety campaigner I see the report deny cancer sufferers even being seen as patients, with rights, choices, intelligence. I believe your conclusions are outdated. Mri and biopsy guided diagnosis and treatment is what occurs today. Of course they need funding and other resources. That can be the only explanation of your rationing agenda of the most common cancer in men. As well as many other disorders of prostate will be affected, confused by men. You must re think this whole strategy please and improve comms re it as men will be put off life saving and quality of life enhancing interventions they could benefit from. I could say more but have illusions who reads or notes this at all. In frustration and exoerience based anger. *****. To the Members of the UK National Screening Committee, I am writing to express my deep concern regarding the Committee's draft recommendation against introducing a national screening programme for prostate cancer. I do so both as a patient-safety campaigner and as someone whose life was directly saved by timely access to the very diagnostic pathway this decision would limit for other men.

			My experience illustrates the critical role of PSA testing as an entry point to modern prostate-cancer diagnostics. A minor, unrelated injury brought me back to my GP, who repeated my PSA test. Over only 18 months, my PSA had risen substantially. That single measurement triggered an evidence-based diagnostic sequence: a multiparametric MRI followed by a targeted fusion biopsy. This contemporary pathway—safe, precise, and scientifically robust—identified a clinically significant Gleason 3+4 adenocarcinoma in both lobes of my prostate. Because it was detected early and accurately, I had access to the full range of treatment options. I was not suitable for focal therapy; a radical prostatectomy with nerve-sparing techniques offered the best chance of cure. I now enjoy excellent functional outcomes with minimal side-effects—outcomes that contradict outdated portrayals of radical prostatectomy as inevitably causing severe incontinence or impotence. The Committee’s report appears to rely on assumptions about prostate-cancer diagnosis and treatment that no longer reflect clinical reality. It underestimates the transformative impact of multiparametric MRI, which dramatically reduces unnecessary biopsies and guides precise sampling. It does not fully recognise that the era of blind, saturation biopsies is over. PSA is not a diagnostic tool in isolation; it is the essential first step in a sophisticated, risk-stratified pathway that is both safer and more accurate than in the past. I am particularly concerned by the public-facing summary accompanying the draft recommendation. Presenting PSA testing as something that “leads to avoidable impotence and incontinence” is misleading and risks deterring men from seeking advice. Such messaging denies men autonomy by implying they cannot weigh benefits and risks in partnership with their clinicians. This approach is paternalistic and may inadvertently contribute to later diagnoses and poorer outcomes. It is difficult to avoid the conclusion that resource constraints form an unspoken backdrop to this position. If so, transparency is essential. We must confront the true cost of inaction: prostate cancer remains the most common cancer in men and causes around 12,000 deaths annually in the UK. A modern, targeted monitoring programme—using PSA intelligently as an initial risk marker—could detect clinically significant disease earlier and prevent many of these deaths. For these reasons, I strongly urge the Committee to: 1. Reconsider the draft recommendation in light of current clinical practice, particularly the role of MRI-guided diagnostic pathways.

			2. Commission an updated evidence review that fully reflects contemporary imaging, biopsy techniques, and treatment outcomes. 3. Revise public communications to be accurate, balanced, and supportive of informed patient choice rather than risk-averse to the point of being discouraging. My experience is not an outlier; it reflects what modern prostate-cancer detection and treatment can achieve when men are given timely access to assessment. I urge the Committee not to close the door on these opportunities for others. Yours sincerely, ***** I consent to this submission being published in full and welcome continued engagement on this important issue
S18	Tim Dudderidge		It would make sense to me that from the outset this group of men should be screened with both PSA and bi parametric MRI scan reported using a protocol suitable for a screening situation and that research be embedded from the outset to evaluate whether PSA or PSA and MRI screening combined should be undertaken in the long run. This will help to inform not only screening of high risk groups but also will provide valuable real world information that can inform the potential future population screening programs. To start screening this group with PSA only using established age linked thresholds would be in my view a very backward approach and although this is the basis on which the evidence base supports screening of this group the world has moved on and MRIs are much better by marker for detecting clinically significant disease?
S19	Thomas Walton		Dear Sir/Madam, I read with interest the proposed UK NSC screening recommendations for prostate cancer testing in men with BRCA1/BRCA2 mutations. There is certainly no doubt that these men have a higher risk of getting prostate cancer and harbouring aggressive disease compared with the members of the general population without such mutations. As a practising clinician in the field, my issue is that most men will be entirely unaware that they harbour such mutations, and therefore targeted testing will be extremely difficult. The CanRisk score has been advocated for screening families of men with prostate cancer (see below), however in practice it is unwieldy and complicated to use. A more simple screening tool along the lines of the Amsterdam Criteria will be needed to identify at risk men for further germline testing.

			Tom Walton R430 Testing Criteria • Proband diagnosed with prostate cancer at <50 years • Ashkenazi Jewish ancestry and prostate cancer at any age • ≥1 grandparent from Whalsay (Shetland) and prostate cancer at any age • Proband diagnosed with metastatic prostate cancer <60 years • Proband diagnosed with prostate cancer with a CanRisk score of >10% and where they do not meet criteria for R208, R207 or R210 – see overlapping Clinical Indications
S20			There are are few things missing which I think should be taken into account in the modelling. Deaths from prostate cancer have been modelled against harms from overdiagnosis. But nowhere does death from overdiagnosis seem to have been considered. With osteoporosis being one of the potential harms, and 1/3rd with an osteoporotic hip fracture dying within 1 year, an estimation of deaths caused from overtreatment should be feasible and would add a huge counterweight against the lives saved. Other genetic risk factors should also be considered. There are 8 genes on the prostate cancer gene panel R430 and a large polygenic component to the risk of prostate cancer (polygenic scores). Polygenic scores for prostate cancer have a similar predictive value to that of the PSA test, but don't seem to have been considered here. It also isn't considered the knock-on impact on the healthcare service. Every biopsy performed that does not find cancer is pushing time-critical aggressive cases further down the waiting list, delaying treatment for those who do need it.
S21	EDUARD O XAVIER HIAS POZZOB ON		I believe the role of PSA in prostate cancer screening is not yet defined. Prospective, randomized studies comparing PSA, MRI, and mutation testing are needed to determine the cost-effectiveness of screening.
S22	Adrian Chenzbra un		The recent UK recommendations against screening for prostate cancer are worrying by rejecting it for practically everyone including high-risk individuals. The Committee are correct to emphasise that the balance between benefit and harm is questionable and that there is only one country with a national screening plan: Lithuania. They are also correct that screening had been associated with only

		a modest reduction in mortality. Beyond that, however, they offer a biased approach to support their position. They ignore the fact that the balance between harm and benefit may be tilted one way or the other by the quality of the medical system within which the screening is offered, by the changing landscape of available diagnostic and treatment modalities and by each country's human development index (HDI). You would expect that in a high HDI country such as UK the balance would be seen as at least tilting toward benefit. They ignore the fact that, overall, screening has been associated with a, even if modest, decrease in mortality and that, as a matter of principle, individuals should be offered the option of informed choice between possible risk of overdiagnosis/complications and possible premature avoidable death due to prostate cancer. They cherry-pick the available evidence: they quote the 2012 USPTF guidelines that are against routine screening but fail to mention that these guidelines have been superseded by the 2018 ones of the same body that now support individualised approach/shared decision making, in line with the position of all the other updated guidelines: 2010 American Cancer Association Guidelines, 2023 American Urology Association Guidelines, 2025 European Association of Urology Guidelines and up-to-date CDC advice. Selectively quoting in 2025, only 2012 guidelines and ignoring more recent ones as listed above is difficult to justify. The Committee decided to ignore generally acknowledged risk factors such as family history and African descent, thus deviating from all the available contemporary international guidelines. This decision, based on modelling and convoluted argumentation is even more egregious when only screening based on presence of high-risk genes is suggested instead, though carriers of such genes would, usually, not be aware of their status. One has the feeling that the Committee had preponderantly in mind economic considerations and the limitations of the UK medical system rather than what would be the best medical approach and public interest and relied heavily on modelling. Indeed, none of the authors of the Sheffield Report on Cost-effectiveness of Prostate Cancer Screening on which these recommendations are based, is a Urologist or at least a medical practitioner: they are modellers, statisticians, and health economics specialists. We saw during the COVID pandemics what was the value of such modelling devoid of clinical insight and detached from social reality. It is my concern that, if adopted in their present form, these recommendations will be seen by GPs at large as a justification to be even less proactive in initiating screening and to discourage even individuals at risk from undergoing it. The outcome will be to add prostate cancer to the already existing list of malignancies for

			which UK citizens have lesser chance of survival/cure than citizens of countries of similar socio-economic level.
S23	James Nevin		Any screening program is going to impact massively on national MRI services. Can the NHS afford this? Can proponents of screening provide reassurance that this will not cause harm to patients without prostate cancer screening? Can the quality of MRI reporting be guaranteed?
S24	Joshua Forman	Jnetics	Jnetics is a UK-based charity dedicated to educate about and screening for Recessive Genetic disorders that disproportionately affect those of Jewish ancestry. We are also official outreach and engagement partners of NHS England on the NHS Jewish BRCA testing programme. We have been the key organisation linking the community (those of Jewish ancestry, with at least 1 Jewish grandparent) and the NHS testing programme. Therefore we have communicated about the risks of BRCA gene variants, signposted to the NHS BRCA testing programme and have become a first port of call for many regarding information around BRCA testing. We have worked closely with clinicians and health professionals to ensure that our language is both scientifically accurate and empathetic, in this specific context. Almost 44,000 people registered for BRCA testing during the 3 year pilot programme. Jnetics welcomes the UK National Screening Committee's (UK NSC) public consultation on prostate cancer screening strategies and strongly supports the proposed recommendation in favour of targeted prostate cancer screening for men with confirmed BRCA1 and BRCA2 pathogenic variants, as set out in the draft recommendation of the evidence review [p7, para 2]. Jnetics is firmly of the view that the evidence presented in the 2025 UK NSC prostate cancer screening evidence review supports approval and implementation of a risk-stratified screening programme for men with BRCA1 and BRCA2 variants, with screening every two years from age 45 to 61, as proposed by the modelling analysis [p5, para 2; p6, para 1]. This targeted approach appropriately balances benefit and harm and is clearly distinct from population-wide PSA screening, which the UK NSC has repeatedly found does not meet screening criteria [p1, para 2; p4, para 1]. The evidence review clearly documents that the longstanding concerns regarding PSA-based screening—namely high rates of false positives, overdiagnosis, and overtreatment—apply predominantly to average-risk populations.

			[p2, paras 1–3; p4, para 1]. From a clinical perspective, the evidence review makes clear that the balance of benefit and harm for prostate cancer screening varies substantially by risk group, and that genetically defined populations warrant separate consideration from the general population [p3, para 3; p4, para 2]. Men with confirmed BRCA1/2 variants represent a clearly identifiable group already engaged with genetic services, making implementation of targeted screening both feasible and proportionate. Ethically, Jnetics believes that failure to offer screening where modelling demonstrates net benefit risks denying high-risk individuals access to potentially life-saving early diagnosis, contrary to the principles underpinning risk-stratified screening endorsed by the UK NSC. [p3, para 4]. Jnetics welcomes the launch of the TRANSFORM trial and supports its aims to improve prostate cancer screening through MRI-based pathways and incorporation of genetic risk [p6, para 1]. However, we emphasise that the review does not position TRANSFORM as a prerequisite for action on BRCA1/2 screening, but rather as complementary research that may further refine future strategies [p6, para 2]. We support the UK NSC's proposal to proceed with BRCA1/2 screening while continuing to evaluate emerging evidence to optimise programme design [p6, para 3]. Jnetics urges the UK NSC to move forward with approval and implementation of this targeted approach as a proportionate, ethical, and evidence-based application of risk-stratified screening.
S25		Sutton Coldfield Group Practice	UK National Screening Committee Consultation: Prostate Cancer Screening (2025) 1. Introduction GP practices support evidence based approaches to cancer prevention and early diagnosis, and recognise the importance of addressing prostate cancer mortality and inequalities. However, any national screening recommendation must carefully balance benefit against harm, cost, and deliverability within a system where primary care capacity is already significantly constrained. 2. Impact on GP workload and demand 3. 1 Direct workload implications Even where the screening test itself is a blood test, the majority of operational workload sits in primary care. This includes identifying

		eligible patients and maintaining accurate coding such as BRCA status, operating call and recall systems, managing reminders and follow up of non-responders, providing pre-test counselling and shared decision making, delivering phlebotomy appointments and result communication, safety netting and repeat testing, onward referral, and managing anxiety, false positives, and opportunistic testing requests. This workload is clinically and administratively intensive and cannot be assumed to be absorbed into existing GP capacity. 4. 2 Demand amplification and spillover effects Experience with PSA testing shows that organised screening increases opportunistic requests from men outside eligibility criteria, follow up consultations for borderline or fluctuating PSA results, and patient contacts relating to delays or outcomes in secondary care. Even a targeted programme risks creating spillover demand that disproportionately affects primary care, particularly in smaller or under-resourced practices. 5. Costs and risk of cost shifting to Primary Care 6. 1 Unfunded activity From a GP practice perspective, a major concern is the risk that significant activity is transferred to primary care without dedicated funding. This includes clinical time for counselling and consent, phlebotomy capacity including staff, rooms and consumables, administrative time for call and recall and results handling, and IT and coding changes to support eligibility and monitoring. Without explicit funding mechanisms such as a nationally commissioned enhanced service, this represents unfunded work and is not sustainable. 7. 2 Identification of BRCA carriers The evidence review notes that the economic modelling does not include the cost or pathway for identifying BRCA1 or BRCA2 mutation carriers. If identification relies on GP-led family history taking, genetic test ordering or referral, and chasing and interpreting genetic results, then the true cost and workload would be substantially higher than modelled, undermining affordability and feasibility. We would strongly recommend that any BRCA targeted screening programme uses a genetics-led or specialist-led identification pathway, relies on central flagging of known carriers from existing genetics records, and does not place responsibility for case finding on GP practices without full resourcing.

			8. Practical Implementation Issues 9. 1 Eligibility, coding and data flow Clear national standards are required for recording and validating BRCA status in GP records, interoperability between genetics services, secondary care and primary care systems, and handling men with results from private or overseas testing. Without this, practices will face inconsistent data, disputes over eligibility, and increased administrative burden. 10. 2 Patient communication and informed choice Given the known risks of overdiagnosis and overtreatment, GP practices will require nationally consistent patient information and decision aids, clear messaging on absolute benefits and harms, and materials suitable for use in short primary care consultations. Inadequate national communication will inevitably result in increased GP consultations to manage uncertainty and anxiety. 11. 3 Inequalities While targeted screening may reduce risk for specific groups, it may also widen inequalities if uptake is lower in deprived populations or access depends on digital systems or proactive health seeking behaviour. Equity must be built into programme design, with monitoring of uptake by deprivation and ethnicity, and proactive support for underserved groups. 12. Downstream and long-term impacts returning to Primary Care Even when diagnostics and treatment occur in secondary care, GP practices manage waiting time queries and result chasing, post biopsy complications and infections, and long-term consequences of treatment such as incontinence, erectile dysfunction, and mental health impacts. High rates of overdiagnosis therefore translate into long term primary care workload, which must be factored into decision making. 13. Conditions for GP Support of a BRCA targeted screening programme General practice would support a BRCA targeted screening recommendation only if the following are clearly specified. 14. A national operating model for identification, invitation, testing and results, not left to local interpretation.

			15. Genetics led identification of BRCA carriers, with no expectation that GP practices undertake unfunded case finding. 16. Full funding of all primary care activity, including administration, phlebotomy, IT changes and clinical time. 17. Clear boundaries of GP responsibility, including how opportunistic PSA requests will be managed. 18. Robust monitoring and evaluation, including impact on GP workload, secondary care capacity, uptake, inequalities and patient harm.
S26	Neil Smith		Evidence supports screening for at risk groups. The World Health Organization now recognize Firefighting as a level 1 occupational risk for cancers due to exposure to carcinogenic materials in the line of work. Prostate cancer screening should be an option for all Firefighters aged 40 and over as a matter of urgency. Look at the study conducted by the University of Central Lancaster – Professor Anna Stec in the first instance.
S27	John Trott	Leonardo Helicopters	I'm writing to express my disappointment with the recent screening committee decision regarding prostate screening. I sincerely hope that, in the end, the government will make the right decision to support high-risk groups beyond BRCA1 and BRCA2 – including firefighters. As you know, the evidence of increased risk is clear. Tests and studies have shown up to a four-fold higher risk in firefighters compared with the general public. This surely makes it both a logical and humane decision to provide screening for those who spend their careers protecting others, while also saving the country money through earlier detection and intervention.
S28	Julian Barwell	United Against prostate Cancer led by University Hospitals of Leicester and East Genomics	Prostate Cancer Screening in High-Risk Groups: Current Status, Challenges, and Recommendations from the United Against Prostate Cancer group. National organised screening for prostate cancer is set to be offered to men carrying inherited BRCA1 and BRCA2 pathogenic variants. This is a pivotal step, particularly for BRCA2 carriers, who have a markedly elevated risk of developing aggressive disease at a younger age, which screening can help detect. It is well recognised that BRCA2-associated prostate cancers not found through screening are often diagnosed at a late stage, resulting in poor outcomes. Limitations of the Screening Programme Despite this progress, the screening will not be extended to other high-risk groups such as men with a strong family history of prostate cancer, those with Lynch syndrome, or individuals of African or African-Caribbean ancestry. This exclusion is troubling and raises concerns about equity. Scientific evidence indicates that

		men with MSH2 Lynch syndrome mutations face an even higher and earlier risk of prostate cancer than those with BRCA1 mutations. The decision to limit screening is justified by the need for further research into targeted screening methods, such as MRI-guided biopsies and appropriate watchful waiting, to ensure benefit and avoid harm. However, it is discouraging that many men will continue to suffer while waiting for data that may quickly become outdated as technology advances. Innovation in risk assessment, biopsy methods, watchful waiting, and targeted screening often outpaces the accumulation of survival data, meaning study results can become obsolete as practices evolve. Additionally, there is concern that stakeholders and campaigners for broader screening have not been sufficiently consulted in the decision-making process. Points of Acknowledgement • A normal PSA result can provide false reassurance. • Biopsies carry inherent risks. • Screening tends to detect slower-growing disease, leading to a risk of overtreatment with no survival benefit. • There is a significant burden on NHS resources, including scanners, urology, oncology, and genetic services. Additional Information for Consideration ATM c.7271T>G Variant Men with the ATM c.7271T>G variant (p.Val2424Gly) have a substantially increased risk of prostate cancer, with studies estimating a 2.5 to nearly 5-fold higher risk compared to the general population. This translates to a cumulative risk of approximately 43% by age 80, compared to about 12-14% generally, and the potential for earlier onset. This high-risk missense variant justifies increased screening and management, similar to other hereditary cancer genes. • Odds Ratio (OR): Around 2.58 to 4.84, indicating much higher risk. • Cumulative Risk by Age 80: About 43% (vs. 12-14% in the general population). The IMPACT Study The IMPACT study is an international, prospective screening programme for men with pathogenic mutations in BRCA1, BRCA2,

		and Lynch syndrome genes (MLH1, MSH2, MSH6). Key findings for MSH2 include: • Men with Lynch syndrome caused by a MSH2 mutation (an inherited DNA mismatch repair gene mutation) have a significantly increased risk of developing prostate cancer, which is often more aggressive and diagnosed at a younger age (average age 58) compared to the general population. • Based on findings from the IMPACT trial, which utilized an annual prostate-specific antigen (PSA) threshold of >3.0 ng/mL for recommending biopsies in men with Lynch syndrome, the following risks were identified: • Higher Prostate Cancer Risk: MSH2 carriers with a PSA > 3.0 ng/mL were roughly eight times more likely to be diagnosed with prostate cancer than non-carriers. • Incidence Rates: In the study, 4.3% of MSH2 carriers were diagnosed with prostate cancer, compared to 0.5% in MSH2 non-carrier controls. • Aggressive Disease: Cancers in MSH2 carriers are more likely to be clinically significant (aggressive and potentially life-threatening), with one study finding that 85% of prostate cancers in MSH2 carriers were “clinically significant”. • Predictive Value: For MSH2 carriers, a PSA threshold of 3.0 ng/mL resulted in a high positive predictive value for finding cancer, with reported rates of 48.1% to 72.2%. • Long-Term Risk: By age 75, the cumulative incidence of prostate cancer in MSH2/EPCAM carriers is estimated to be as high as 46%. Tumours occur at a younger age (average 58 versus 66 years for non-carriers) and are more likely to have aggressive, clinically significant tumours. * Recommendation for High-Risk Individuals: Due to these findings, researchers recommend annual PSA screening starting at age 40 for men with MSH2 mutations to detect cancer earlier and potentially access life-saving treatment. Key Questions for the Committee • How will overall survival or metastatic disease survival be validly assessed, considering ongoing improvements in risk stratification, imaging, biopsy techniques, watchful waiting, and treatments? • How will men with significant family history be managed? Should screening advice be discontinued altogether? Recommendations

			1. Clearly define the level of risk and disease aggressiveness by age. Specify the evidence required to demonstrate screening effectiveness, e.g., a 20% risk of significant disease by age 60 and 30% of men with a PSA over three having significant disease at biopsy. 2. Outline the rationale and evidence for the chosen screening ages and frequency of PSA measurement, with or without MRI. 3. Develop methods to build trust in men of African and African-Caribbean descent for future research trials. Recognise that limiting availability to certain regions, such as the West Midlands, will negatively impact perceived equity of access and awareness in these communities. 4. Provide assurance that men with prostate cancer and those who are at increased risk due to family history, genetic risk, and ancestry will be included in evidence review. Accept that many high-risk men will now struggle to access screening support via their GP, who may feel understandably emboldened by national recommendations. It is documented that individuals from BME groups face barriers to accessing genetic services and testing, especially if relatives are overseas. 5. Acknowledge that men of African and African-Caribbean descent have previously been underserved by NHS and research services. Review the criteria for study participation regularly, as excluding those with prior PSA tests may undermine study validity due to the inverse care law, reducing participation rates and introducing bias. 6. Restore perception of scientific credibility to the review process by separately considering BRCA1 and BRCA2, rather than combining them as BRCA1/2, since their disease characteristics and risks are distinct. The use of the term BRCA1/2 is concerningly inappropriate and inaccurate in this setting. 7. Include heterozygous carriers of pathogenic variants in ATM and MSH2 in screening programmes, given their significantly increased risk of early and aggressive disease. Lynch syndrome has been studied for over a decade, and many families affected feel devastated by current exclusion decisions. 8. Acknowledge that many men with Lynch syndrome who participated in the IMPACT study, where their risk of aggressive prostate cancer was clearly demonstrated, will feel let down that their disease was omitted from the screening report. We would suggest that the scope of a report should be based on clinical risk and experimental evidence. 9. Recognise that all research to date is limited by evolving risk stratification, biopsy techniques, use of MSI, watchful waiting, and emerging technologies.

		10. Accept that randomised, double-blind trials are impossible for invasive procedures like biopsies, necessitating surrogate endpoints. Retrospective genetic analysis of control groups should be performed at study conclusion to assess whether screening down-staged disease in those at equivalent risk. Appendix 1: United Against Prostate Cancer Genomic Medicine Service Alliance Nurse-Led Project This collaborative project had three main aims: 11. Unite stakeholders to raise awareness about screening opportunities for men at high risk of aggressive prostate cancer—particularly those with a family history and African descent—and support them through testing and treatment. This included creating a steering group, glossary, and community events with educational videos. 12. Develop a tumour tissue BRCA testing pathway and downstream germline testing to prepare for future research and personalised treatment. This involved consent materials, pathology capacity improvements, quality controls in genomic laboratories, and establishing a patient identification and testing pipeline. 13. Create legacy materials and videos for national dissemination, establish links with other centres, and develop peer patient champions to support ongoing campaigns and patients. This project builds on previous initiatives such as the Macmillan Cancer Support Project and the 100,000 genome project PPI group, with a holistic approach integrating education, clinical, laboratory, outreach, insight, lobbying, and support to improve awareness and access to services. Notable achievements include the first clinical genetics YouTube channel, a medical supermarket model for access to allied health services, population awareness efforts via social and traditional media, lobbying and contributions to national reports, educational events, recruitment aids, and community-specific outreach such as clinics, leaflets, comics, and videos involving community champions. Key collaborators include University Hospitals of Leicester, University of Leicester, East Genomics, Prostaïd, National Hereditary Breast Cancer Helpline, Colin Mcfarlane (Prostate Cancer UK spokesperson), Play Dominoes Talk Prostate Cancer, B'ME Cancer Now (Rose Thompson Foundation), Leicester Rangers Football Club, Lord Mayor of Leicester, and Leicester City Football Club. Appendix 2: Analysing the Pros and Cons of Cancer Screening for Prostate Cancer in Males of African Descent

			Introduction Prostate cancer is a significant public health issue, with Black men experiencing a notably higher disease burden. Across high-income settings, there are marked ethnic disparities in mortality, with Black men facing a roughly 4-5% lifetime risk of dying from prostate cancer, compared to 3-4% in White men and about 2% in many Asian groups. For example, in the United States, prostate cancer death rates are two to two-and-a-half times greater in Black men than White men. Ethnic Disparities in Prostate Cancer Mortality UK data from a primary-care cohort of over 730,000 men show that Black men with raised PSA levels have a higher prostate cancer diagnosis rate (24.7%) within one year compared to White men (19.8%). Epidemiological studies consistently indicate higher age-specific risk in Black men, attributed to both biological susceptibility and differences in access to diagnostic testing. Comparison with Other Cancer Screening Unlike prostate cancer, breast and cervical cancers benefit from organised national screening programmes, which have demonstrably reduced mortality through systematic invitation, recall, and quality assurance. Prostate cancer currently lacks such a programme, leading to variable PSA testing and lower participation among high-risk groups, including men of African descent. Limitations of Current Prostate Cancer Screening Large, randomised trials of PSA-based screening show a 20% relative reduction in prostate cancer mortality, equating to about one fewer death per 1,000 men screened over a decade. Modelling studies suggest that earlier and more intensive screening in Black men could reduce mortality by 25-35%, while structured programmes could prevent additional deaths compared to non-stratified approaches. The absence of organised invitations and follow-up contributes to later-stage presentation and persistent disparities. Risks and Harms of Screening PSA screening carries the risk of overdiagnosis, with European cohorts estimating that 20-50% of detected cancers are indolent. Historically, these have often been treated aggressively, resulting in high rates of long-term erectile dysfunction, urinary incontinence, and bowel or urinary side effects. MRI-based diagnostic pathways reduce unnecessary biopsies and low-risk cancer diagnoses, but overdiagnosis remains a concern, necessitating careful consideration in high-risk groups.

			Advances in Diagnostic Technologies Traditional screening relies on PSA testing and digital rectal examination, both of which have limitations. Recent innovations, such as multiparametric MRI and MRI-targeted biopsies, allow more precise identification of clinically significant cancers. Personalised risk stratification incorporating ethnicity, family history, and genetic markers is rendering older trial data less applicable to contemporary screening in African-descent populations. Screening Guidelines for Men of African Descent New guidelines recommend earlier and more frequent PSA screening for Black men, starting baseline testing at ages 40 to 45. Earlier onset of prostate cancer in this group justifies regular screening through approximately age 70, with projected mortality reductions of around 30% without a significant increase in overdiagnosis. Impact on Healthcare Systems Broader screening for men of African descent will increase demand on oncology, radiology, and urology services. Greater use of MRI and targeted biopsies requires investment in infrastructure and workforce. While screening can detect cancers at more treatable stages and reduce advanced disease, it may also lead to overdiagnosis, patient anxiety, and increased costs. Robust risk stratification is essential to minimise these effects. Structured screening could substantially increase service demand, with modelling suggesting several-fold increases in annual PSA tests and 20-40% rises in biopsy rates. In already stretched systems, increased MRI and biopsy requests may lengthen waiting times and delay treatment, potentially limiting the mortality reduction benefits. However, by shifting diagnoses to earlier stages, screening can reduce the proportion of metastatic presentations and subsequent demand for costly therapies. Challenges in Screening Uptake and Community Engagement Uptake and engagement are ongoing challenges. Culturally sensitive education, community involvement, and consistent clinician support are vital to overcoming mistrust and misinformation. Improved adherence to screening leads to earlier detection, enabling less aggressive treatments and better outcomes. Opportunistic PSA testing is currently suboptimal, with participation among Black men lagging behind White men despite higher risk. National breast screening programmes achieve much higher attendance rates. Closing the gap in prostate screening uptake is essential to realise the projected mortality reductions.

			Economic and Resource Considerations Widespread screening incurs significant costs, including diagnostic procedures, follow-up, and potential overtreatment. Personalised screening algorithms, active surveillance, and regular evaluation of outcomes in terms of mortality reduction, quality-adjusted life years, and cost-effectiveness are needed to mitigate these financial challenges. Conclusion Prostate cancer screening in men of African descent involves balancing benefits and risks. Evidence and guidelines support earlier, targeted screening to address disproportionate disease burden, using advanced imaging and risk-based protocols. Realising these benefits requires enhanced clinical infrastructure, tailored community engagement, and robust policy frameworks to optimise health outcomes and minimise harms.
S29			Everyone who has serious symptoms related the prostate must have prostate screening. Regardless the age.
S30			Dear Mike and Anne We attach our response to the draft NSC document on prostate cancer screening which we hope is helpful. We have also been in communication with CGG, PCUK, BAUS, RCR and GIRFT hence the cc's but they of course will be considering their individual responses.

Response to the NSC draft prostate cancer screening announcement 25.1.26

and *****

(this is a personal response and not on behalf of *****)

Considerations:

What is the optimal endpoint?

To date, screening guidelines have required an improvement in survival to be approved. In prostate cancer, data show that survival is reduced in those with metastatic disease (50% at 5 years for M+ versus 95-100% at 5 years for disease localised to the prostate [1]) therefore metastasis free incidence is now suggested for an outcome of a screening programme in prostate cancer. The TRANSFORM study investigators have discussed this with the NSC previously. This is also reflected in the NHS plan aim of achieving a stage shift in cancers to 75% of cases being diagnosed at stage 1 or 2 [2].

Definition of harm

It is noted that the estimates of harm are based on historical series of side-effects of radical treatments (i.e. radical prostatectomy and external beam radiotherapy). However, surgical techniques and side-effect profiles have improved [3]. Furthermore, diagnostic biopsy techniques favour the transperineal approach and the sepsis rates are so low that antibiotics are rarely indicated [4].

Who is at increased risk and therefore which populations would harbour more cases in a targeted population screening programme?

There is an increased risk of prostate cancer in those with prostates who have:

- (i) A family history of the disease as defined in our research as a first degree relative with prostate cancer at <70 years of age or second degree at this age if through the maternal line [5]. We have shown using UK data from the UK Genetic Prostate Cancer Study (UKGPCS) that those with a family history of this definition or more cases (two cases where one is <60 years or three or more cases at any age) have a better survival if they are not the first case in the family whereas this was not seen if they were the first familial case [5]. This is evidence that knowledge of the family history improves survival and is likely to be due to uptake of PSA screening or early investigation of symptoms.
- (ii) Those of African ancestry irrespective of family history. Data internationally show that the incidence is twice that of those with European origin. The draft guidance reports that there is not enough evidence that the disease is more aggressive and this is based

on SEER data which are from the USA. Although the UK data show increased incidence, they are conflicting on whether the disease occurs at a later stage, but some reports do confirm this [6].

(iii) Those with pathogenic variants in *BRCA1* and *BRCA2* and some other DNA repair genes. The strongest evidence is for *BRCA2*. There is evidence for increased incidence from *BRCA1* variants, but this is lower [7]. The use of Biobank data for assessment of incidence of *BRCA1* variants could be problematic as there could be a 'healthy cohort' effect which would artificially lower the frequency of variants. Although there are data on increased incidence of prostate cancer in other gene mutation carriers (e.g. *MMR*, *ATM*, *CHEK2*), we do not consider that these should be included in a targeted screening programme outside of clinical trials at present as further data are needed on the type of variant and risk and clinical outcome (e.g. there are data on differing risks depending on the type of mutation in *ATM* [8] and a difference on disease aggressiveness depending on type of mutation in *CHEK2* [9]). Whilst we have strong baseline data indicating higher incidence of aggressive disease in those with *MSH2* and *MSH6* pathogenic variants at a baseline PSA test, we do not yet have outcome data of annual PSA screening to demonstrate a stage-shift and this should be available within the next year to inform screening guidelines.

The IMPACT studies have shown that annual PSA in *BRCA1* and *BRCA2* pathogenic variant carriers aged 40-69 years identifies prostate cancers that are more likely to be aggressive as determined by Gleason score and NCCN classification [10,11]. The latest submitted analysis at 5 years of **annual** PSA screening has not identified any case with M+ disease in 1816 *BRCA1* or *BRCA2* carriers [12]. Terminating screening at age 61 would miss 49% and 43% of the prostate cancers detected in the IMPACT studies in *BRCA1* and *BRCA2* respectively. Starting at age 45 rather than 40 would miss 3%, but although the incidence of prostate cancer is lower at these younger ages, prostate cancer diagnosed under 45 years is likely to have a poorer outcome if not diagnosed at stage 1 [13,14]. The IMPACT data showed that prostate cancers were detected in each screening year (except year 4 in *BRCA1*) so we would not advocate 2 yearly screening.

The unpublished data sent from the database in Manchester (Prof Evans) are from unscreened individuals so presumably these were individuals not enrolled into IMPACT. The most optimal real-world peer-reviewed dataset is the IMPACT study, which includes participants from Manchester who have been screened and are therefore not included in the unscreened set. The Manchester unscreened data show that survival is worse in those with *BRCA2* than *BRCA1* pathogenic variants which support international data on this point. However, the Manchester data also show clearly that the survival for both *BRCA1* and *BRCA2* pathogenic variant carriers is worse than that for localised prostate

cancer and therefore support the arguments outlined above that if disease is detected at an earlier stage, then survival should be improved.

BRCA1 and *BRCA2* are different genes with different cancer risk profiles and should not be analysed together; each gene should be considered on its own evidence-base.

(iv) Those with a higher polygenic risk score from international data. To date the only real-world data are from the BARCODE1 study in European men only [15] and we consider that further studies and longer-term outcome data such as that from TRANSFORM are needed.

Note on EAU

The EAU guidelines were published in 2021 and 2024 recommending targeted PSA **annual** screening for those with germline pathogenic *BRCA2* mutations from **40-69** years based on the baseline and 4-year outcome data from the IMPACT studies [10, 11, 16,17].

Outcome data from IMPACT in *BRCA1* and *BRCA2* pathogenic variant carriers at 5 years are under review at European Urology with a resubmission deadline of 19th January 2026 to reply to the statistical review (reply to the overall reviews has already been considered) [12]. There is no statistically significant increased incidence of prostate cancer in *BRCA1* carriers, but there is a statistically significant increased incidence of *unfavourable* prostate cancer on NCCN classification in *BRCA1* carriers, and this is the type of prostate cancer that would reduce mortality. The draft of this paper was submitted to the NSC prior to the draft guidance.

Summary response taking into account these considerations

We would respectfully recommend that any consideration for targeted screening for prostate cancer in the UK should not ignore the existing published, peer-reviewed UK trial data which are not referenced in the current document (specifically the UKGPCS and IMPACT studies [5,10-12]).

From these data we would recommend that:

- Targeted PSA screening should be offered to those with prostates and a pathogenic germline *BRCA2* variant from 40 to 69 years and the PSA should be annual and not 2 yearly.

- Based on our 5-year data we would also recommend targeted annual PSA screening for those with prostates and a pathogenic germline *BRCA1* variant from 40 to 69 years and the PSA should be annual and not 2 yearly. We recognise that the paper supporting this is still under review, but we hope to have a decision by the end of January.
- Those with a family history as stated above do have an improved survival with the conditions noted and this is a large study and is of UK data. We recognise that more data may be preferred and, in that instance, would encourage recruitment to the TRANSFORM trial. Of note, those who have already had a PSA test will not be eligible and many men with a family history will live outside TRANSFORM recruiting areas. Consequently, we are advocating for an update to the current guidance to GPs to make clear that they should have an annual informed discussion about PSA testing with men with a family history using the UKGPCS definition.
- Those with Black African ancestry. We recognise that more UK data may be preferred and therefore we are working with PCUK which is obtaining further UK data. We would encourage recruitment to the TRANSFORM trial. Of note those who have already had a PSA test will not be eligible and many men with African ancestry will live outside TRANSFORM recruiting areas. Consequently, we are advocating for an update to the current guidance to GPs to make clear that they should have an annual informed discussion about PSA testing with men with Black African ancestry.

References

- [1] Cancer Research UK (2026) <https://www.cancerresearchuk.org/about-cancer/prostate-cancer/survival>
- [2] NHS England (2025) <https://www.england.nhs.uk/cancer/strategy/>

- [3] Alibhai SM, Leach M, Tomlinson G. Impact of hospital and surgeon volume on mortality and complications after prostatectomy. *J Urol*. 2008;180(1):155-162. doi:[10.1016/j.juro.2008.03.040](https://doi.org/10.1016/j.juro.2008.03.040)
- [4] Pilatz A, Cornford P, Bonkat G, Kranz J. Transperineal Prostate Biopsy Without Antibiotic Prophylaxis: The New Gold Standard? Recommendations from the European Association of Urology Guidelines on Prostate Cancer and Urological Infections. *Eur Urol*. 2026 Jan;89(1):91-92. doi: 10.1016/j.eururo.2025.10.002. Epub 2025 Oct 23. PMID: 41136277.
- [5] Brook MN, Ní Raghallaigh H, Govindasami K, and Eeles RA. Family History of Prostate Cancer and Survival Outcomes in the UK Genetic Prostate Cancer Study. *Eur Urol*. 2023 Mar;83(3):257-266. doi: 10.1016/j.eururo.2022.11.019. Epub 2022 Dec 16. PMID: 36528478.
- [6] Delgado C. Black men have higher rates of late stage prostate cancer, audit shows. *BMJ*. 2025 Jan 10;388:r50. doi: 10.1136/bmj.r50. PMID: 39793992.
- [7] Nyberg T, Tischkowitz M, Antoniou AC. BRCA1 and BRCA2 pathogenic variants and prostate cancer risk: systematic review and meta-analysis. *Br J Cancer*. 2022 Apr;126(7):1067-1081. doi: 10.1038/s41416-021-01675-5. Epub 2021 Dec 28. PMID: 34963702; PMCID: PMC8979955.
- [8] Karlsson Q, Brook and Eeles RA, Kote-Jarai Z. Rare Germline Variants in ATM Predispose to Prostate Cancer: A PRACTICAL Consortium Study. *Eur Urol Oncol*. 2021 Aug;4(4):570-579. doi: 10.1016/j.euo.2020.12.001. Epub 2021 Jan 9. PMID: 33436325; PMCID: PMC8381233.
- [9] Leongamornlert DA, Saunders EJ, and Eeles RA. Germline DNA Repair Gene Mutations in Young-onset Prostate Cancer Cases in the UK: Evidence for a More Extensive Genetic Panel. *Eur Urol*. 2019 Sep;76(3):329-337. doi: 10.1016/j.eururo.2019.01.050. Epub 2019 Feb 15. PMID: 30777372; PMCID: PMC6695475.
- [10] Page EC, Bancroft EK, et al, and Eeles RA. Interim Results from the IMPACT Study: Evidence for Prostate-specific Antigen Screening in BRCA2 Mutation Carriers. *Eur Urol*. 2019 Dec;76(6):831-842. doi: 10.1016/j.eururo.2019.08.019. Epub 2019 Sep 16. PMID: 31537406; PMCID: PMC6880781.
- [11] Bancroft EK, Page EC, et al and Eeles RA. Targeted prostate cancer screening in BRCA1 and BRCA2 mutation carriers: results from the initial screening round of the IMPACT study. *Eur Urol*. 2014 Sep;66(3):489-99. doi: 10.1016/j.eururo.2014.01.003. Epub 2014 Jan 15.

- [12] Bancroft EK, Page EC, et al and Eeles RA. Targeted prostate cancer screening in men with BRCA1 and BRCA2 detects clinically significant disease. 2026 UNPUBLISHED: Under review at European Urology.
- [13] Salinas C.A., Tsodikov A., Ishak-Howard M., Cooney K.A. Prostate cancer in young men: An important clinical entity. *Nat. Rev. Urol.* 2014;11:317–323. doi: 10.1038/nrurol.2014.91
- [14] Orzechowska MJ, Bednarek AK. Molecular Landscape of Prostate Cancer Across Age Groups: Impact on Prognosis and Treatment Outcomes. *Int J Mol Sci.* 2025 Oct 8;26(19):9777. doi: 10.3390/ijms26199777. PMID: 41097041; PMCID: PMC12524801.
- [15] McHugh JK, Bancroft EK, and Eeles RA. Assessment of a Polygenic Risk Score in Screening for Prostate Cancer. *N Engl J Med.* 2025 Apr 10;392(14):1406-1417. doi: 10.1056/NEJMoa2407934. PMID: 40214032; PMCID: PMC7617604.
- [16] Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer-2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. *Eur Urol.* 2021 Feb;79(2):243-262. doi: 10.1016/j.eururo.2020.09.042. Epub 2020 Nov 7. PMID: 33172724.
- [17] Cornford P, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on Prostate Cancer-2024 Update. Part I: Screening, Diagnosis, and Local Treatment with Curative Intent. *Eur Urol.* 2024 Aug;86(2):148-163. doi: 10.1016/j.eururo.2024.03.027. Epub 2024 Apr 13. PMID: 38614820.

S31		Furness Prostate Cancer Support Group	We are a Prostate Cancer Support Group based in the Furness area of NW England, our membership has now exceeded 100 people and many of these have joined within the last 5 years or so. In 2023 the Group held it's first ever PSA Testing Day which attracted 110 men and we know from them 4 men required treatment, 2 of these needed urgent treatment as they had reached Stage 4. We held further testing days in 2024 and 2025 and each year the number has risen, as has the number requiring treatment. As part of the testing day Group Members talked at length with the men in attendance asking specifically why they had come to our event rather than going to see their own GP, the answers were startling as more than we anticipated had been refused a test at the GP despite being over 50yrs and/or with a family history, the reason for the majority of these refusals was based on just one reason they didn't have any symptoms. If you look at the NICE Guidelines it does not at any point tell GPs they should refuse and as should be common knowledge to all GPs at Stage1 and 2 of PCa there are no symptoms and at the time when there are it is usually too late and men are at Stages 3 or 4 meaning more expensive treatment is required and their chance of being cured is dramatically reduced and more often than not it will lead to long term continued treatment bringing about a much heavier burden on the NHS, a burden that could have been avoided had the GP tested at the early Stages meaning a full cure at a reduced cost. We have a man in the Group who was denied a test on several occasions, eventually he had one and was at Stage 4, he has had already a great deal of treatment and requires on-going medication which he calculated at over £40k per year, had the GP offered the PSA Test the first time he asked he would now not face a shorter life expectancy and the cost to the NHS would have been minimal, looking at this as a business decision it makes no sense not to test early. I wrote to our local ICB after hearing his story, my reason was as heart breaking as his story is I had heard it that often I was no longer shocked and therefore I simply suggested to the ICB that GPs are killing men by their continuous refusals and the time had come for action. I met with the ICB a few weeks later and explained in detail what was happening in the GPs office when men are asking for a test, when the Dr refuses immediately without full consultation with the patient using the "no symptoms" excuse it's a serious concern, the GP should know there are no symptoms at the early stages and by refusing it suggests 2 things, firstly the GP actually has no idea about PCa or they are simply telling lies to the patient and I don't know what is the worst answer.

		I listened to an interview on Radio Lancashire a few months ago, a very eminent Uro-Oncology Prof. suggested the problem is too many GPs knowledge of PCa dates back to their days in medical school and diagnosis and treatment has come on so much in recent years the answer is to refer men to the Urology dept. sooner, I heard one Clinical Lead from the Humberside area, he has told GPs in his area he wants men with family history to be referred when they have a PSA of just 1.5. I had a conversation with a Phlebotomist based at a GP surgery, her lead GP has recognised the seriousness of not testing and has given the Phleb permission to test any man over 50 yrs who is already in the surgery having blood taken for whatever, she asked the GP about the conversation that needed to be had prior to taking the sample, that being the does and don'ts and his answer was shocking, why because he had no idea what she was talking about which begs the question how could he make the decision to test or not to test a man requesting a PSA when he has little or no idea on the subject, I would love to tell you this is a rare event but sadly it's not and as a direct result men are dying and will continue to do so all because of a test costing a few pounds. I fully understand and acknowledge the PSA is flawed at the moment but unless we are going to offer an MRI to every man over 50 yrs it is the only cost effective test, the time has to come to firstly have an extensive program educating GPs about PCa and secondly revise the Guidelines which are very out dated and start offering the test to every man over 50, I have 2 sons one who is approaching 40yrs and I know of a man who was diagnosed at just 32 which is concerning for my son and as such I will be prompting him to be tested after his next birthday to set a base number and then get him to be tested every year after that, not waiting until he gets to 45yrs. How many more men are going to die unnecessarily before you do something to stop this, I met a man in 2022 who was repeatedly refused a test and when he finally had it he ended up in hospital within a few weeks of the test, scans showed extensive mets and he was told he only had 6 to 12 months to live, he sadly died just 12 weeks later and having spoken with him on many occasions I came to the conclusion the GP who repeatedly refused directly caused his death, had the GP tested a year earlier when he first asked he would be here today telling you his story, at this moment I say shame on the GPs but if you allow this to continue in the way it is then shame on you.
S32	Prof David S Morrison	I would ask the Committee to encourage the authors of the European Randomised Study of Screening for Prostate Cancer (ERSPC) to publish the all-cause mortality results from their 23-year follow-up study. The ERSPC published prostate cancer and "other cause" mortality rates, finding a reduction in the former but no difference in the latter between screened and non-screened

			men. Deaths from other causes greatly outnumber those from prostate cancer. In brief, I've had some correspondence with the lead author of the ERSPC in which I've learned that there was no significant difference in all-cause mortality between the intervention and control arms of the trial. The trial was widely reported to show that screening saved lives but arguably it did not; it reduced the attribution of death to prostate cancer among those who were screened but made no significant difference to their survival.
S33	Andrew Vickers		To whom it may concern: Please see attached form. Best Andrew

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name:	Andrew Vickers	Email address:	*****
Organisation (if appropriate):	*****		
Role:	*****		
Do you consent to your name being published on the UK NSC website alongside your response?		Yes	
Section and / or page number	Text or issue to which comments relate	Comment <i>Please use a new row for each comment and add extra rows as required.</i>	

I am a biostatistician who has worked on prostate cancer early detection for over 20 years, including involvement in microsimulation modeling as a consultant to CISNET. I have numerous concerns with the SCHARR model. For instance, the estimate of the proportion of prostate cancers that are grade group 1 is nearly twice reported in contemporary practice (e.g. PRECISION trial gives 19% of patients have grade group 1; SCHARR model is ~35% for men of screening age). This may be why the overdiagnosis rates given by SCHARR are higher than has been typically estimated.

However, that is not what I would like to focus on in this submission. However we might quibble about model inputs, there is a more fundamental problem with the SCHARR model that, in my view, means that it should be completely discounted from serious discussion of UK policy on PSA screening. In brief, **the approach to PSA screening evaluated in the SCHARR model is one that makes little sense and has never seriously been advocated.** The SCHARR report never expressly addresses this point – and that might be the problem right there – but I have confirmed with the authors directly concerning how they dealt with what is called “opportunistic screening”, the background PSA testing that is going on right now in the UK.

Specifically, current NHS policy is that “anyone aged 50 or over with a prostate can ask for a PSA test”[<https://www.nhs.uk/tests-and-treatments/psa-test/>]. Moreover, as part of national guidelines on recognition of suspected cancer[<https://www.nice.org.uk/guidance/ng12/resources/suspected-cancer-recognition-and-referral-pdf-1837268071621>], a PSA test is recommended for men with lower urinary tract symptoms, erectile dysfunction or hematuria. The former two indications are near ubiquitous in older men. As a result, there are very high rates of PSA testing in the UK. In a paper published in the British Medical Journal [doi: 10.1136/bmj-2024-083800], following ~10m men in England for a mean of ~8 years, 1.5m had close to 4m PSA tests. The authors also noted that PSA testing was much higher for men in their 70s, 80s and 90s compared to those aged 50 – 70 years. For instance, about 25% of men aged 80 – 89 have a PSA test each year. This is highly problematic because older men have the highest risk of overdiagnosis, and best evidence is that they do not benefit from PSA screening[doi: 10.1136/bmj-2022-071082].

The approach used by SCHARR is to assume that implementation of a population-based screening program would make no difference to men’s opportunistic

screening behavior and there would be zero other changes in NHS policy. With respect to behavior, take an example case of a man who, under currently policy, would ask his GP for a PSA test at age 62. When the SCHARR investigators evaluate a program where men get a PSA at age 60, the assumption made is that, unless cancer is found as a result of the PSA test at age 60, the man would go to his GP at 62, ask for PSA test, and the GP would order it for him. This is obviously rather implausible. With respect to policy, the SCHARR assumes that the NHS would implement, say, a one-time PSA at 60 but change nothing else, whether “you can get a PSA test if you ask for one” or recommending PSA tests for men with erectile dysfunction. On the contrary, guidelines would naturally be revisited if a population-based screening program were to be implemented. One would expect the NHS to end opportunistic testing once a PSA screening program was in place. PSA would not be available in primary care: if a man wanted a PSA test, he would have to do that through the NHS prostate program.

When discussing PSA testing policy, academics distinguish between no PSA being available, a population-based screening program or opportunistic testing. Population-based screening plus opportunistic testing is simply not a reasonable approach and has never been part of the academic conversation. In more than 20 years working in this field, I have never heard any serious academic propose, for instance, “a screening program with PSAs every 4 years from 50 to 70, but also let men get a PSA test whenever they want”. Similarly, I’ve never previously seen “PSA program plus PSA screening at will” proposed in a guideline or evaluated in a modeling study. A slight caveat is that a personal decision is sometimes recommended in small subgroups, such as age 70 – 75 with higher PSA, or men 40 – 50 with family history but obviously this is very different to what is evaluated by SCHARR.

The SCHARR report concludes “Screening men in [the general population] England may lead to some benefits in mortality reduction but will also result in substantial overdiagnosis”. This is inaccurate. How this conclusion should read is “adding screening to opportunistic testing in the general population may lead to some benefits in mortality reduction but will also result in substantial overdiagnosis”. But, of course, this is a completely uninteresting finding: no-one should want to know the effects on mortality and overdiagnosis of adding some additional PSA testing to our current disorganized approach, a policy that makes little sense, has never been formally proposed and would never happen in practice.

There has been only one country that has rolled out a population-based screening program, Lithuania, and they have reported a close to 80% fall in PSA testing in men over the age of 70[doi: 10.3390/jcm9123826], a group that does not benefit from PSA screening but is at high risk of harm from overdiagnosis. Partly on this basis, a group of academics have proposed that implementation of population-based PSA screening in countries where there is currently opportunistic testing would reduce both the number of PSA tests given and rates of overdiagnosis[doi: 10.1136/bmj-2022-071082]. A formal modeling study evaluating a sensible policy of introducing population-based screening coupled with limits on opportunistic testing has recently been published as a preprint [<https://doi.org/10.64898/2026.01.23.26344710>]. The headline findings are that PSA tests would be reduced by 25% and overdiagnosis by 25% by such a policy. The brief explanation for this finding is that the increase in PSA testing and overdiagnosis in men of screening age (50 – 69) related to population-based screening in this group would be far less than the reduction in PSA testing and overdiagnosis in older men related to restricting opportunistic screening. The paper also should that a policy that was more aggressive about limiting testing in older men, by dramatically restricting the indications for PSA outside of screening, overdiagnosis rates could be reduced by up to 50%.

I would urge the UK NSC to reject opportunistic testing – “you can have a PSA test if you want” – as a political compromise that has failed. In addition to leading to high rates of PSA testing and overdiagnosis, it has led to gross disparities with one recent paper[doi: 10.1136/bmjnc-2024-000643] reporting a 10% difference in prostate cancer mortality between highest and lowest deprivation quintiles, attributable primarily to differences in PSA screening. The only reasonable alternatives are either (i) end PSA testing altogether, or (ii) implement a population-based screening program alongside a policy that would reduce opportunistic testing by ending the availability of PSA in primary care.

Please return your completed form to the UK NSC Inbox UKNSC@dhsc.gov.uk by 11.59pm GMT on 20 February 2026.

S34	Duncan Carins	Prostate Cancer Victims	Dear NSC, Please find attached your proforma form with my comments contained within. I also attach the original word document file. I hope that these comments are acceptable .Please advise. Knd regards

Comments to National Screening Committee (NSC) Prostate Cancer(PCa) regarding recommendations

The group “Prostate Cancer Victims” being an unincorporated association and I take the role of quasi secretary who help circulate information relating to PCa within the group. There have been around 24 people within the group, mostly friends, colleagues, friends of friends and relatives. All have their own story of poor treatment for their PCa investigation and treatment from the NHS, most relating to the appalling service from their GPs.

Executive summary

It is clear that the NSC recommendations have issues and flaws because they are based on outmoded and inaccurate information based on a retrospective and introspective analysis of the real position taking little or no account of the current medical practices. If the actual current medical position is used then the harms of treatment are much less than what is stated. “Overdiagnosis and overtreatment” is not an issue if correct clinical pathways are properly followed. “False positive PSA test” is a misnomer created by the improper assignment of the actual role of the PSA test.

The modelling is not clear or transparent and it is difficult to understand or know exactly what modelling parameters were actually used, and unless the model is released as an open source publically interactive model whereby people can upload the model and run the model themselves using the parameters that they can justify then transparency of how the recommendations have been arrived at is not publically transparent or accountable.

With regards to the BRCA1 and BRCA2 recommendation it does seem as if it has been introduced because it is the least expensive option with the aim to placate public outcry for a national screening program. It is not clearly laid out what the actual screening program would entail. It appears to be modelled on thin evidence and woolly modelling parameters all of which are not clear.

The TRANSFORM trial is used as an excuse to “kick the can further down the road”. If we wait for the study to finish around 240,000 men will have died from PCa. A screening program would currently save 2 lives per 1000 men screened so in 20 years, assuming no betterment of screening mortality results, then a screening program would save around 22,000 men’s lives.

From sources that have expertise in modelling it appears that there are many criticisms surrounding the modelling and economic exercise as presented.

Overall there is an urgent need to have a national screening programme. It seems as if the introduction of a screening program is fairly imminent in Europe because the emerging results of their trial within 5 member states all point towards nations being tasked with rolling out a national screening program.

Brief overview of current recommendation

The UK NSC's draft recommendation is to:

- offer a targeted national prostate cancer screening programme to men with confirmed BRCA1 or BRCA2 gene variants every 2 years, from age 45 to age 61
- not recommend population screening
- not recommend targeted screening of Black men
- not recommend targeted screening of men with family history
- collaborate with the [Transform screening research trial](#) team to:
 - answer outstanding questions on screening effectiveness for black men and men with a family history – as soon as trial data becomes available
 - await results of the study to develop and trial a more accurate test than PSA alone, to improve the balance of benefit and harm of screening

There are several documents which have been lodged on the website

1. the model study
2. narrative paper Cancer Research UK Modeling the outcomes of PCa screening
3. evidence review coversheet
4. infographic

Looking at the infographic

Points for consideration.

Comment 1

It states that the majority of the information used comes from the GOTEBOG -2 trial (1). Having to pay for the privilege to obtain a copy of the New England Journal of medicine since the information is not open source which maybe the NSC might have been able to provide free links to since it bases most of its assumptions on this paper plus a few others also on the NEJM .

It states in the Goteborg paper that the main objective of the research was *“whether a strategy of omitting systematic biopsy in men with a PSA > 3 and performing only targeted biopsy of MRI positive lesions would reduce the risk of detecting clinically insignificant PCa while still enabling the detection of clinically significant PCA at a curable stage.”*

The trial which commenced in 2015 had 3 groups of men. 2 groups only being considered in the paper; one for the groups of men who underwent a MRI targeted biopsy and the other group of men underwent a systematic biopsy ie a random collection of 12 core samples from the prostate. Each group had around 6500 men aged between 50 and 60. An age group not best selected for PCa since the average age of when a man is diagnosed as having PCa is 64, hence this trial does not adequately reflect what the most likely screening population should be for PCa is the most common years of diagnosis has

not been included . The population was from Sweden and hence the vast number of men were white and hence does not in reflect the multiracial mix that pertains to the UK.

In both groups around 10% of men had an elevated PSA of >3. In the group of men who had a targeted MRI biopsy, 226 had a positive MRI scan that showed a lesion. 224 men then had a targeted biopsy. Of the 417 men who did not have a lesion showing on their MRI scan only 9 men had a targeted biopsy. In the systematic biopsy group 685 men had an elevated PSA test (>3) of which 219 had a positive MRI scan 213 went on for a non targeted biopsy. Of the 430 men with no lesion showing on their MRI scan 359 men went on to have a biopsy.

The trial found that after screening for 4 years then in the MRI targeted biopsy group 2.8% were found to have cancer yet the group which offered the non targeting biopsy found that 4.5% of the group had cancer. Looking at table 2 of the paper

	MRI targeted group	systematic group
Clinically significant cancer	1.8%	2.1%
Clinically insignificant cancer	1%	2.4%
All PCa	2.8%	4.5%

Within the paper they advise that those who have grade 2 cancer and above were classified as having clinically significant cancer. We are advised on page 1 of the report that *“the primary outcome was the detection of clinically **insignificant** (International Society of Urological Pathology [ISUP] grade 1 PCa; detection of clinically significant (ISUP greater than or equal to grade 2) PCa was a secondary outcome”*

It does seems bizarre that when looking at all documents within the report then the NSC has predicated all the results and findings based on one half of the Goteborg report ie the findings that were produced within the MRI targeted biopsy group. It is clear within the infographic where all the figures used for modeling have derived from eg “2.8% will have cancer” the breakdown of those with insignificant cancer 10, 18 with significant cancer.

However this appears to be a bizarre contradiction of the Goteborg report in that had NSC selected the findings from the other group ie the systematic group 4.5% of men in that group had cancer then translating that to the current study this would have resulted in 45 men out of the 1000 with cancer 24 with insignificant cancer at the time of screening and 21 with significant cancer and hence if these figures had been used within the model then a totally different result would have been created. There has been questions raised about the Goteborg study over the fact that most men went on to have a non targeted biopsy even if they had a negative MRI yet only 0.5% of men who had a negative MRI within the targeted group opted for a standard biopsy. Hence the question has be asked as to what is the purpose of screening, is it the case that screening is to identify all cases of cancer since it is clear that over time many people who have grade 1 PCa go on to develop clinically significant PCa in their lifetime and hence any good screening system needs to ensure that all people identified with any form of PCa have a clearly defined clinical pathway to follow be that active surveillance or treatment.

It was interesting to note from the “Man in the Van” trial as reported in the Int J cancer 2024 trial showed a 3.6 % rate of prostate cancer in the population , 67% having grade 2 PCa

It is very interesting to note that the current EU beating cancer screening trials have commenced in 5 different countries in Europe, including Ireland. The trial before it is rolled out to member states is called PRAISE-U. There has been some feedback provided about the early results of the trials and the information released shows that out of 1000 men coming forward then 100 -150 men will have an elevated PSA (>3). It is interesting to note that the country with the highest level (150) being Ireland. The PRAISE U trial then undertakes a 4Kscore test before offering a MRI and hence this “liquid biopsy” test looks at a range of parameters in the blood plus other physical factors and produces a risk score of the likelihood of an aggressive cancer. If a person has such a high risk then they then go to having a MRI scan.

Hence, if these results are used instead of the infographic figures of 150 men with a possible PSA test then using the percentages thereafter would result in 42 men with prostate cancer, 16 of which would have grade 1, 20 having grade 2 and 6 having grade 3-4. It is suggested that this demonstrates the importance of having a dataset that better aligns to the inherent native population of the UK and it is suggested that the population within Ireland is a far closer fit to that of Ireland based on the 2016 study that estimated that the average citizen in the UK has 48.9% Celtic ancestry. This is compared to the “Viking” (Danish /Swedish/ Norwegian) genetics which account for 6%. Hence specific Swedish genetics making up a third equates to only 2% genetic input into the UK population. It is disappointing that there is no mention of any close working with the EU over this matter and I am sure that had the correct approaches been made then better and more update information from the current PRAISE U trial could have informed the NSC report.

The information within the NSC reports makes mention of having a positive PSA test result and then this leads to a MRI scan and if that is positive a biopsy. The only mention made about targeted biopsy is within the key information document which states

“ men with a PSA level >3 will undergo a targeted biopsy”

Clearly this statement is incorrect. If a person has an elevated PSA test then they are offered a MRI scan and only if the MRI shows that there is a lesion then a biopsy would be offered. It is patently wrong to suggest that a screening pathway would go directly from a PSA test to biopsy and miss out the MRI scan. It is suggested that any published information is factually correct otherwise the public would quickly lose confidence in what they read and or be put off from participating in any PCA screening program if they are to think that an elevated PSA would then be faced with an immediate biopsy.

The NSC suggestion being that all biopsies will be transperineal (TP). It might be the case that in England currently around 70% of prostate biopsies are TP but in Scotland 95% of biopsies are still performed through the transrectal (TR) route. Yet cost modeling has gone for all biopsies being TP when because of problems of sampling through the rectum then there is a higher likelihood of more complications be it sepsis or bowel function. It is hopefully encouraging that all biopsies within the NHS are to be performed TP. This clearly has benefits if we look at Sweden, in 2021, when there was an outrage in the press

following on from a TR prostate cancer biopsy death from sepsis which thereafter resulted in all prostate biopsies being performed TP and to date there have been no record of deaths from prostate biopsies.

As with many medical papers there can be issues with what is contained within if the results are not used in line with the aims of the study and it has been suggested that there are several unexplained lacunas within the study. That being the case it is a fundamental failing of the review not to attempt to make provision for these failings of a study that is not four square with the matter in front of us since the main aim of the study related to seeing the effect of using a targeted biopsy only in relation to insignificant (Gleeson 6) cancers. The Goteborg report concludes that further studies are needed in relation to the use of MRI on the safety and efficacy of screening for PCa.

Comment 2

It is stated in the key information paper that “47% of cancers will be grade 2 and are likely to be offered surgery, radiotherapy or active surveillance. Clinical experts suggest many of these diagnosed with grade 2 disease are likely to be over detected and over-treated (over treated being defined in the document as the treatment of a cancer that would not have gone on to cause harm in a person’s lifetime. Treatment has associated physical harms as outlined in the infographic but can also have psychological ,social and economic impacts on the patient)

12 % of PCa will be grade 3-4. These are likely to be clinically significant”

It is clear from the above that there is reluctance to classify grade 2 PCa as significant. Yet throughout the Goteborg paper they classified PCa , grade 2 and above as clinically significant and only labeling grade 1 PCa as clinically insignificant.

It is further interesting to note that reference is made to “clinical experts suggestions” yet there are no medical papers provided which put forward the position as to why these medical experts come to their view apart from a statement later on that suggests that the estimates of over diagnosis and over treatment are based on a mixture of clinical expertise and the Protect trial (treatments undertaken over a decade ago). That being the case it seems as if the model has been downgraded and only to consider grade 3 -4 as clinically significant cancers. This appears to be another flaw in the modeling process.

Comment 3

Historical retrospective; It appears from the information provided that much emphasis of the report focuses on information supplied within historic (greater than 10 years) medical reports which fails to adequately reflect the actual current medical position especially in relation the harms. There have been significant advances in the way that treatment for PCa is being applied and because of that most data presented in the papers takes an introspective hand retrospective standpoint then much of the information should be considered outmoded and not truly reflecting the actual current position going forward.

I can provide anecdotal views of the members of the group. Most of the members of our group live in London and the SE. Some men have had radiation treatment at the Royal Marsden while many of the

group who opted for surgery have had a Retzius Sparing RARP (RS-RARP) at NHS bodies such as ,Royal Surrey Guildford, Royal Marsden, UCLH, Imperial, Royal Berkshire and Frimely hospital. It seems that London and the SE are blessed with NHS facilities performing RS-RARP however further afield eg Scotland, Wales, NI there appears to be no centres where RS-RARP is routinely performed. I note with interest that many peer reviewed papers have been written by surgeons operating in and around London/SE undertaking this procedure as far back as 2018 (a). Many other international medical papers dating back a decade eg Lim in 2014 show massive improvements in post operation recovery and the reduction of post operative harms. Eden reported in his 2018 paper that Retzius-sparing RARP is faster than the anterior approach to the prostate, allows a shorter catheterization time and produces dramatically better continence results at four weeks compared to RS-RARP (3 x higher pad rate) with 90% of patients being pad-free 4 weeks after surgery and 7.5% of patients needing only 1 pad/day after 4 weeks and 2.5% needing 2 pads / day.

The men in our group also stand testimony to these figures in that everyone who had a retzius sparing RARP has reported full continence within 4 weeks, many cases sooner and hence never had to resort to wearing pads at all since full continence followed directly on from the removal of the catheter.

It is interesting to note that your modeling of harm uses the figure of **20%** of men will continue to have continence issues and 50% experience erectile problems 5 years on from surgery. Radiotherapy; 40% erectile problems and 5% bowel problems. In the accompanying “narrative paper” which provides the link to the NICE document NG131 where the information was lifted; this is produced below

“For example, after just 6 months: (9) • For men undergoing prostate surgery: - 71% (nearly three quarters) will find it difficult to control their bladder - 19% (almost 1-in-5) will be unable to control their bladder (moderate to severe urinary incontinence) - 3% will have moderate to severe impacts on their bowel habits - 66% (two thirds) will experience moderate or severe erectile dysfunction • For men undergoing radiotherapy: - 38% (nearly 2 in every 5) will find it difficult to control their bladder - 6% will have moderate to severe urinary incontinence - 5% will have moderate to severe impacts on their bowel habits - 48% (nearly half) will have moderate or severe erectile dysfunction.

(9). [Recommendations | Prostate cancer: diagnosis and management | Guidance | NICE](#)

NICE guidance 131 document states

What effect does each treatment option have on urinary function?

There is some evidence that urinary function is better for people offered active surveillance or radiotherapy than those offered prostatectomy.

At 6 months, problems with urinary continence were reported in:

- 39 out of 100 patients offered active surveillance
- **71 out of 100 patients offered radical prostatectomy**
- 38 out of 100 patients offered radical radiotherapy.

At 6 years, problems with urinary continence were reported in:

- 50 out of 100 patients offered active surveillance
- **69 out of 100 patients offered radical prostatectomy**
- 49 out of 100 patients offered radical radiotherapy.

At 6 months, moderate to severe urinary incontinence problems were reported in:

- 4 out of 100 patients offered active surveillance
- **19 out of 100 patients offered radical prostatectomy**
- 6 out of 100 patients offered radical radiotherapy.

At 6 years, moderate to severe urinary incontinence problems were reported in:

- 8 out of 100 patients offered active surveillance
- **13 out of 100 patients offered radical prostatectomy**
- 5 out of 100 patients offered radical radiotherapy.

Note on these figures; it is hard to see where the 20% figure comes from as stated in the infographic. It is also deeply concerning to discover how NICE does not keep abreast of the current state of play in their guidance documents as detailed above with actual information about commonly used procedures such as retzuis sparing RARP and their outstanding results in relation to continence. NICE fails to describe within the section of their guidance where they have obtained their figures from by suggest that there is *“some evidence that urinary function is better for people offered active surveillance or radiotherapy than those offered prostatectomy”* yet looking at these figures it is difficult to understand that after 6 years 8% of men report severe or moderate problem compared to 5% after the “offer” of radiotherapy (was radiotherapy given or just offered?). NG131 comments on biopsies being performed TR and goes on to state that TP not being part of the assessment and only being trialed. It all goes to show just how antiquated, retrospective, inaccurate and dangerously misleading these documents are when considering the position in terms of practice procedure and results.

As stated above, most of the myths that get circulated and promulgated about PCa surgical procedures hark back to experts discussing figures that were obtained from performing operations that invaded the Retzuis region where many important features for continence are contained. The NSC directs us to look at various historical studies which are reporting on PCa treatments that were performed around the turn of the century and are now looking at the follow up studies of how men fared 12 or 15 years post their treatment undertaken in the early 2000s. Looking back at data of the period, it had been reported by BAUS that in 2009/10 52% of PCa open radical retropubic prostatectomy procedures (2529) were performed using an open surgical technique ie a large 20cm incision in the lower abdomen and then through the retzuis area to gain access to the prostate. The other 48% of surgery was carried out laparoscopically (robot assisted or not). in 2009/10 This represented a 80% increase in the use of laparoscopic surgery from the previous year. A few years later the move over to RARP was virtually completed however there may be the rare occasions where RARP cannot be used and open surgery is required. However RP surgery now is undertaken by LARP and it seems that there is a steady push

towards using the RS- RARP procedures which it is hoped , in the near future will soon become the “gold standard”.

Therefore it is clear that surgical techniques dating back in the early 2000s were much more “brutal” and they resulted in chronic post operation problems relating to continence and hence the figure that is commonly trotted out that 69% of men will still be suffering from incontinence 6 years post surgery, which may have been the historical context but currently and moving forward then men can be confident that following surgery then incontinence is not the issue it once was. It is also anecdotally reported by men that have been suffering for years from nocturia or chronic flow, hesitancy, urgency because of prostate problem and many were wrongly told by their FGPs that it is not cancer but a benign prostate hyperplasia (BPH), who then spent years living with disturbed sleep, frighten to leave home unless they knew where a wc was, but then discovering that the GP had misdiagnosed them and it was not a BPH but rather PCa. They then went on to have a retzuis sparing RARP and thereafter recovered a quality of life in that they no longer get up at night and have a solid 7 hours sleep at night, have no urgency problems and have a strong consistent flow and have no fear of leaving the house in case they cannot find a wc or having to wear pads. It is odd that all we ever hear about are the harms post operation and there has been no expression of the positive physical benefits to continence that emerge following surgery when there were worse continence issues beforehand.

The point that is being made is that the modeling presented has been carried out using the harms caused by a surgical practices used two decades ago and bear little resemblance to the true position currently seen and reported on.

Also in terms of radiation treatment then it is clear that over the last 20 years there have been significant advances in targeting and radiation dose control resulting in fewer cases where collateral damage has occurred especially in relation to bowel problems.

Throughout the medical world there have been advances in imaging be that PSMA PET scans or 3D scinitgraph; whole body SPECT scans that can detect tiny bone metastases that other scans do not pick up. Those radiations beams can be focused precisely and controlled to even take account of a person movement caused by breathing and adjust accordingly. Different radiation dose regimes are applied. Hence, as with surgery, many of the problems previously reported a decade ago have long since been improved upon and the post radiation treatment problems of old are not as prevalent as before.

Hence it seems reprehensible that any screening model developed regarding a future screening program looks at outcomes and harms from open surgery and radiation performed 20 years ago when the real challenge to any fit for purpose model is to consider what is currently available and instead of using the figure of 20% of men will have continence issues 5 years after surgery when it is suggested that the model should be populated and run with a more realistic figure of around 3% of men could have a continence issues related to post surgical problems.

(a)journal of clinical urology 2018urinary continence for weeks following Retzius sparing RARP; the uk experience Eden Moschonas and Soares

Comment 4

False positives, overtreatment and over-diagnosis; it is stated

- False positives: this is when a high PSA result suggests that cancer is present when it is not. This can lead to unnecessary tests such as prostate biopsies, which carry a risk of rectal bleeding, blood in urine, blood in semen, infection, urinary difficulty, pain and worry.
- Over-diagnosis: true positive PSA results for cancers that would never have caused symptoms or affected length of life. Over-diagnosis causes unnecessary worry to men and other psychological harms such as anxiety, fear of cancer, and undue stress lasting long periods of time. It also exposes men to unnecessary treatment, which can sometimes cause lifelong side effects
- *over treated being defined as the treatment of a cancer that would not have gone on to cause harm in a person's lifetime. Treatment has associated physical harms as outlined in the infographic but can also have psychological, social and economic impacts on the patient)*

These are concepts that have been entirely self-generated by the dismal failure of the medical profession over the years and as a result many of these issues could be immediately addressed and prevented if there is a concerted effort to not use sloppy language and a purge on over-diagnosis and over-treatment.

In terms of the lie that is perpetrated by the medical world of a **false positive PSA test** then maybe someone needs to simply understand the actual function of a PSA test. In real terms the PSA test result is simply an accurate test result to determine the level of PSA within the blood. It is not a determinative test for PCa. In current terms if a person has LUTS (lower urinary tract symptoms) and an elevated age related PSA (NICE) or if they have no LUTS and an elevated PSA (elevated being considered >3) under PCRM (Prostate Cancer Risk Management Program) then they should be referred from their GP to urology for further investigations ie MRI and if the MRI indicates a problem then a biopsy. It may be that a person has an elevated PSA but on further investigation there is no indication of PCa from either their MRI and or biopsy

It is the case that the PSA is not a definitive test and nothing positive can be taken from the test result all it does is open a gate to a further suite of tests and only once these further tests are performed can a person be given any diagnosis of PCa or not. So for years the medical world have been framing the PSA wrongly by calling an elevated PSA test where no PCa is found as a false positive when all that needs to be said about a PSA test is that the result shows that it is elevated, no conclusions can be made as to why it is elevated until further secondary investigations are carried out by urology. If the medical world actually focused on the precise use of language rather than being slapdash banding about the concept of a false positive from a PSA test and maybe they should replace with the phrase with something like "elevated PSA result on further investigation showed no PCa" and hence remove any stigma associated to imbibing the PSA test with being positive or negative.

It is odd that no mention is made of the phrase “false negative” where by men are told that because their PSA test is not elevated then they do not have PCa. This is the dangers or prescribing the PSA with the attributes of a PCa defining test. It was interesting to note from the REIMAGINE trial that 48 of the men were discovered with significant PCa ,50% had a PSA result of less than 3 and hence in a normal setting this would **not** have triggered a referral from their GPs. Professor Moore ,the chief investigator of the REIMAGINE study, made the comment “ *half the men with a significant PCa would have been reassured by a low PSA test result is a sobering thought indicating a need for comprehensive screening program*”. If the key results of the Goteborg -2 trial data are considered where they looked at a group of men with low PSA levels ie 1.8 to 3 then that study found 41% of men within this group who had a positive MRI scan were found to have prostate cancer. Hence, it is axiomatic that significant amounts of PCa has been found in men below the normal threshold of 3 set for screening programs and hence commentators has suggested that PSA results are not a useful tool for screening and the PSA testing should be reserved for monitoring PSA levels post treatment .

Maybe it is very convenient to not mention this since all the modeling is predicated on the myth that an elevated PSA is the gateway to screening for PCa. It is true that elevated PSA test results especially when they are high do help to identify PCa eg Gretzer advises that a PSA level of 10 will show around 7 in 10 men to have PCa and an elevated level of 3 will show 1 man in 4 will have a PCa .

It is stated in the infographic “*This can lead to unnecessary tests such as prostate biopsies, which carry a risk of rectal bleeding, blood in urine, blood in semen, infection, urinary difficulty, pain and worry*”.

It does seem that unnecessary scaremongering is deliberately selected to create a narrative to fulfill the recommendation that is sought. It is odd that little mention is made of the fact that there are a range of mechanism within screening programs that all lead to ensuring that men only head off for hopefully a TP biopsy (see above). It is the case that following an elevated PSA test men in the PRAISE U trial undertakes a 4Kscore test. If this indicates a higher risk of an aggressive PCa then a man will have g a MRI. Only if the MRI reveals a positive indication of potential PCa will a man be offered a biopsy. As with the modeling figures around 3.5% of men will eventually have a biopsy 85% of men will be diagnosed with PCa. Hence out of 100 men with an elevated PSA, 6 will have gone through the process to discover that they had a suspicious MRI but the biopsy confirmed that there was no PCa. It is difficult to see how the word *unnecessary* fits in. It is suggested that any person told that they have an elevated PSA, a suspicious MRI, would not want to go onto have a biopsy to confirm or deny that there is cancerous material present and I am sure that men in this situation do not see the biopsy step as *unnecessary* since they just want to know what the position is as part of the overall investigation. The necessity depends on perspective. People agreeing to a biopsy are informed of the potential side effects but it is the case that people are keen to find out one way or the other if they have PCa or not. As with any procedure or medicine there always is an associated risk. It is difficult to see why rectal bleeding is being suggested if all biopsies are to be TP.

It is suggested that yet again medicine uses sloppy and biased language to create the false narrative sought. It is further suggested that it could be simply said that “TP biopsies can reveal or not the detection of PCa however in having a TP biopsy there are associated, risks blood in urine, blood in

semen, infection, urinary difficulty". Again it be interesting to know what difference to the modeling program would be if the correct position was actually used such?

Overdiagnosis/overtreatment

Yet again another historical problem of the medical world own making. Why did the medical world over-treat when the traits of PCa have been known for decades? There is no need to dive deeply into the reason for the potential negligence of the medical world in the past but there is now the opportunity to correct the wrongs of the past in that it has long been established that group 1 PCa has been designated as clinically insignificant. Some commentators suggest have used the word "wart" to describe the clinical significance of the cancerous material in the prostate in order to give a layman's perspective in that many people happily live with a wart on their skin. Hence it is only PCa that fall within groups 2 and above that need further detailed consideration. For years it has been the accepted practice that PCa which is classified as none aggressive, low PIRADs score and contained within the prostate should be effectively monitored by having a 3 monthly PSA test. If a 3 monthly PSA test shows a significant increase then a further MRI scan and possibly a further TP biopsy will be taken to get an understanding of the situation and if there is concern from these further tests then curative options will be offered.

Hence the bad old days of overtreatment and overdiagnosis should be consigned to the bin and the clear structured treatment pathways should be used and if patients have the treatment pathways laid out then there will be no doubt because everyone will understand where they are namely group 1 know they have an insignificant PCa and routine checks will be made to establish if there has been any movement. As with group 2 a clear clinical decision is made in that a patient could be on active surveillance or offered treatment dependant on exactly what has been discovered. Group 3 and above will have their own treatment paths laid out.

As suggested above if the medical world within the UK unanimously adopted these simple steps are followed then there should be no overtreatment or overdiagnosis. On the basis of that the NHS is currently applying the correct medical discipline and adhering to the use of their own guidance then it must be the case these the modeling inputs are amended o take account of the fact that overdiagnosis and overtreatment should be mostly irradiated especially for the purpose of screening modeling.

Comment 5

International screening.

No mention is made whatsoever of the PRAISE U trial currently underway in 5 countries in Europe. All we are told that in 2012 USA rejected calls for screening, that Lithuania is the only country with a screening program. Internationally prostate screening is rare which “reflects shared concern”. (a comment too far?)

It is suggested that *“various countries offer opportunistic PSA testing or, as in the UK, provide guidance that supports individual decision making for men on PSA testing.”*

The section then details some very none international screening information on internal NSC work.

It is clear from information on the prevalence of PCa that many countries do not have the same numbers of deaths pro rata. Other countries do not have a unified national health service which is free at the point of entry. Because of such certain basic fundamental difference then there are specific reasons as to why they are reluctant to consider screening programs for PCa eg in Asian countries where mortality rates are reported to be as low as 2 men per 100,000 cf the UK being 25 deaths per 100,000.

It is further interesting to note the comment on opportunistic PSA testing in the UK as highlighted above. This seems to suggest that in the UK we do not offer opportunistic PSA testing but rather simply provide guidance that supports individual decision making for men on PSA testing. It appears that the NSC are not actually aware of what is currently on offer within the UK. The Government (Health and Social Care) website (see link below) considers that men who are asymptomatic with an elevated PSA test result >3 should be clinically assessed for consideration for referral to urology by GPs under the Prostate Cancer Risk Management programme (PCRM). As from 12th December 2024 a man of any age can ask his GP for a PSA test and if elevated his GP should consider a referral to urology. However, just like the NSC it appears that the NHS does not was to tell their GPs about this referral route since all 21 cancer Alliances in England and Wales only ever mention how to refer men with LUTS using the NICE age related thresholds.

Link to UK Gov DoH “advising men without symptoms of prostate disease who ask about the PSA test”

<https://www.bing.com/ck/a?!&&p=921c01201a050828ffd5ac7d829f0b66c246e27874176f937bd0ee974812e0eJmItdHM9MTc2OTA0MDAwMA&ptn=3&ver=2&hsh=4&fclid=1790aed2-9116-6134-0763-bb6c90316056&psq=advisinf+men+without+symptoms+of+prostate+disease+who+ask+about+the+psa+test&u=a1aHR0cHM6Ly93d3cuZ292LnVrL2dvdMvYbm1lbnQvcHVibGJiYXRpb25zL3Byb3N0YXRILXNwZWNPZmIjLWFudGlnZW4tdGVzdGluZy1leHBsYW5hdGlubi1hbmQtaW1wbGVtZW50YXRpb24vYWR2aXNpbmctd2VsbC1tZW4tYWJvdXQtdGhlLXBzYS10ZXN0LWZvci1wcm9zdGF0ZS1jYW5jZXItaW5mb3JtYXRpb24tZm9yLWdwcmw>

It is suggested that for the last 6 years the NHS has effectively only been referring men with LUTS under the NICE referral route then any figures supplied by the NHS that are used by the NSC to model the problem of PCa are not to be relied on because they only depict the story of men who report symptoms to the GP, (GP acknowledges and understands the clinical implications of such symptoms), and have elevated PSA test results as rated against the NICE age threshold and thereafter referred to urology. Therefore, this is a whole raft of people who have PCa have been ignored since GPs have a basic lack of knowledge on the subject because they are not being adequately directed by their Cancer Alliances.

Comment 6

Recommendation that a targeted national PCa screening program to men with confirmed BRCA1 or BRCA2 gene variants every 2 years, from age 45 to age 61.

Any screening recommendation is welcomed, however it appears that this recommendation has been poorly developed and worked up within the modelling exercise since it seems that its inclusion is to try and placate those calling for national screening. There is much to criticise as to how the study came to its findings however it does seem that it is being served up because it could be the least expensive screening option to implement and a fob.

What it appears that we are being told;-

1. That it is a scheme for people aged between 45 to 61. However, it was found in the IMPACT trail that 49% of the PCa discovered was found in men aged 62-69. It is also noteworthy that the European cancer program suggests that screening should be applied up to the age of 69. If there were to be a screening program it should be for men aged up to 69 and not 62 as proposed since the current scheme would only screen for half the men with PCa from this gene mutation.
2. That screening will be carried out every 2 years. However to be effective then research shows that because of the aggressive nature of PCa associated with BRCA1/2 gene mutations a 2 year cycle would be too long since these aggressive PCa could progress so much in this interval that would prevent the use of curative options because the PCa had advanced too far. Hence if there was to be a screening program for BRCA1/2 it should be every year.
3. Costs – From the information supplied it seems very difficult to get a fully appreciation of what is being proposed as to how all these men with the potential of having a BRCA1 and BRCA2 gene are going to be found. It seems that the suggestion is that whole swaths of men would come forward because they already have spent around £1000 to find out privately if they have a BRCA1 or BRCA2 gene mutation by conducting their own medically valid genetic test. By way of a simple straw poll no one within our group has had a genetic test to discover if they have a BRCA1/2 gene mutation. Obviously cheaper ancestry tests do not detail if a person has such a gene mutation. It is then further revealing that there is no cost allocation within the model for the NHS to carry out the genetic screening. So the question has to be asked as to how is the whole

screening scheme going to work, how are men able to find if they have one or both of these genes? One would like to think that if there was an economic costing of the feasibility of a screening program then a massive part must be the cost associated with genetic testing. It is suggested that the NHS must have these figures to hand since the NHS currently operates a scheme (The NHS Jewish BRCA testing program) for the Jewish community whereby any Jewish person 18 or over with one or more Jewish grandparents could receive a test kit and have their genetic material analysed for BRCA1/2 genes for free. Hence the information on the cost of testing must be available. The number of men in the UK with a BRCA1/2 gene mutation is suggested to be 32,000, hence it seems that it is not a hard calculation to get to the bottom of in terms of providing a robust exercise, if indeed the pathway of implementation has been fully thrashed through?

4. The risk factors used within the model. On page 87 we are told that the figure of 1;200 being the prevalence of the BRCA1/2 gene within the general population. Whereas earlier within the modelling paper we are told the precise figures; BRCA1, 1;382 and BRCA2, 1;277. It does seem bizarre that having such clear figures of the precise numbers of people who will have the gene mutation the model then goes on to use a surrogate which effectively almost double the risk factors in the case of BRCA 1 and hence it is considered that by not using the precise figures in the model then it will significantly skew the results. It is further interesting to note on the risk of having a BRCA1/2 gene is that if both parents have the gene mutation and have 4 children then 3 out of the 4 children will inherit the gene. Obviously 3:4 risk factor is very significant. Within your report Petrucelli in 2023 suggested that men with a BRCA2 mutation face a 47% risk of developing PCa. Some commentators suggest the risk can be as high as 61%. It will be interesting to know as to the risk figures used in the model.
5. Page 34. Family history. It seems that family history for modelling purposes relates to having either a father or brother with PCa because the increased risk figure of 1.94 is used. Is this the figure used in the model? What if the person has father and brother then the risk dramatically increases to 3.51%, yet there is no mention of this. Obviously there are other family history combinations and factors eg mother/ sister with breast cancer adding to the risk factors. In the absence of clarity it does seem as if the figure of 1.94 was used in the model which clearly has limitations.
6. The whole concept seems very predicated and reliant on one medical research paper by Nyberg. This whole area of screening for BRCA1/2 does not have the body of evidence that other areas of PCa screening has and it is suggested that if such a novel approach is being taken based on limited new evidence then maybe the same novel approach should be taken for PCa in general and the NSC should look at the actual current medical position rather than looking back at outdated historical medical papers that reported on events that happened 20 years ago or waiting for 20 years to get the results of TRANSFORM and hence look to push the boundaries?

Comment 7

“£42 million TRANSFORM trial, the biggest prostate cancer screening trial in 20 years, could save the lives of thousands of men each year”.

What is clear is that the TRANSFORM trial is being used as an excuse to “kick the can down the road.” Do we wait another 20 years and 6 more rounds of the NSC sitting on their hands waiting for the conclusion of the TRANSFORM trial? As we all know the number of PCa cases is on the rise with 63,000 cases of PCa detected last year a rise of 9% on the previous year. The numbers of deaths from PCa is also predicted to rise over the next decade. In 20 years at say 12,000 deaths per year then around a quarter of a million men will have died from PCa. We are told that 2 men’s lives could be saved per 1000 men screened. Looking at the UK male population of screening age then screening would save 22,000 men’s lives.

It does seem unconscionable that the PSA test is being considered within the 20 year study. It is clear that the PSA test is not a test that screening should hang its hat. The person who first discovered PSA actually warned the medical world years ago that it should not be used as a cancer testing because its lack of specificity. There are many better mechanisms already on the market and approved such as the PSE test (blood sample only) which has been used extensively within the field especially in the USA over the last 3 years and reports on its accuracy within the field validated its trial data in that it has found to be 94% accurate for early detection of PCa. Medical studies (PSE blood test reduces unnecessary prostate biopsies; a real world clinical study) in 2025, also verified that it improves PCa detection by reducing unnecessary biopsies by up to 79.1% in clinical setting. I believe that this demonstrates just how badly conceived the TRANSFORM trial is to not even have the PSE test within the trial.

Comment 8

It has been reported that PCUK have commissioned York Health Economic Consortium to look at the model and have produced a report highlighting the NSC modelling irregularities.

It is further understood that Wes Streeter and Prof Witty have had separate discussions since they seem to be of the view that there are fundamental failings with the report and its recommendations.

Comment 9

Sexual discrimination. It has long been suggested that there is blatant sexual discrimination being created in that men’s health has been ignored for years and direct decimation has occurred because men have been treated less favourably than women. It is only now that a light has started to be shone on the issue and for the first time in decades men’s health is starting to creep up in prominence. However after decades of damage and maltreatment it is suggested that in order to attempt to correct the imbalance then the NSC should simply recommend the introduction of a prostate screening program. Both PCa and breast cancer have similar surrounding statistics in that both cancers will kill around 25-28 deaths per 100,000 (the number of deaths from breast cancer is decreasing whereas men’s PCa deaths are set to rise), that the screening program for breast cancer will also save around 2

lives per 1000. Yet there is a reluctance to create parity and treat the male and female populations equally.

Conclusion

It is disappointing that after 6 years of a 3 year cycle between reports that the NSC has produced such a rancid report with glaring mistakes and inappropriate recommendations. It is suggested that the public has lost faith in the NSC and as such consideration needs to be given to allowing a fully independent body whose members have no involvement or connection with the NHS to look at the matter and provide a report that people can have faith in.

Duncan Carins

S35	Mr Simon Bott MD, FRCS(Uro I).	There are three options on how PSA testing for prostate cancer can proceed. 1. We continue as we are – with disorganised screening – this has had minimal or no effect on prostate cancer mortality in this country. It leads to over diagnosis and over treatment, causing significant harm, particularly in men >70 years old, due to side effects inherent in all prostate cancer treatments. Between 25-50% of men diagnosed with prostate cancer in the UK would have lived out their natural life without the diagnosis if they had not had a PSA check – 10,000 men unnecessarily diagnosed and potentially treated in the UK each year. It further enhances health inequality as PSA testing is higher in more affluent and educated groups (Vickers BMJ 2023). 2. We stop PSA testing altogether – this was tried in the US when the US Preventative Services Task Force advised against using PSA to test for prostate cancer in 2012. Over subsequent years there was a rise in men presenting with more advanced local disease and in men presenting with metastatic disease. This decision has now been reversed. In favour of this policy, we have not seen a rise in prostate cancer mortality in the US and there was significantly less over treatment. However, the 'cat is already out of the bag', so if this was adopted in the UK in 2026 educated and more wealthy men would simply pay to have a private PSA, whilst others would not be tested, further exacerbating the issues with the disorganised screening we currently have. 3. Population or targeted population based screening – when this is done, starting at age 50-55 mortality from prostate cancer drops by 71% (Goteborg 1 Screening study). This reduction compares favourably with other screening programs in the UK and would have a significant impact on mortality of the most common male cancer. Men should be invited aged 50-55 for a PSA test and then risk stratified based on that result to an MRI, or re-testing at 2 years or 5 years. This approach would 4. Reduce number of PSA tests by 25% 5. Reduce over diagnosis by 25% and also costs of over treatment 6. Would reduce costs of treatment for metastatic disease 7. Reduce regional/economic variation (Vickers 2026 www.medrxiv.org) It should be organised by a national body so that GPs no longer check PSAs as in other screening programs. This will free up GP time and ensure the right men are being tested.

			The SCHARR report has been widely criticised for fundamental errors and assumptions. I would strongly urge the NSC to talk to International biostatisticians, epidemiologists and urologists who have worked in the field of prostate cancer screening for decades – including Monique Roobol (ERSPC study), Andrew Vickers (published 150 peer reviewed papers on PSA screening), Jonas Hugosson (Goteborg screening study) and Sigrid Carlsson (Division Head of the Clinical Epidemiology of Early Cancer Detection at German Cancer Research Center). Population based PSA screening can save lives now, before the results of the TRANSFORM study produces any meaningful results. It can be done at less cost and with less overdiagnosis/treatment and harm.
S36	Tanimola Martins		The committee is commended for the substantial time and expertise invested in the development of these recommendations, while acknowledging that some of the conclusions reached may be disappointing to certain stakeholders. However, having considered the accompanying evidence and rationale, the recommendations appear broadly reasonable in the context of the current evidence base. The recommendation to offer targeted screening to men with a known BRCA gene mutation seems appropriate, reflecting clearer evidence of increased risk and potential net benefit in this group, although a small number of other genetic mutations may also warrant consideration as the evidence evolves. Family history of prostate cancer, or cancer more broadly, could be conceptualised within a comparable risk-stratified framework. However, this is often poorly captured in healthcare records, as many men are unaware of their family history or its clinical relevance. As such, the feasibility of using family history alone as a basis for organised screening is currently limited. In practice, this limitation is partially mitigated by existing clinical guidance, which encourages men with a known family history of prostate cancer to discuss prostate specific antigen (PSA) testing with their GP. Further efforts to improve awareness and recording of family history may therefore be sufficient at this stage, without the need for a formal population-level screening recommendation. The decision not to recommend targeted screening for Black men is more complex and likely to generate heated debate. However, it can be justified as being in the best interests of Black men, rather than as a failure to acknowledge their elevated risk. Black men in the UK have a higher lifetime risk of developing prostate cancer than men from other ethnic groups, consistent with evidence from the United States and elsewhere. However, increased incidence alone does not constitute sufficient justification for population screening, particularly where the balance of benefits and harms remains uncertain. Importantly, UK evidence does not clearly demonstrate that Black men are more likely to present with advanced-stage disease at diagnosis. Emerging evidence,

			including from ongoing research at the University of Exeter, suggests that survival outcomes for Black men may be comparable to, or potentially better than, those observed in White men. These findings challenge the long-standing assumption that Black men in the UK necessarily experience poorer prostate cancer outcomes. Such considerations are directly relevant to screening policy, as the justification for screening rests not only on disease incidence but also on evidence of reductions in advanced disease and mortality. Consideration must also be given to PSA biology and test performance. Black men tend to have higher baseline PSA levels, independent of clinically significant cancer. Screening approaches that apply uniform PSA thresholds may therefore result in higher false-positive rates in Black men, leading to unnecessary biopsies, overdiagnosis, anxiety, and downstream harms. In the absence of appropriately adjusted PSA thresholds or risk algorithms, PSA-based screening could disproportionately expose Black men to harm without a corresponding improvement in clinical outcomes. Taken together, while the elevated risk of prostate cancer among Black men is well recognised, the current evidence relating to stage at diagnosis, survival outcomes, and PSA dynamics does not support a blanket recommendation for targeted screening at this time. The committee's cautious approach is therefore consistent with established screening principles, particularly the requirement to demonstrate that benefits clearly outweigh harms. Future modelling and policy development would benefit from more granular, UK-specific data on ethnicity, baseline PSA variation, disease aggressiveness, and long-term outcomes. Continued research, including large prospective studies and improvements in routine data collection, will be essential to determine whether more refined, risk-adapted screening strategies could deliver net benefit for Black men in the future. Crucially, many arguments in favour of targeted screening implicitly assume that Black men would take up prostate cancer screening at sufficiently high levels for the programme to deliver population-level benefit. This assumption is ambitious and not well supported by experience from existing screening programmes. Even within long-established, well-resourced national screening programmes such as breast and bowel cancer screening, uptake remains socially patterned, with consistently lower participation among ethnic minority groups and those experiencing socioeconomic disadvantage. There is little reason to believe that prostate cancer screening, which is associated with invasive follow-up tests, diagnostic uncertainty, and potential long-term harms, would achieve higher or more equitable uptake. Evidence also suggests that distrust of healthcare systems and health professionals remains prevalent within some Black communities, shaped by historical and contemporary experiences of discrimination and unequal treatment. These factors are likely to act as substantial barriers to engagement with an organised screening programme, even if eligibility were restricted to a higher-

			risk group. In addition, men are generally less likely than women to engage with preventive health services, and prostate cancer carries particular stigma related to masculinity, sexual function, and continence. Fear of life-changing treatment side effects may further deter participation, especially when the benefits of screening are uncertain or poorly understood. Importantly, screening uptake is not merely a matter of access or invitation, but of trust, perceived relevance, and confidence in net benefit. Introducing a targeted screening programme in the absence of clear evidence of mortality reduction risks generating low and uneven uptake, thereby limiting effectiveness while concentrating harms among those who do participate. Given that fewer than 10 percent of cancers in the UK are currently diagnosed through screening, it is unlikely that the introduction of prostate cancer screening would substantially improve the detection of clinically significant disease. Instead, there is a real risk that such an initiative would divert resources, exacerbate diagnostic bottlenecks in primary and secondary care, and inadvertently widen existing inequalities by benefiting a more health-engaged subset of the population. From an equity perspective, improving timely presentation, diagnostic pathways, and symptom awareness among Black men may offer greater potential benefit than the introduction of a screening programme with uncertain uptake and unclear net advantage. In conclusion, while concerns regarding prostate cancer risk among Black men are legitimate and warrant continued attention, the committee's current recommendation represents an evidence-based and proportionate response to uncertainty and appropriately avoids the introduction of a screening programme that could result in unintended harm. Ongoing surveillance and research will be critical to ensure that recommendations evolve as the evidence base strengthens.
S37	Jeanette Smalley	CancerHelp (Preston) Ltd	Hello, Working at a cancer support centre that hosts a prostate cancer support group, I am acutely aware of the number of men locally being diagnosed with prostate cancer. Currently, there is no agreed nationwide screening programme for men. As a result, it is often up to individuals to visit their GP if they experience possible symptoms. Many symptoms may be attributed to the ageing process, and without a baseline PSA level, it can be difficult to determine what constitutes a PSA result that requires further investigation. I would like to highlight one example from our centre. One of our contractors, in his early 50s, had recently undergone follow-up for melanoma. Not long afterwards, he attended a routine 'Well Man' check at his GP practice and was referred for further tests. He was subsequently diagnosed with prostate cancer that had already

		spread beyond the prostate. He is otherwise fit and active – an Ironman and regular half marathon runner with a healthy diet. I recently saw coverage around the decision not to introduce a national PSA screening programme. The discussion focused on potential harms, such as infection following a biopsy. While these risks exist, they are associated with follow-up procedures rather than the PSA test itself. Presenting this distinction clearly is important for public understanding, particularly for men who may be reluctant to engage with health services. At our cancer support centre, the prostate cancer support group has previously run several PSA screening sessions attended by over 300 men that has been funded largely by local construction companies – at the most recent one, just under 500 men attended. There is a want to engage with this, despite men often being described as not exhibiting help seeking behaviour. As a result of these sessions, several men were diagnosed with prostate cancer earlier than they might have been otherwise, increasing the likelihood of curative or life-prolonging treatment. Anything that can increase the chances of timely detection and access to effective treatment deserves consideration. The Cancer Plan that was launched today emphasises 'patients' priorities', and early detection of prostate cancer is a priority for many patients and support groups. Thank you for considering this perspective. Yours Jeanette
S38		The PSA is not suitable as a screening tool, the money implementing a screening programme would be far better invested in developing an accurate marker for prostate cancers, genetic markers for high risk prostate cancer and public campaigns for awareness especially amongst groups at higher risk, and training for AI healthcare apps and allied healthcare professionals.
S39		Dear Sir Please find attached my response on the draft report on prostate cancer screening produced by the NSC. With many thanks Best wishes

Dear Sir

I would like to respond to the draft NSC report on prostate cancer screening following the recent Round Table discussion with the Secretary of State on 28th January 2026 which I attended.

The data used in the SCHARR model is out of date. The targeted screening data from our recent (2026) published study of over 18,300 men using a modern an NHS approved cancer diagnostic pathway would provide up to date UK data for modelling. **Ref 1.**

Rates for detection of clinically insignificant prostate cancer are underestimated in the SCHARR model. Below is a comparison from our targeted screening program using a modern MRI first pathway and LA TP biopsies.

- The targeted screening program PSA positivity rate was 4.7% rather than the NSC estimated 10.4%.
- 42% of men who had an MRI had an abnormality requiring an LA TP biopsy rather than their figure of 33% (implying 58% of men were reassured after their scan).
- 1.4% of men targeted screening program who had a PSA test had prostate cancer, the NSC report quotes 2.8%.
- Only 16% of the cancers we detected were grade Grade Group 1 rather than the NSC estimated figure of 37% figure and significantly higher grade cancers were detected than they estimated, see below.
- There were no episodes of post-biopsy sepsis and to our knowledge no harm was caused from the diagnostic pathway.

	Grade Group 1	Grade Group 2	Grade Group 3 +4	Grade Group 5
NSC estimates	37%	47%	12%	4%
Our UK data	16%	51%	25%	7%

In view of the work by Andrew Vickers, see **Ref 2, 3**, on modeling UK prostate cancer screening, the NSC report is flawed as it did not model for the cessation of the existing unregulated opportunistic screening program that currently existing. Any new screening initiative must also mandate that chance opportunistic screening, especially in Primary care must stop.

The current guidance to GPs, through PHE stating that unless an asymptomatic man requests a PSA it should not be offered, should be reversed immediately as PHE's own guidance states that early prostate cancer is usually symptomless. The current advice unfairly disadvantages men of a lower socio-economic group who may not know to ask for a test, despite perhaps being Black or having a strong family history of prostate cancer. There should be a national prostate cancer screening

program, men aged 50-70 ys of age, and from 45yr in men with a strong family history (First degree relative), Black ethnicity or BRCA 2 positive status.

To do nothing but leave the current system intact (irrespective of targeting the tiny minority of men who may know the BRCA status) is not a neutral position. The current unregulated, opportunistic screening regime that exists in the UK, is known not to reduce prostate cancer mortality **Ref 4**.

The risks regarding Family History are well documented and summarized below **Ref 5,6,7, 8**. The metric should be having a first degree relative with prostate cancer to start having PSA screening at the earlier age of 45yr compared to the standard age of 50.

In the UK a black man has twice the life time risk of prostate cancer (1 in 4) compared to a white man (1 in 8) and the risk of prostate cancer related to family history is, as below:

Scenario	Relative Risk	Approx. Lifetime Risk	"1 in X" shorthand
Background (white men)	1×	12–13%	1 in 8
One first-degree relative (any age)	2–3×	25–35%	≈1 in 3–4
One first-degree relative diag. young (< 60 yrs)	3–4×	35–45%	≈1 in 2–3
Two or more first-degree relatives	4–6×	45–60%+	≈1 in 2

Whilst the exact risk of prostate cancer is difficult to interpret from the current data, our targeted screening program showed that there was an increased risk of the disease and of the disease being clinically significant **Ref 1**. More data will come to light as a future screening program progresses. It is not acceptable to exclude Black men from early screening.

In summary, there should be a national prostate cancer screening program in men aged 50-70 ys of age and from 45yr in men with a strong family history (first degree relative), Black ethnicity or BRCA 2 positive status. Primary care should equally be stopped from providing opportunistic PSA testing in an unregulated fashion.

Prof of Urology

February 2026

References

- 1 Targeted Prostate Health Checks, a Novel Screening System to Identify Men at Risk of Prostate Cancer :Real-worldEvidencefromMorethan18000Prostate-specificAntigenTests Langley SEM et al, *Eur Urol Oncol* 9 (2026) 93-100. doi.org/10.1016/j.euo.2025.10.007
- 2 Effect of implementing population-based prostate-specific antigen screening on testing rates and overdiagnosis in England: a statistical modelling study. Vickers A & Brentnall A. 2026; <https://www.medrxiv.org/content/10.64898/2026.01.23.26344710v2>
- 3 Current policies on early detection of prostate cancer create overdiagnosis and inequity with minimal benefit Vickers A et al. *BMJ* 2023;381:e071082. <http://dx.doi.org/10.1136/bmj-2022-071082>
- 4 Opportunistic testing versus organized prostate specific antigen screening: Outcome after 18 years in the Goteborg randomised population-based prostate cancer screening trial. Godtman RA et al. *Eur Urol* 2015 (68) 354-360
- 5 Hemminki, K., Försti, A., Sundquist, K., & Barlow, L. (2005). "A systematic review and meta-analysis of familial prostate cancer risk." *European Urology*, 48(4):508-513.
- 6 Bruner, W., Moore, D., Parlanti, A., Golbeck, E., & Garber, J. (2003). "Relative risk of prostate cancer for men with affected relatives: Systematic review and meta-analysis." *International Journal of Cancer*, 107(5):797-803.
- 7 Whittemore, A. S., Kolonel, L. N., Wu, A. H., John, E. M., Gallagher, R. P., Howe, G. R., & His, F. T. (1995). "Family history and the risk of prostate cancer." *Cancer Epidemiology, Biomarkers & Prevention*, 4(6): 485-492.
- 8 Prostate cancer risk prediction based on complete prostate cancer family history(Hjelmberg et al., 2015). *Prostate* Mar 1;75(4):390-8. doi: 10.1002/pros.22925.Epub 2014 Nov 18

S40	Chiara De Biase	Prostate Cancer UK (PCUK)	Good afternoon I'm very pleased to present the Prostate Cancer UK submission for the public consultation on screening for prostate cancer. Best Wishes Chiara Chiara De Biase

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name:	Chiara De Biase	Email address:	*****
Organisation (if appropriate):	Prostate Cancer UK		
Role:	Director of Fundraising and Health Strategy		
Do you consent to your name being published on the UK NSC website alongside your response?		☒ Yes	☐ No
Section and / or page number	Text or issue to which comments relate	Comment <i>Please use a new row for each comment and add extra rows as required.</i>	
SCHARR Cost-effectiveness report, section 8.1; General Population. and Prostate Cancer Screening Evidence Review 2025 Narrative, section 5.1.	Screening for the general population	While we acknowledge and respect the UK NSC recommendation for the general population, we also share the public's deep disappointment that evidence remains insufficient to establish a screening programme for all men. We recognise that current evidence demonstrates screening reduces prostate cancer mortality, however, we understand this benefit must be weighed against ongoing substantial overdiagnosis and the risk of overtreatment. Further research is essential to identify the optimal mechanism for safe and accurate prostate cancer diagnosis. The TRANSFORM trial and its associated translational research programme will be instrumental in achieving this goal. In the absence of a screening programme in the non-BRCA risk groups, the DHSC, UK NSC and NHS must take action to address an inadequate status quo by engaging and consulting with key stakeholders to establish an early detection programme which provides all men at risk of prostate cancer, fair and equitable access to the information needed to make an informed choice about whether to have a PSA blood test or not. That should include the following steps: 1. An update to the current GP guidelines (Prostate Cancer Risk Management	

		Programme, PCRMP). Updates must reflect the latest evidence, SCHARR modelling, and clinical practice in the UK. We need an early detection programme which provides all men at highest risk of prostate cancer fair and equitable access to the evidence-based information needed to make an informed choice about whether to have a PSA blood test or not. 2. Replacement of the current, ineffective PCRMP patient information, with the Prostate Cancer UK online Risk Checker tool (that will be redeveloped to reflect the latest evidence from this evidence review and SCHARR modelling) to ensure that men can access clear, evidence-based information to help them understand their risk factors, and the pros and cons of a PSA blood test to support a genuine informed decision. 3. To ensure that all at risk men have equitable access, a recommendation that GPs should proactively start conversations about the pros and cons of the PSA test with men at highest risk as determined by this review. Primary care should be given the necessary resources to fund this activity. 4. Investment in targeted risk awareness campaigns to ensure relevant groups of men know their prostate cancer risk and know they can make an informed choice about PSA testing and diagnosis
SCHARR Cost-effectiveness report, section 10.1 Discussions and Conclusions; Men of Black ethnicity: Conclusions, p.174., Prostate Cancer Screening Evidence Review Cover sheet, 7. Draft recommendation, page 7.	'Data uncertainty' to justify not recommending targeted prostate cancer screening in Black men	While we accept that the results of the SCHARR model reflect the data and evidence used as inputs, we challenge the assertion that uncertainty in the data inevitably means that UK NSC could not recommend prostate cancer screening for Black men. This uncertainty could have been mitigated through analysis of NHS electronic health records. The failure to pursue this reflects a lack of curiosity and planning within the review process. There is data in the NHS ecosystem that could have been used to fill key evidence gaps on prostate cancer in Black men in the UK. Prostate Cancer UK has a programme of work underway to access this data to address the evidence gaps outlined in this section and will make the findings available to the UK NSC to update the SCHARR model within a year. With the uncertainty that has resulted from this missed opportunity, we don't believe it is right to lower the evidence threshold for Black men and make a premature decision to screen. Instead, the UK NSC should update the SCHARR model using Real-World Evidence and reevaluate their screening recommendation for Black men, as soon as our data is available.

SCHARR Cost-effectiveness report, section 10.1 Discussions and Conclusions; Men of Black ethnicity: Conclusions, p.174.	Filling in remaining evidence gaps to understand the harms and benefits of Prostate cancer screening for Black men	Some of the data uncertainty cited in the SCHARR report arises from specific components of the natural history model, as well as from limited evidence on screening uptake among Black men. Some uncertainties are genuine gaps; for example, the natural history of prostate cancer in Black men may differ from that of the general population, with implications for the applicability of overdiagnosis estimates. There is also lack of clarity on screening uptake for Black men as Black men have been underrepresented in past prostate cancer screening trials. We also note that natural history models are predicated on incidence rates, which are themselves impacted by differences in testing rates. PSA testing rates can differ due to a combination of factors such as ethnicity, age, area level deprivation and geography. Recent data suggest historical disparities in rates of testing at the population-level (age-adjusted) have narrowed in England and are comparable between Black and white men. However, after examining ethnic differences in rates of testing in Black men compared to white men and adjusting for multiple variables, Black men have been reported as more likely to be tested.¹ We do not know if this is attributable to awareness activity and the impact it has on both tumour stage and grade at diagnosis in Black men. It is important to note that the higher testing rate cannot explain why the prostate cancer specific mortality for Black men is double that of white men, or why NPCA data shows significantly higher incidence of late-stage disease in Black men. There is also uncertainty in the generalisability of natural history disease parameters for Black men diagnosed in the modern UK setting. For example, local anaesthetic trans perineal (LTP) biopsy may impact diagnostic assessments of tumour aggressiveness in Black men as LTP is associated with improved sampling of anterior tumours.² The improved detection of these tumours is important as the presence of anterior tumours has previously been postulated as being a contributing factor to pathological upgrading after radical prostatectomy in Black men. We actively seek the UK NSC's support in our efforts to fill in the remaining evidence gaps and identify solutions. Those efforts include the TRANSFORM trial and we seek support to maximise the potential of that programme, and our Real-World Evidence programme.
Prostate Cancer Screening Evidence Review Cover sheet, 7. Draft	Establishing a dedicated prostate cancer evidence taskforce	Prostate cancer UK are actively working to address the data gaps to reduce the data uncertainty through our Real-World Evidence programme and the TRANSFORM trial. We are well placed to work with DHSC, OHID, UK NSC, NHS England and other partners to fill these evidence gaps quickly and to the necessary standards of data quality and certainty. In order to do so, we urgently need rapid

recommendation, page 7.		and regular access to routine prostate cancer data which includes ethnicity, Gleason Grade distribution, and mortality outcomes. Data innovation needs to be leveraged to establish a mechanism to integrate these data points into the Rapid Cancer Diagnostic Dataset. We ask that a dedicated taskforce is established to achieve these goals in as timely manner as possible and to reduce the risk of future evidence generation leaving avoidable evidence gaps, especially for Black men with and at risk of prostate cancer. This should include immediate prioritisation of investment and access to Real-World Data sources, and additional long-term investment to improve access to clinical trials for Black men.
SCHARR Cost-effectiveness report, section 8.2.2. Men of Black ethnicity: repeat screening scenarios. and section 10.1. Summary of the Modelling Results.	Black men draft recommendation/cost-effectiveness planes	The lack of data availability on disease progression and screening uptake for Black men led to wide probabilistic uncertainty for Net Monetary Benefit (NMB) in the model, with a mean incremental NMB of £148 (95% CrI: –£1,137 to £829) for repeat screening. Given that prostate cancer screening for Black men aged 50-62 every 4 years was associated with 81% of probabilistic runs being cost-effective and with a mean incremental NMB of £99, the UK NSC should clarify the level of certainty required to consider an intervention as cost-effective. It also warrants urgent acquisition of UK data on Black men to demonstrate the true cost-effectiveness of screening for UK Black men.
SCHARR Cost-effectiveness report, section 10.4. Data limitations and requirements, p.181.	Use of US data on aggressive disease in Black men	As highlighted in sections above, data uncertainty on Black men stems in part from reliance on US data. Importantly, studies have shown that Black men are associated with more aggressive disease at diagnosis even in equal access setting, as reported by Navarro, S et al. (2022); a study which was cited in the SCHARR report.³ However, we know there are conflicting findings on whether Black men are more likely to present with more aggressive disease at diagnosis or experience adverse outcomes following treatment, compared to white men.^{2,4,5} For example, in one equal-access US study investigating treatment outcomes, although a higher proportion of Black men were diagnosed with Gleason score of 7 at baseline, a lower proportion were diagnosed with Gleason 8 or more, compared to white men, with no ethnic differences subsequently reported in either 10-year cumula-

		tive incidence of biochemical recurrence or metastatic disease, following definitive radiation treatment.⁵ Study reports both within and outside of the US generally fail to define aggressive disease in a consistent manner, making the evaluation of the strength of these findings difficult. Similarly, different classification systems have been historically reported to denote aggressive disease, ranging from descriptions based on levels of 'differentiation' of biopsy sample cells to those focused on the post-2014 Gleason Grade classification system, further adding to difficulty of interpreting inter-study findings.^{6,7} Furthermore, we acknowledge that US data from equal access settings is subject to selection bias based on criteria to enrolment for programmes such as Medicare, and uncertain (and potentially inequitable) access to pre-biopsy MRI. For these reasons, we do not consider US data to be directly applicable to the UK context. We therefore agree with the SCHARR report that there is <i>'a clear need for UK-specific data on the Black population, particularly regarding Gleason Grade Group distribution by age at diagnosis, stage at diagnosis by age, incidence-to-mortality ratios, and uptake of and response to opportunistic and organised screening programmes.'</i> As part of our Real-World Evidence programme, we are undertaking a data study that will shed light on the Gleason Grade Group distribution of prostate cancer diagnosis and ethnicity and provide data on the absolute and relative risk of aggressive prostate cancer for Black men. The results from this study will be available within a year and will provide the missing data to better understand the natural history of prostate cancer for Black men and reduce the reported data uncertainty. This data may strengthen or weaken the UK NSC draft recommendation on Black men, depending on whether results demonstrate increased or decreased risk of aggressive disease and therefore shift cost-effectiveness analysis to be more or less cost effective.
SCHARR Cost-effectiveness report, section 8.2.1. Men of Black ethnicity: single screening at different ages, p.109 (Figure	Concerns on potential overdiagnosis of Black men.	We do not know what the true rate of overdiagnosis is in Black men due to historical underrepresentation of Black men in clinical trials. Given that overdiagnosis was defined as excess incidence/screen detected cases in the SCHARR modelling rather than based on detection of clinically significant prostate cancer, this measure does not fully represent the rates of Black men who are diagnosed with a prostate cancer that would not have caused any harm if left untreated.

37).		Importantly, our ability to infer overdiagnosis (defined as men who are diagnosed with low grade disease that would not have caused any harm if left untreated) in Black men using real-world data continues to evolve due to historic underreporting of both clinical T stage and grade of disease in a UK setting. For example, multiple US studies in equal access settings have reported that Black men may present with stage T1 disease but have a higher proportion of biopsy-detected Grade Group 2-3.^{8,9} In the short term our Real-World Evidence programme will provide data on Gleason Grade Group distribution by ethnicity within a year. This data can be used to help inform the model and provide estimates of excess incidence by stage and grade at diagnosis if screening were implemented for Black men. Therefore, the UK NSC must commit to reviewing the findings from our Real-World Evidence programme work to inform future iterations of the model. To further strengthen the evidence, the first set of results from TRANSFORM, will provide an up-to-date measure of Gleason grade distribution in the whole population and in Black men, in a screening population. These results will be available in under two years. The findings from these early results must also be incorporated to inform future iterations of the model.
SCHARR Cost-effectiveness report, section 6.8.4. Screening uptake, p.69.	Applicability of CAP trial uptake rate	We are concerned that the uptake rate of 36% observed in the CAP trial may not be representative of a screening programme implemented now. The CAP trial tested the efficacy of a single prostate cancer screening round under the old prostate cancer diagnostic pathway and did not include pre-biopsy MRI between 2002 and 2009. There have been significant changes in awareness around prostate cancer and associated pathways. However, we recognise that the CAP trial is the best indication we currently have on likely uptake rates for prostate cancer screening. Prostate Cancer UK is committed to improving the evidence on this assumption and the first stage of TRANSFORM, anticipated to report by the end of 2027, will provide up-to-date, UK-specific and screening population-specific information on background PSA testing rate, and acceptance of an invitation to screening (in a trial). We welcome the UK NSC's commitment to reviewing these findings and using them to inform future iterations of the model as soon as possible.
Prostate Cancer Screening Evidence Review 2025 Narrative,	UK NSC draft recommendation for men with a BRCA variant	We accept and welcome the committee's recommendation to screen men with a BRCA variant, as SCHARR's modelling shows clear benefit for this cohort which outweighs the risk of harm. We urge the UK NSC to pursue this draft recommendation.

section 5.3. Targeted screening for men with a known BRCA1/2 gene variant.		Prostate Cancer UK is well-placed and ready to be a key strategic partner in the development and rollout of the programme if the recommendation is confirmed. We see this as a positive opportunity to develop an initial quality assured pathway that is acceptable to other groups of high-risk men further down the line.
UK NSC Cover sheet, section 6. Next steps, p.7.	Whether a strategy focusing on genetic risk should include men with BRCA 1 and 2 variants or just BRCA 2 variants	The UK NSC has requested specific views on whether the approach should include both BRCA1 and BRCA2 variants, or just BRCA2 variants. BRCA2 variants are more strongly associated with an increased risk of prostate cancer than BRCA1 variants, but results from the IMPACT study indicate that both types of gene variants are associated with an increased risk of aggressive prostate cancer, with pathological upgrading to greater than Gleason Grade Group 2 following radical prostatectomy. We welcome the decision to look at both variants in this modelling but recognise the importance of assessing them separately if the committee considers that the available evidence allows this. Regarding a screening strategy, an assessment by the UK NSC would need to be made on the practicalities, feasibility and efficacy of grouping men with a confirmed BRCA1 and BRCA2 into the same screening algorithm or different algorithms. We are aware of emerging data which suggest that other rare variants may confer even stronger risk of aggressive prostate cancer and prostate cancer mortality. We encourage the UK NSC to develop a mechanism to assess the strength of evidence for these emerging (non-BRCA) variants quickly and, if appropriate to add them to the screening-eligible cohort.
SCHARR Cost-effectiveness report, section 6.4.2. BRCA1 or BRCA2 mutations, Known BRCA1,2 status, p.31.	Use of known BRCA status in the modelling and need for increased awareness of genetic testing eligibility	SCHARR's modelling uses men with a known BRCA variant as the eligible population. To ensure that all men with a BRCA variant benefit from this recommendation (including those who don't currently know their BRCA status), increased awareness of eligibility for genetic testing will be key, as will ensuring that the system can support increased testing uptake and associated costs.
SCHARR Cost-effectiveness report, section 8.4.5 BRCA	Clarification on the upper age limit of the draft recommendation for men with a BRCA variant	It has been highlighted that the current age range of the draft recommendation would miss a substantial number of clinically significant cancers detected beyond age 61 (49% of BRCA1 cancers and 42% of BRCA2 cancers based on IMPACT data). The modelling considered scenarios with an upper age limit of 68 but did

screening - impact on population, p.149.		not take these forward into the probabilistic analysis. We recognise that these scenarios were associated with higher overdiagnosis rates and would like to request clarification on whether this was the reason why scenarios with a more restricted age range were favoured. Information on the Gleason Grade distribution of the excess incidence cases would be helpful to better understand the consequences of an upper age limit of 61. There are also practical considerations about how to appropriately counsel men with a known BRCA mutation who have been eligible for PSA screening, once they reach age 61 under this scenario. If the probabilistic analysis shows likely overall benefit in an extended age range for this group of men, we would be supportive of screening to a later age for this group of men more in line with the IMPACT age range.
SCHARR Cost-effectiveness report, section 6.4.3. Family history of prostate, breast, and ovarian cancers, p.32.	Definition of 'Men with Family History' and population size included in this cohort	Family history is complex, and not all family histories are the same. Further work is needed to understand how different types of family history impact aggressive prostate cancer diagnosis, late-stage diagnosis and death. We believe the family history definition used, including all men with 'one or more first-degree relatives previously diagnosed with prostate, breast, or ovarian cancers' was too broad, particularly because BRCA populations were excluded but breast and ovarian cancer had only been included in Prostate Cancer UK's original targeted screening proposal as a proxy for BRCA risk. The very broad definition of family history used here has two impacts. Firstly, it broadens the group of men meeting this definition to 1/3 of the population over 60. Secondly, it likely dilutes the excess risk of prostate cancer seen in this group compared to men selected by a narrower definition of family history. The high overdiagnosis rates in this broad group of men with family history is likely exacerbated by this dilution of risk. Further work must be done to explore whether alternative, narrower definitions of family history could identify men with a higher risk of aggressive prostate cancer and death, who would benefit more from prostate cancer screening.
SCHARR Cost-effectiveness report, section 8.3. Men with familial	On Results: Recommendations for future family history modelling	In subsequent iterations of the model, we wish to see results for men with a family history of prostate cancer only (removing the men included in this broad group through family history of breast and ovarian cancer) to understand how that changes the harm to benefit ratio. However, we accept that, even for that

risk, p.121. and Section 10.1, Summary of the Modelling results, Familial risk: conclusions, p.173.		group there is a mixed evidence picture in terms of whether excess diagnoses are of clinically insignificant, or clinically significant disease. Prostate Cancer UK is actively working to develop a clearer, evidence-based definition of familial risk, and is currently undertaking a rapid systematic review to understand if there are specific cohorts of men with a family history that are more likely to benefit from screening interventions. The findings of this review will be published and presented to the clinical community to support consensus on what constitutes a relevant family history for prostate cancer. We propose that, as a matter of urgency, the UK NSC works in partnership with Prostate Cancer UK to integrate the findings from this consensus process and, if possible, apply the agreed definition to recalibrate the model. Our suggestion is that family history definitions based on prostate cancer death, or metastatic prostate cancer, or prostate cancer treatment at young age may offer improved risk to benefit ratios. However, those definitions are new, and so it is unlikely that we will be able to find robust evidence of harms and benefits of screening for men defined by those tighter criteria outside a trial setting. TRANSFORM gives us the opportunity to test those once the consensus work has been done to define them.
SCHARR Cost-effectiveness report, section 7.2. External validation, p.81.	On methodology: Use of data and evidence in external validation of model	We agree that the methods provide a sound demonstration of internal and external validity. We see that the use of CAP and ERSPC trial arms as comparison are appropriate, given data availability. This validation against CaP and ERSPC does, however, highlight a major problem currently facing any attempt to model prostate cancer screening. Namely there is a dearth of up-to-date evidence from high quality clinical trials. Neither CaP nor ERSPC included pre-biopsy MRI and so fail to reflect current practice. While the model does attempt to correct for this shortcoming it is essential that more up to date trial data can inform future iterations of the model. TRANSFORM will provide that new data about the current (and possible future) pathways used in the UK population and based on modern treatment paradigms. The first read out from TRANSFORM – providing up-to-date information on diagnostic accuracy, background testing rates, harms from diagnostic procedures and treatments, and resource usage - will happen as early as the end of 2027 and we are pleased to see the commitment from NSC to begin to incorporate that evidence as soon as possible. Even more stark is the systemic lack of high-quality trial data from Black men at all. Again, TRANSFORM is designed to address that

		evidence chasm, and we seek continued support from NSC, NIHR and DHSC more broadly to ensure that we maximise the opportunity to finally deliver the evidence base that Black men, more than any other group, need urgently.
SCHARR Cost-effectiveness report, section 7.3. Determining the characteristics of the simulations, p.83-84.	On methodology: 7.3.1 addressing stochastic uncertainty	We acknowledge that given the constraints, a full incremental analysis of all screening strategies and scenarios cannot be conducted and believe that the screening strategies selected for probabilistic analysis for each modelled high-risk group are reasonable. We agree that the numbers of individuals simulated are reasonable to address stochastic uncertainty. The scenarios set out in the scenario analyses are appropriate.
SCHARR Cost-effectiveness report, section 8. Modelling results: PSA screening with threshold 3ng/ml, p.115-116.	Clustering in cost-effectiveness planes, specifically in targeted screening of Black men under imperfect uptake	We recognise that the 'clouds' of runs in several cost-effectiveness planes are acknowledged to be associated with uncertainty in the underpinning natural history disease (NHD) parameters. Clustering suggests that parameter combinations reflect heterogeneous specifications of NHD. While this propagates to all reported cost-effectiveness analyses, we note its particular impact on the modelling for Black men in which some clusters consist of runs that are entirely cost-effective and some entirely not (for example, Figure 44 for 4-yearly screening from ages 50-62), resulting in this strategy's 81% probability of being cost-effective. This contrasts with a hypothetical case where there are no distinctly separated clusters and some runs within the distribution are cost-effective. This highlights the importance of epidemiological data that accurately reflects the characteristics of UK Black men, as the interpretation of cost-effectiveness is sensitive to small changes in model parameters, and we believe more steps could have been taken to increase the certainty in the modelling for Black men. We encourage the UK NSC to commit to incorporating high-quality data from trials and real-world epidemiological sources, including our own, when/where they are available to increase certainty of the NHD parameter distributions.
SCHARR Cost-effectiveness report, section 10.4 Data limitations and requirements, p 183-186	Clinical Presentation Rate and Opportunistic Screening Coverage	We recognise that measuring the impact of an organised prostate cancer screening programme on opportunistic PSA testing requires accurate and consistent data coding. Collins et al have provided updated estimates of PSA testing rates; however, limitations in available data meant they were unable to precisely distinguish opportunistic testing from other indications. ¹ To robustly identify the reasons for PSA testing in the UK, test indications need to be systematically and prospectively coded within healthcare records.

		The narrative that an organised screening programme could substantially reduce PSA testing rates is undermined by evidence by Merriel et al, who paired PSA testing data with symptoms as a proxy for symptomatic PSA testing. The study found that approximately four-fifths of prostate cancers in the UK are diagnosed following symptomatic presentation. PSA testing rates were 3 times higher in patients aged 70-89 when compared to those aged 50-59.¹⁰ This suggests that even if population screening is introduced for men aged 50-59, PSA testing rates outside of a screening programme would continue to be driven by the population aged 70 and over. Moreover, PSA testing is widely accessible over the counter and through private healthcare, and uptake is likely to increase in the future, rather than decline. In this context, we agree with the model's acknowledged limitations regarding opportunistic PSA testing and recognise that the authors have made reasonable efforts to account for PSA testing interactions given current data limitations.
UK NSC Cover sheet, section 6. Next steps, p.6.	Screening for prostate cancer overall and on the standard of the modelling study	We believe that whether screening for prostate cancer is implemented should be based on the available evidence and consider both the potential harms and benefits. We appreciate that the committee's draft recommendations have been guided by SCHARR's findings and consider the modelling to have been undertaken to a high standard.
UK NSC Cover sheet, section 6. Next steps, p.6.	Whether the evidence and data used in the model are appropriate	Above we have outlined several areas in which we have concerns around the modelling inputs, including how the eligible population is defined for men with a family history and that steps have not been taken to rectify cited data uncertainty in the modelling for Black men. We strongly recommend that effort is focused on finding ways (in partnership) to improve these shortcomings and strengthen assumptions in future. Other than in these cases, and for the present model, we consider the evidence and data used in the modelling to be appropriate.
	Collaborate with the TRANSFORM screening research trial team to: - answer outstanding questions on screening effectiveness for Black men and men with a family history – as soon as trial data becomes available - await results of the study to develop and trial a more accurate test than PSA alone, to improve the	We welcome this recommendation and look forward to continued collaboration with the UK NSC to assess findings from the TRANSFORM trial in a timely manner. We need to understand how these findings impact the cost-effectiveness modelling and benefits/harms of screening in the higher-risk groups of men as soon as possible and as detailed above, initial results will be available in 2027. We also recognise the commitment of NIHR and DHSC to support the trial to that point and in the definitive stage. That definitive stage will be powered, and funded, to follow men up long enough to determine longer term outcomes up to

	balance of benefit and harm of screening	and including prostate cancer specific mortality. We are encouraged by conversations to date about the use of meaningful endpoints that can be measured at earlier timepoints to drive screening decisions – notably the avoidance of metastatic prostate cancer. We would encourage continued engagement on that point in particular. We also welcome the ongoing input of DHSC, NIHR and UK NSC colleagues into TRANSFORM as it moves from stage 1 to stage 2. The trial has been designed to be adaptable, and we look forward to working collectively to explore any opportunities to leverage the work that has gone into TRANSFORM to make bigger or faster progress for men.
	Any other views – Active Surveillance	We strongly believe active surveillance plays a crucial role in the reduction of overtreatment in men with early, low-risk prostate cancer and will be a key part of the quality assured screening pathway in future. Our research has highlighted huge variations in how surveillance is done in practice, and deviation away from current NICE guidelines (NG131). There is good evidence that well-structured active surveillance, including patient education, can support uptake and compliance. There should be a concerted effort by experts and key stakeholders, including DHSC, NICE, UK NSC, Prostate Cancer UK and the NHS to address variation and establish standardised active surveillance protocols so that they are fit for purpose and can be included in future screening pathways.
UK NSC Cover sheet, section 2.1. Concern with PSA testing, p.2	Terminology describing the PSA test as 'not very reliable'.	We wanted to provide some feedback on some of the concerns that men have shared with our Supporter Care and Specialist Nurse teams following the publication of the UK NSC draft recommendations. The public narrative that resulted from the UK NSC announcement in November was that the PSA test was 'not a very good test'. e.g. the cover sheet describes the test as being 'not very reliable'. We are seeing the negative consequences of this language in our contacts from men - including several men diagnosed with prostate cancer who have been advised by their clinical team to go on active surveillance, expressing concerns as their monitoring would mostly be done via the PSA test - and they had heard it was 'not very reliable'. It is important that language about the PSA test recognises that it is a very good

		test for monitoring men post diagnosis, in addition to setting out its limitations in the pre-diagnostic stage. Prostate Cancer UK can support the UK NSC going forwards on messaging relating to the PSA test, to ensure men aren't left confused or worried.
	Any other views – quality assurance	Our statistical modelling shows that deaths from prostate cancer will increase regardless of whether an organised screening programme is implemented or not. To improve the quality of life of men diagnosed with prostate cancer and reduce mortality, we formally request the hugely variable treatment pathway in England to undergo an immediate, formal quality assurance process to further reduce regional, racial and socio-economic inequities highlighted from the most recent National Prostate Cancer Audit data.
	Any other views – update PCRMP	Whilst this review (with the notable exceptions outlined above) has provided a comprehensive overview of the evidence around screening, it has not considered the current status quo and the extent to which it is resulting in both over and undertesting of men. The evidence is clear that the current outdated guidelines (PCRMP) add further confusion to the broader challenges for early diagnosis.^{1,11} It is essential that the guidelines are overhauled to recognise the latest evidence of both clearer pros (PSA testing reduces prostate cancer mortality) and cons (around half of diagnoses are for a disease that would not have killed if left undetected). There must then be a considered approach to closing health inequities through an early detection programme which equitably provides all men with tailored information about their own risk, their risks of harm and the chance of benefit associated with PSA testing. That work is urgently needed now. Longer term, we request that the UK NSC continues to engage in a timely manner with Prostate Cancer UK and with other experts bringing forward relevant, high quality peer reviewed evidence (from trials and from high quality real world evidence studies) to reduce data uncertainties in the current model and continue to assess whether population wide, or targeted screening for prostate cancer provides a safe, effective way to reduce the number of men who die or are harmed because of a late diagnosis of prostate cancer.

References

1. Collins KK, Oke JL, Virdee PS, Perera R, Nicholson BD. Prostate specific antigen retesting intervals and trends in England: population based cohort study. BMJ. 2025 Oct 8;391:e083800.

2. Sundi D, Kryvenko ON, Carter HB, Ross AE, Epstein JI, Schaeffer EM. Pathological examination of radical prostatectomy specimens in men with very low risk disease at biopsy reveals distinct zonal distribution of cancer in black American men. *J Urol*. 2014 Jan;191(1):60–7.
3. Navarro S, Hu X, Mejia A, Ochoa CY, Pickering TA, Ballas L, et al. Racial/ethnic disparities in patient experiences with care and Gleason score at diagnosis of prostate cancer: a SEER-CAHPS study. *Cancer Causes Control*. 2022 Apr;33(4):601–12.
4. Klebaner D, Courtney PT, Garraway IP, Einck J, Kumar A, Martinez ME, et al. Association of Health-Care System With Prostate Cancer-Specific Mortality in African American and Non-Hispanic White Men. *J Natl Cancer Inst*. 2021 Apr 23;113(10):1343–51.
5. Leapman MS, Freedland SJ, Aronson WJ, Kane CJ, Terris MK, Walker K, et al. Pathological and Biochemical Outcomes among African-American and Caucasian Men with Low Risk Prostate Cancer in the SEARCH Database: Implications for Active Surveillance Candidacy. *J Urol*. 2016 Nov;196(5):1408–14.
6. Taksler GB, Keating NL, Cutler DM. Explaining racial differences in prostate cancer mortality. *Cancer*. 2012 Sep 1;118(17):4280–9.
7. Freeman VL, Durazo-Arvizu R, Arozullah AM, Keys LC. Determinants of mortality following a diagnosis of prostate cancer in Veterans Affairs and private sector health care systems. *Am J Public Health*. 2003 Oct;93(10):1706–12.
8. Freedland SJ, Sandin R, Sah J, Emir B, Mu Q, Ratiu A, et al. Treatment patterns and survival in metastatic castration-sensitive prostate cancer in the US Veterans Health Administration. *Cancer Med*. 2021 Dec;10(23):8570–80.
9. Effect of healthcare system on prostate cancer-specific mortality in African American and non-Hispanic white men. | *Journal of Clinical Oncology* [Internet]. [cited 2026 Feb 4]. Available from: https://ascopubs.org/doi/10.1200/JCO.2021.39.6_suppl.23
10. Merriel SWD, Pocock L, Gilbert E, Creavin S, Walter FM, Spencer A, et al. Systematic review and meta-analysis of the diagnostic accuracy of prostate-specific antigen (PSA) for the detection of prostate cancer in symptomatic patients. *BMC Med*. 2022 Feb 7;20(1):54.
11. Vickers A, O'Brien F, Montorsi F, Galvin D, Bratt O, Carlsson S, et al. Current policies on early detection of prostate cancer create over-diagnosis and inequity with minimal benefit. *BMJ*. 2023 May 17;381:e071082.

Please return your completed form to the UK NSC Inbox by 11.59pm GMT on 20 February 2026.

S41			I support not offering Prostate screening until a better test is available. However, the current situation where GPs are instructed to offer it to patients who want it is also unsatisfactory as there are so many groups (charities, celebrities, politicians) telling people to get a test that they often don't believe the actual evidence that there is no or minimal benefit from screening and it is likely to cause harm. PSA testing should be reserved for men with symptoms, following a proper assessment.
S42	DESMOND GEORGE POWE	Friends & Bredrins Prostate Cancer Support Charity	Online Response to the UK National Screening Committee's recommendations. A fully referenced more comprehensive response is available on request from Dr Des Powe PhD, ***** We wish to respond to the UK NSC's call for views concerning the 'Next Steps' document (page 6, Screening for prostate cancer). It addresses: (1) Whether the evidence and data used in the model are appropriate (2) Whether the conclusions drawn from the evidence, data and model are appropriate, in particular: * whether targeted screening in men with higher genetic risk should be pursued? * towards this end, which questions might be addressed by further evidence synthesis work such as reviews and modelling * whether a strategy focusing on genetic risk should include men with BRCA1 and -2 variants or just BRCA2 variants * how research and evaluation might help develop and define a screening strategy based on genetic risk 1) UK NSC: Whether the evidence and data used in the model are appropriate. RESPONSE: Could more data have been sourced for modelling Black men with prostate cancer? a) US African Americans and African Caribbean men may share a common West African ancestry UK NSC acknowledge the lack of strong evidence from large trials about the harms and benefits of over-diagnosis with consequent over-treatment in UK Black men (1). The lack of data concerning prostate cancer in Black African/Caribbean men is a contributory factor for prostate cancer health inequity affecting this population. UK NSC state of the previously published data that much relates to US studies involving Black African American men. Even so, the UK population and UK

		Caribbean men will share a common ancestry due to the trans-Atlantic slavery legacy. Could US-based study data have been used for modelling purposes? What evidence is there to suggest US data is not suitable? b) Utilisation of UK based NHS and GP datasets If UK NSC only wanted to use UK-based data in modelling targeted PSA screening for UK Black men, could they have accessed datasets from the NHS National Disease Registration Service (NDRS)(2) and GP (Clinical Practice Research Datalink (CPRD)) to obtain data for modelling? From these datasets UK NSC could identify the prevalence of BRCA1 and BRCA2 variants and its association with tumour aggressiveness in UK Black men because they contain accurate figures for cancer susceptibility genes (CSG; BRCA?), incidence, prevalence, demographics (including ethnicity) and geography. The primary purpose of the NHS NDRS data repository is to support service planning and ensure health and treatment equity. Failure to use this data risks missing men within the high-risk Black population that are susceptible to developing aggressive prostate cancer requiring early treatment intervention. c) Is variant BRCA gene expression increased in the UK Black population? If so, could an existing NHS programme for BRCA screening be used to accommodate UK Black patients to identify deleterious BRCA mutations? Hereditary prostate cancer accounts for 5-10% (3) of newly diagnosed prostate cancer, with BRCA2 being among the most frequent pathogenic variant (PV) within the DNA Damage Repair gene class (4,5). The prevalence of BRCA gene mutation in the UK population varies, but a frequency of 1:250 to 1:400 is reported, but the prevalence is as high as 1:40 in the UK Jewish population (6,7). Variant BRCA2 gene carriers have double to five times the risk of developing aggressive (high Gleason grade) prostate cancer compared to the general population (8). Real World Evidence (RWE) cancer data is collected in a repository administered by The NHS National Disease Registration Service (NDRS) (2). Data in this resource has identified a 2.1% prevalence of the cancer susceptibility gene BRCA in the UK Jewish population. Consequently, the NHS Jewish BRCA Testing Programme (9) was established and between 2023-25 more than 11,000 patient saliva samples have been analysed for BRCA DNA. Deleterious BRCA expression is associated with increased risk of developing breast, ovarian and prostate cancer. Increased BRCA prevalence is also identified in Black West African women with breast cancer. A meta-analysis study reported 45% Black West African women (compared to 10-15% White European women) develop aggressive breast cancer, at earlier age, with a 'triple negative breast cancer' (TNBC) phenotype (10). BRCA

		mutations are associated with TNBC, with BRCA1 showing a stronger association (11). Black Caribbean men commonly have West African ancestry due to a historic legacy of the trans-Atlantic slave trade. The UK NSC state the prevalence of BRCA1 and BRCA2 in the UK Black population is unknown and, because the available data emanates from US studies of the African American population, the data was not used. However, Kanamaya et al identified a BRCA2 prevalence of 1.92% in Black African American men, remarkably similar to that identified in the UK Jewish population (2.1%) (12,7). In another study, BRCA2 prevalence was shown to be higher, approaching 5% (13). Aggressive prostate and breast cancer characteristically develop at younger age in Black men and women, respectively. 2) UK NSC: Whether the conclusions drawn from the evidence, data and model are appropriate? PROPOSAL: We propose targeted BRCA genetic screening in UK Black men age 40-61 could identify men most at risk of developing aggressive prostate cancer requiring early treatment. Implementation of this proposal could feasibly reduce prostate cancer health inequity. UK NSC concede a lack of significant data from large clinical trials for the UK Black population. We propose the UK NSC to consider recommending the proposal of targeted BRCA genetic screening for Black men age 40-61, as an extension to the existing NHS Jewish BRCA Testing Programme. This will contribute valuable Real World Evidence data to the NHS National Diagnosis Registration Service, needed for service planning and achieving equity in future genetic testing and treatment pathways. In addition, it will address UK NSC's question concerning the significance of BRCA1 versus BRCA2 variant expression, and their respective association with prostate cancer development and progression. Black men with African ancestry, including Caribbean men, have double the risk (1:4) of developing prostate cancer and have increased mortality rates compared to White (1:8) and Asian (1:12) men. High PSA levels in Black men are more likely to correlate with prostate cancer diagnosis (14), and yet paradoxically a UK report found Black men are less likely to receive life-saving cancer treatment compared to men with White ethnicity (15). UK NSC did not model if testing for the BRCA gene itself is cost-effective. Here, we ask UK NSC to perform such a costing model for Black men age 40-61 based on the NHS Jewish BRCA Testing Programme. The cost to the NHS of running the NHS Jewish BRCA Testing Programme could not be identified. However, the NSC concludes 'screening of Black men has higher probability of cost-effectiveness in probabilistic analyses than screening men of general risk,' because of their high risk. Furthermore, the children (sons and

		daughters) of men identified with BRCA variants would be eligible for BRCA screening and counselling due to their increased risk of cancer development. This is in agreement with NHS National Diagnosis Registration Service objectives, and could facilitate early-stage cancer prevention and minimise need for treatment. It would benefit patients and impact materially on NHS economies. We urge the UK NSC to model the population size of Black men (African, Caribbean and mixed ethnicity) age 40-61 to be considered for BRCA1 & 2 variant genetic screening. Based on 2021 Census data, it is estimated that a modest 406,220 UK/Welsh Black men age 40-60 would require initial BRCA screening, resulting in a potential 2,843 – 7,108 (2-5% BRCA prevalence) number of BRCA carriers requiring annual (16) follow-up PSA blood testing. From this group of patients, it is estimated that 995 – 2,488 men will subsequently develop aggressive prostate cancer needing treatment, based on a 35% development rate (17). CONCLUSION We call on the UK NSC to run further models to determine the benefits and harm of extending BRCA1 and BRCA-2 genetic screening to UK's Black African and Caribbean men age 40-61, based on a similar model to that used in the NHS Jewish BRCA Testing Programme. POSSIBLE BENEFITS: * Increased numbers of Black men offered BRCA screening and identified with oncogenic BRCA variants * Increased numbers of high-risk BRCA positive patients PSA screened for prostate cancer, correlating with earlier detection and treatment * Earlier identification of possible increased cancer risk to sons and daughters, facilitating screening and earlier treatment * Commitment to tackle health inequity in the UK Black population * Providing Real World Evidence BRCA data to the NHS National Diagnosis Registration Service, assisting future treatment planning Adoption of the proposal provides an NHS plan of what can be done now to reduce mortality and harmful side-effects in the high-risk group of UK Black men prior to recommendations from the TRANSFORM clinical trial for prostate cancer. These BRCA variant positive patients characteristically develop high grade aggressive prostate cancer requiring immediate treatment. UK NSC did not perform a costing model for BRCA testing in the UK Black population but concludes 'screening of Black men has

		higher probability of cost-effectiveness in probabilistic analyses than screening men of general risk.' This is because male mutant BRCA carriers have a strong association with development of aggressive prostate cancer requiring treatment, thereby reducing the risk of over-treatment. The benefits of such an approach are increased because it provides a procedure for identifying future BRCA carriers in the children of affected men. Subsequently, this could reduce health disparities seen in the Black population who are susceptible and at increased risk of prostate, breast, and ovarian cancer. A protocol for BRCA genetic testing is established: The NHS BRCA Jewish Testing Programme. A similar but separate programme for targeted BRCA screening of Black men age 40-61 could be modelled on this, or the existing programme could be scaled up to accommodate the additional cases. REFERENCES 1 SCHARR report prepared for the UK National Screening Committee. Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk. 2025 University of Sheffield. 2 National Disease Registration Service – NDRS. https://digital.nhs.uk/ndrs 3 Genetic susceptibilities to prostate cancer. Cancel-Tassin G & Cussenot O. 2005; British Journal of Urology International, 96, 1380–1385. 4 Germline Genetics of Prostate Cancer: Prevalence of Risk Variants and Clinical Implications for Disease Management. Doan DK et al. Cancers; 2021; 13, 2154. 5 Updates in Prostate Cancer Research and Screening in Men at Genetically Higher Risk. Bancroft EK et al. Current Genetic Medicine Reports. 2021; 9:47–58. 6 Prostate Cancer UK: BRCA. https://prostatecanceruk.org/about-us/news-and-views/2025/11/brca-genes-and-prostate-cancer 7 Macmillan, UK. https://www.macmillan.org.uk/cancer-information-and-support/worried-about-cancer/causes-and-risk-factors/brca-gene 8 Prostate Cancer Risks for Male BRCA1 and BRCA2 Mutation Carriers: A Prospective Cohort Study. Nyberg T et al. Eur. Urol. 2020; 77, 24–35. 9 NHS Jewish BRCA Testing Programme. https://www.england.nhs.uk/2025/01/hundreds-of-people-at-increased-cancer-risk-identified-by-new-nhs-brca-testing-programme

			10 Triple-negative breast cancer prevalence in Africa: a systematic review and meta-analysis. Hercules SM et al. British Medical Journal Open. 2022;12(5). bmjopen.bmj.com/content/12/5/e055735 11 Triple-Negative Breast Cancer Risk Genes Identified by Multigene Hereditary Cancer Panel Testing. Shimelis H et al. Journal of the National Cancer Institute. 2018; 110(8), 855–862. 12 Clinical and Functional Analyses of an African-ancestry Gain-of-function HOXB13 Variant Implicated in Aggressive Prostate Cancer. Kanayama M et al. European Urology Oncology. 2024; 7(4), 751-759. 13 Prevalence of germline variants in prostate cancer and implications for current genetic testing guidelines. Nicolosi P et al. JMAOncol. 2019; 5,523–528. 14 Association between patient ethnicity and prostate cancer diagnosis following a prostate-specific antigen test: a cohort study of 730,000 men in primary care in the UK. Down L. 2024; BMC Medicine 22:82. https://doi.org/10.1186/s12916-024-03283-5 15 National Prostate Cancer audit 2024 (pub 2025). www.natcan.org.uk/wpcontent/uploads/2025/10/NPCA-SotN-2025.pdf 16 The Institute of Cancer Research. https://www.icr.ac.uk/about-us/icr-news/detail/men-with-brca1-and-brca2-gene-mutations-should-get-annual-prostate-cancer-screening 17 Cancer Research UK. Cancerresearchuk.org
S43	Janine Aldridge	The Royal College of Pathologists	With prostate cancer being one of the most common cancers affecting men globally, there is need for a multi-pronged approach to tackling a disease that affects 63,000+ men in the UK alone per year. The ethnic differences in prostate cancer mortality and morbidity are a concern. Black men face a higher rate of diagnosis and high grade disease (which means a tumour is likely to grow and spread faster). Improving prostate cancer outcomes without triggering a wave of overdiagnosis requires a nuanced approach. The College supports the introduction, in the future, of smarter screening of high risk groups, better biopsy strategies, and AI-augmented diagnosis. These need to be implemented with care. Pathologists are vital for almost every aspect of patient care, from diagnostic testing and treatment advice to using cutting-edge genetic technologies and guiding risk-stratified management. Their workload must be respected and supported with staffing, technology, and training.

		To truly improve men's health without fuelling overdiagnosis we recommend: • Focus screening efforts on high-risk groups, such as black men, those with BRCA1/2 mutations and those with a family history of the disease, rather than blanket screening. • Implement MRI diagnostic pathways, ensuring biopsies are only taken when imaging suggests clinically significant disease. • Invest in training and retaining histopathologists and expand the use of digital pathology to reduce bottlenecks. • Use pathology data to refine prognostic models, incorporating histological, molecular, and imaging features to personalise treatment. • Promote active surveillance for low-risk disease, relying on clear criteria and regular monitoring rather than immediate treatment. • Encourage trials such as TRANSFORM to examine the utility of these newer techniques rather than blanket adoption. Stratified screening and risk-based approaches Current discussions around prostate cancer screening in Europe and the UK centre on risk-stratified approaches. Large-scale studies, such as the European Randomized Study of Screening for Prostate Cancer (ERSPC), have shown that PSA screening can reduce prostate cancer mortality by around 20%, but at the cost of high overdiagnosis and overtreatment. Histopathology can support better stratification by integrating emerging diagnostic tools: • MRI-targeted biopsies, rather than random systematic sampling, are improving diagnostic yield for significant cancer and reducing unnecessary biopsies. • Molecular biomarkers and genomic classifiers (e.g., Decipher, Oncotype DX) may help predict tumour behaviour and guide active surveillance versus intervention. Implementing these tools at scale, however, introduces workload and training demands on pathology departments. The rise in prostate biopsies, especially with the introduction of pre-biopsy MRI and fusion-targeted biopsies, has increased the complexity and volume of cases that pathologists face. The College workforce census 2025 found that 47% of pathologists are aged 50 and over, suggesting a potential retirement cliff edge within the next decade. 78% of pathologists do not believe current staffing levels are adequate to ensure long-term stability of pathology services and to meet growing demand. Simultaneously,

		prostate cancer incidence continues to increase, and the push for early detection intensifies. Digital pathology and AI solutions offer some promise. AI tools trained to detect and grade prostate cancer are being piloted and validated, including solutions like Paige Prostate and Ibex, which have demonstrated non-inferiority to human pathologists in detecting malignancy and grading. But adoption is still slow, and regulatory frameworks and trust remain barriers. The role of pathologists in diagnosis and management Histopathology is central to the diagnosis and grading of prostate cancer. Following a prostate biopsy – often triggered by raised PSA (Prostate-Specific Antigen) levels – pathologists assess the tissue, assign Gleason scores (a system to evaluate the aggressiveness of prostate cancer), and determine prognostic grade groups. These grades guide treatment, from active surveillance to radical intervention. Not all prostate cancers behave in a predictable manner. Many are characterised by slow growth and would not cause clinical harm during a man's lifetime. Early diagnosis may not alter disease course (the lag time) and thus men may suffer unnecessary harm in terms of earlier surgery and psychological harm from the knowledge of a cancer diagnosis. Histopathology also has a pivotal role in distinguishing between clinically significant and insignificant disease. Challenges of overdiagnosis and overtreatment Overdiagnosis is a critical issue. PSA testing, while simple and accessible, lacks specificity. It detects many slow-growing tumours that would never progress to symptomatic or lethal disease. As a result, many men undergo biopsies and even radical treatments that may have long-term side effects – such as incontinence and impotence – without survival benefit. Autopsy studies suggest that incidental prostate cancer is found in up to 70% of men over 80, yet most of these men die with, not from, the disease (Sakr et al., 1996). Thus, any public health strategy to reduce mortality must avoid increasing detection of these slow growth cases. We need to ensure that more men at high risk of clinically significant prostate cancer are diagnosed early. However, the diagnosis of insignificant cancers that never become a danger to men's lives is a great concern. There are trials underway such as TRANSFORM to help this. Pathology input in major clinical trials for screening studies has not been funded or accounted and there has not been any discussion or planning for the anticipated increase in pathology work load that

			this will create. With most trusts and management undergoing staff shortages and recruitment freezes, the decision to screen or not screen should come with responsibility and reassurance of adequate and appropriate staffing of specialist teams from managerial structures. If overdiagnosis leads to large number of patients with clinically insignificant disease on active surveillance, then this could affect availability of scans and clinic appointments for other patients with clinically significant disease (not just prostate cancer). This would be particularly true if blanket screening (which fortunately RCPATH and the screening committee do NOT recommend) programme was adopted. Screening for cancer is a highly complex activity which risks causing harm as well as benefits. Often the harms of late diagnosis are seen clearly while those of overdiagnosis are not well represented. We hope that the cutting edge UK trials such as TRANSFORM will shed further light on this decision which should be kept under review.
S44		Houston Kiltmakers	Needs to get done
S45			I am currently receiving treatment for prostate cancer that was picked up by a PSA test with no symptoms prior. I am told that the cancer was spreading rapidly into lymph system. Had my GP not authorised an annual voluntary PSA test the cancer would have developed such that treatment could not be effective. Your decision to restrict testing is foolhardy and shortsighted. PLEASE RECONSIDER.
S46			Whilst I value all attempts to to reduce cancer deaths I wonder if we have adequate screening tools at our fingertips to do this currently in a meaningful way. Regarding whether targeted screening in men with higher genetic risk should be pursued my concern is how many men know they are BRCA 1/2 and if men now ask for this screening are we set up and prepared? Based on the evidence presented in the UK NSC review, I don't think that a national population screening programme for prostate cancer should not be introduced at this time. The findings show that PSA-based screening does not demonstrate a clear mortality benefit and continues to carry significant risk of overdiagnosis, unnecessary biopsies, and associated harms. While emerging tools such as mpMRI and risk stratified approaches are promising, at present they lack the consistency required for population screening. Commissioning priorities should probably remain focused on ensuring high quality opportunistic PSA testing, strengthening

			primary care counselling and referral pathways, and maintaining diagnostic capacity within imaging and urology services. Ultimately, continued research, particularly into targeted screening for high risk groups, will be essential to inform any future policy change.
S47	Ola Steinberg	A3p Biomedical	We at A3P Biomedical were surprised and concerned to note that the draft report from the UK National Screening Committee (UK NSC) indicates that the Stockholm3 test was not included in the screening evaluation. Stockholm3 has been evaluated in more than 90,000 men across Europe and the United States and is described in more than 30 peer-reviewed scientific publications. Data from these published studies indicate that Stockholm3 has the potential to detect clinically significant prostate cancer at an earlier stage than current diagnostic pathways, and may, over time, contribute to a stage shift toward more treatable disease, with the possibility of reducing prostate cancer mortality. As a reflex biomarker test intended to improve risk stratification following PSA testing, Stockholm3 represents a potentially relevant component of contemporary screening and diagnostic pathways. To ensure that the necessary data were available for the modelling work, A3P coordinated and facilitated a data-sharing agreement between SCHARR and the Karolinska Institute in Sweden, which holds the underlying research data. Individual-level data were subsequently transferred to SCHARR in order to conduct the analysis. On this basis, we understood that the relevant data required to support modelling of Stockholm3 had been made available to the analysis team. In May 2025 we were informed by SCHARR that that Stockholm3 would not be included in the modelling, following a decision that the UK NSC would not proceed with its inclusion. As we understood it, the stated rationale was that the requested data were not in the public domain. This was unexpected given that the primary studies have been published in high-ranking peer-reviewed scientific journals, including The Lancet Oncology and the Journal of Clinical Oncology, and that individual-level data had been shared directly with the modelling team via the Karolinska Institute. We came to understand from the SCHARR's published report that concerns were raised regarding the status of certain data as not being in the public domain, including conditions relating to publication embargoes. We recognise that such arrangements can arise where research teams intend to publish analyses from primary datasets. However, the use of confidential or non-public data under controlled access arrangements is common in health technology and diagnostic evaluation processes, where analyses may be conducted using data that are not yet publicly available,

			with appropriate handling of commercial or academic confidentiality and redaction of sensitive material in public reporting. In this context, we would welcome clarification regarding the UK NSC's approach to the use of non-public or embargoed datasets within modelling work, and the evidentiary or transparency criteria that determine whether such data can be incorporated into screening evaluations. Greater clarity on this point would help ensure that emerging diagnostic and risk-stratification tools can be assessed consistently where relevant data exist but are subject to standard scientific publication controls. As Stockholm3 is a test designed to support more precise risk stratification following PSA, its omission from the UK NSC's current review process may limit the ability of the modelling to evaluate the full range of relevant diagnostic strategies and screening pathways currently available or under development. Naturally, it is in our interest to ensure that all relevant data are shared to support robust modelling efforts and, ultimately, to contribute to reducing prostate cancer mortality in the UK. We remain fully committed to constructive collaboration and to providing any additional clarification or documentation that may assist the Committee in its evaluation, including for Stockholm3. We would be pleased to provide any further information that may support consideration of Stockholm3 in future modelling updates or sensitivity analyses, should this be helpful.
S48		Norfolk & Waveney Prostate cancer support group	I have now lived with prostate cancer for 20yrs I have to have a psa test every 6 months. My father died from prostate cancer by the time he was given a psa test it was to late! My brother now has prostate problems & needs a psa test every 6 months! So I would like to know how you feel about living with this disease & not knowing when you are going to die! just because you can not get a simple blood test!! Please Please sort this out for us men to have a life without worry!
S49	Katie Snape, Terri McVeigh	UK Cancer Genetics Group	Dear team UKCGG response attached herewith for your consideration – along with the statement shared with our members and our current guidelines – which are dynamic and iterative and can be adjusted as/if required. The statement includes criteria for germline genetic testing as well if helpful. Very many thanks for involving us in these important discussions. Warm regards Dr Terri McVeigh Consultant Clinical Geneticist

			The Royal Marsden NHS Foundation Trust

BRCA2 Germline Pathogenic Variant Carriers

Management Guidelines for Healthcare Professionals

Female BRCA2 Pathogenic Variant (GPV) carrier age-dependent cumulative cancer risks (95% confidence intervals) *			Cumulative risk for contralateral breast cancer by time since first breast cancer *	
Age (years)	Breast cancer (Note population risk to age 80 approx 10%*)	Tubo-ovarian cancer (Note population risk to age 80 approx 1.5%*)	≤5 years	8% (6-12%)
21-30	4% (2-9%)	-	>5-10 years	16% (12-21%)
31-40	13% (9-19%)	<0.5%	>10-15 years	21% (17-26%)
41-50	35% (29-41%)	1-2%	>15-20 years	26% (20-33%)
51-60	53% (46-59%)	7% (4-11%)	>20-43 years	65% (25-98%)
61-70	61% (55-68%)	15% (10-23%)	Patient resources ➤ A Beginner’s Guide to <i>BRCA1</i> and <i>BRCA2</i> (patientinfo.library.royalmarsden.nhs.uk) ➤ breastcancer.org “Someone like me” https://breastcancer.org/information-support/support-you/someone-me-telephone-support ➤ coppafeel.org ➤ https://www.macmillan.org.uk/cancer-information-and-support/worried-about-cancer/causes-and-risk-factors/brca-gene	
71-80	69% (61-77%)	17% (11-25%)†		
†Risk of OC >70 is likely underestimated by referenced study, see management below and FAQ			Notes It is important to manage patients in the context of their family history of cancer. Individualised risk estimates available from https://canrisk.org/ should be used instead of the general risk estimates wherever possible.*See FAQ document for further information and references.	
Other cancers	BRCA2 GPV carrier risk (95% confidence interval)	Population risk*		
Male breast cancer	4% (2-8%) by age 80	Rare		
Prostate cancer [†] Adjusted risk for screening effect, please see FAQ for unadjusted figures	41% (22-54%) by age 85 [†] (Nyberg et al, 2020) 27% (21-35%) by age 80 (Li et al, 2022)	Approx 12% by age 80		
Pancreatic cancer*	Male: Approx 4-5% by age 80 Female: Approx 2% by age 80	Approx 1% by age 80 Up to 1% by age 80		
No significant association consistently found for other cancers.				
Management recommendations				
Screening	Breast: Annual MRI breast from 25 to <40 years*. MRI + mammography from 40 to <51 years. Mammography +/- MRI from 51 to <71 years. Screening in individuals over the age of 71 is available upon patient request. Screening is available to those at 50% risk from age 25 to 30 (to age 50) based on personalised risk assessment. For women with previous breast cancer, as above if residual breast tissue.			
	Tubo-ovarian: Not currently recommended. No evidence based screening programme.			
	Prostate: Annual PSA from 40 with onward referral if PSA >3.0ng/ml.			
	Pancreatic: Not currently recommended outside of research. Consider the EUROPAC study.			
Risk-reducing surgery	Breast: Discuss bilateral mastectomy. Individualised* assessment recommended.			
	Tubo-ovarian: Discuss risk-reducing bilateral salpingo-oophorectomy (RRBSO), offer when childbearing is complete and no earlier than age 40 – 45. Due to continued risk of ovarian cancer at older ages, RRBSO should be discussed with all women, with consideration of general fitness/co-morbidities.			
Hormone replacement	Women undergoing RRBSO with no previous history of breast cancer, should consider taking HRT until 50. For women with previous breast cancer, individualised discussion with Oncologist is advised.			
Chemoprevention	Discuss the pros and cons of chemoprevention. Can be offered if no contraindications. No studies have been conducted to date on efficacy of chemoprevention in BRCA2 GPV carriers.			
Cancer management	BRCA2 GPV carrier status may influence management of current cancers – ensure oncologist aware of carrier status and manage as part of a multidisciplinary team. Consider long term prognosis / competing risks prior to considering risk-reducing surgery.			
Lifestyle information	-Provide information about regular self-breast examination and ovarian cancer symptom awareness. -Provide information on the benefits of smoking cessation, minimising alcohol intake and maintaining a healthy weight to lower the chance of getting cancer. -Contraception: use of oral contraceptive pill (OCP) is not contraindicated, but requires informed discussion and consideration of alternative forms of contraception*.			
Family matters	-Refer to clinical genetics to facilitate genetic testing in at-risk family members. -Refer to clinical genetics for discussions on reproductive options.			
Psychological	-Consider referral to clinical psychology support services if appropriate.			

* Please see FAQ for more information



UK Cancer Genetics Group Statement on the Draft National Screening Committee (NSC) proposal on prostate cancer screening

We note the draft recommendations of the National Screening Committee (NSC) to offer prostate cancer screening to men with a confirmed *BRCA1* or *BRCA2* variant every 2 years between the ages of 45-61([available here](#)). We note that this draft recommendation has entered a formal consultation period, and we have initiated discussions with our clinical, academic community and patient/public representatives to have further conversations, review the evidence and data and submit a formal response.

In the interim period we recommend that individuals who are carriers of *BRCA1/BRCA2* or other genes where there is evidence of association with prostate cancer risk follow our national agreed consensus management guidelines available on our [website](#):

<https://www.ukcgg.org/information-education/ukcgg-leaflets-and-guidelines/>

NHS information regarding PSA testing is available at <https://www.nhs.uk/tests-and-treatments/psa-test/>.

We strongly support the proposal to offer prostate cancer screening to *BRCA2* carriers where the evidence is clear that men develop younger onset, aggressive prostate cancers for which the benefit of screening can be reasonably anticipated to outweigh the harm. *BRCA2* carriers have an elevated risk of developing prostate cancer comparative to other at-risk groups (RR=2.22 (95% CI: 1.63 - 3.03) 27% to age 80¹). We welcome the recommendation from the UK NSC which will enable development and implementation of national infrastructure to safely deliver a standardised and equitable screening programme, with systems for recall, assessment and management. UKCGG are working with the UK NSC, National Disease Registration Service (NDRS), NHS England and the National Inherited Cancer Predisposition Register (NICPR) to support development of pathways to identify carriers and facilitate streamlined entry into a future screening programme. We will work with Devolved Nations as required to support their own programmes of work in this area.

We understand that there are conflicting views in our community about the inclusion of *BRCA1*, and exclusion of other monogenic causes of increased prostate cancer risk, such as *MSH2*-associated Lynch Syndrome. We also acknowledge the conflicting views around inclusion or exclusion of other groups potentially at elevated risk.

We note that UK NSC were not asked to review *MSH2* or other genes at the inception of this process and that it was out of scope. We also note that the [TRANSFORM trial](#) will provide evidence within 3 years around screening in other at-risk groups which will add to the body of evidence and debate around benefit and harms of screening. ***We will continue our discussions around these topics and circulate our formal response in due course.***

We also wish to highlight the avenues for germline genetic testing that are already available to people with prostate cancer through the [National Genomics Test Directories](#). The cancer test directory recommends somatic testing (testing of DNA from the prostate cancer) in affected individuals with metastatic castration-resistant prostate cancer that would be potentially eligible for NICE approved PARP inhibitor (M218.1). Germline genetic testing may be indicated in such patients in the following circumstances:

- Individuals in whom a likely pathogenic/pathogenic *BRCA1/BRCA2* variant of suspected germline (inherited) origin is identified in tumour DNA should be offered a follow up germline test to confirm or exclude this.
- Where somatic testing is unsuccessful or impossible, eligible patients may be offered germline *BRCA1* and *BRCA2* testing (R444.2).
- Patients fulfilling eligibility for diagnostic panel-based germline genetic testing (R430) as outlined below.

The Rare and Inherited Disease Test Directory recommends germline genetic testing of a panel of genes (R430), including *BRCA1* and *BRCA2*, known to increase prostate cancer risk to individuals meeting relevant criteria.

R430 Testing Criteria:

- Individual diagnosed with prostate cancer <50 years
- Individual diagnosed with metastatic prostate cancer <60 years
- Individual with Ashkenazi Jewish ancestry and diagnosed with prostate cancer at any age
- Individual with ≥1 grandparent from Whalsay (Shetland) and diagnosed with prostate cancer at any age
- Individual diagnosed with prostate cancer with a CanRisk score of >10% and where they do not meet criteria for other inherited cancer predisposition panels (R208, R207 or R210)

Genetic testing may also be available through research studies according to study specific eligibility criteria.

People with a personal and/or family history of *BRCA1/BRCA2*-associated cancer(s) may wish to seek a formal family history assessment from their GP/family history service. We would suggest assessment is appropriate where the family history in close relatives includes at least one of the below

- Young onset prostate cancer (<60)
- Young breast cancer (<40)
- Young pancreatic cancer (<60)
- Ovarian cancer
- >1 close relative with prostate, breast, ovarian, pancreatic cancer (under 60)
- >2 close relatives with prostate, breast, ovarian, pancreatic cancer (under 70)

Assessment will not necessarily result in genetic testing but will allow advice and guidance based on the unique personal and family history provided. **Where affected family members are alive, we would recommend they are referred in the first instance.**

Private genetic testing is also increasingly available. Individuals identified as carriers of a confirmed germline likely pathogenic/pathogenic *BRCA1/BRCA2* variant through testing in the private sector are also eligible for NHS referral to be added to the NICPR, as long as the test was undertaken on a sample representative of germline DNA, in an accredited laboratory and a full report can be provided at time of referral to NHS services.

References

¹ Li S, et al. Cancer Risks Associated With *BRCA1* and *BRCA2* Pathogenic Variants. J Clin Oncol. 2022 May 10;40(14):1529-1541. doi: 10.1200/JCO.21.02112. Epub 2022 Jan 25. PMID: 35077220; PMCID: PMC9084432.

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name:	Katie Snape/Terri McVeigh	Email address:	***** or *****
Organisation (if appropriate):	UK Cancer Genetics Group		
Role:	Chair/Secretary		
Do you consent to your name being published on the UK NSC website alongside your response?		Yes	
Section and / or page number	Text or issue to which comments relate	Comment <i>Please use a new row for each comment and add extra rows as required.</i>	
General	Benefits versus harms of prostate cancer screening	We would like to state that we know that undertaking a review of screening for prostate cancer is highly emotive and difficult. UKCGG is strongly aware that the requirements of a screening programme to identify aggressive prostate cancers which will cause death, whilst reducing the very serious and common harms to men from overdiagnosis and over-treatment, (such as bladder incontinence and impotence), if they have an indolent, non-fatal prostate cancer is a very tricky juggling act. We note the TRANSFORM trial has commenced and note the committee recommendation to review the evidence from this trial in a timely and agile way to update and adjust these current recommendations. We feel this is appropriate and very welcome and we look forward to reviewing new guidelines in the relevant timeframes as evidence from TRANSFORM becomes available. We are supportive of the approach to not escalate and scale more broadly to other enhanced risk groups until we have extremely robust evidence on the benefits of screening against the harms.	
Page 5,Section 4.3 (Evidence review coversheet) and SCHARR report phase 3 Prostate cancer modelling,	Targeted screening for <i>BRCA1/BRCA2</i>	UKCGG strongly support the recommendation of screening for carriers of pathogenic variants <i>BRCA2</i> (hereafter known as " <i>BRCA2</i> carriers") and have been recommending this to men through our widely used national guidelines https://www.ukcgg.org/information-education/ukcgg-leaflets-and-guidelines/ This is a very welcome step for men with <i>BRCA2</i> germline pathogenic variants (GPVs), and will enable this cohort to be a pathfinder for the roll out and embedding of a national prostate cancer screening programme, so that any	

future decisions on scaling to other groups can be undertaken with evidence on the logistics and the successful implementation of a national screening programme for prostate cancer. We commend the committee for this decision to include *BRCA2* carriers for national screening. We note the value of the National Inherited Cancer Predisposition Register (NICPR) to facilitate entry of carriers into screening and are happy to support as required to develop national pathways and processes for our high risk *BRCA2* carriers.

We have concerns about the model for carriers of GPVs in *BRCA1*, considering risks associated with such variants are much lower. With respect to the model used for *BRCA1*: use of the Nyberg et al. (2022) paper for *BRCA1* risks is controversial. Neither the IMPACT study nor work by Li et al (2022) support this level of risk. This leaves the committee open to criticism that they have included *BRCA1* carriers at a level of risk for which they have excluded other men at equivalent levels of risk.

The danger of apparent inclusion of *BRCA1* because of overlapping phenotype with *BRCA2*, but without a clear scientific rationale with respect to prostate cancer risk and risk management, is that there is now an obvious inconsistency in the approach and use of available evidence for monogenic prostate cancer susceptibility.

Our main concern is that we feel it was illogical to include *BRCA1* in a national prostate cancer screening programme without considering other, higher-risk monogenic causes of enhanced genetic prostate cancer risk. This is particularly true for GPVs in the *MSH2*, which causes Lynch Syndrome, and for which there is now strong and high-quality evidence from the IMPACT Study for prostate cancer risk and association. Please could the committee explain why they have included *BRCA1*, and not *MSH2*, and whether and when they will look at the evidence for *MSH2* if they are going to make recommendations for monogenic carriers with enhanced prostate cancer risk.

We also note that as a result of these screening recommendations there will be great interest in getting tested for *BRCA2* (and other genes) to access screening. It would be helpful if the committee could make a statement to the effect that ~ only 1 in 400 men are *BRCA2* carriers and that GPVs in this gene mainly confer breast and ovarian cancer risk, such that diagnostic yield of testing is low in men without family history of such cancers. We do not recommend testing outside of the National Genomic Test Directory Eligibility criteria at the current time, but men with a known *BRCA2* variant in the family, or a strong family history of breast/ovarian/prostate/pancreatic cancers may wish to access assessment in the NHS. Other men should only access testing through ethically approved research studies.

Please return your completed form to the UK NSC Inbox UKNSC@dhsc.gov.uk by 11.59pm GMT on 20 February 2026.

S50	Chris Booth	CHAPS	Dear Team, I have pleasure in submitting our Response. Yours sincerely, Chris Booth, MBBS, FRCS.

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name:	Chris Booth	Email address:	*****
Organisation (if appropriate):	CHAPS		
Role:	Clinical Director		
Do you consent to your name being published on the UK NSC website alongside your response?		Yes	
Section and / or page number	Text or issue to which comments relate	Comment <i>Please use a new row for each comment and add extra rows as required.</i>	

Please return your completed form to the UK NSC Inbox UKNSC@dhsc.gov.uk by 11.59pm GMT on 20 February 2026.

I am a retired consultant urologist (Colchester 1984-2006) and with a career-long participation in NHS service development and care pathway integration, including the Cancer Services Collaborative and a series of community-based pilots for the NHS Modernisation Agency. Since 2014, I have been a leader in the charitable provision of risk-based, programmed Prostate Cancer (PCa) screening in the UK and am now on the UK APPG for PCa Screening and the Scientific Advisory Board of the EU PRAISE-U Programme. I am the author of the joint submission to the NSC from CHAPS, ORCHID, PROSTATE CANCER UK & TACKLE Prostate Cancer requesting a National Screening Programme for Prostate Cancer. I also represent a further 20 UK Charities that support this proposal.

My comments address 3 principal areas:

- The SCHARR Report
- The NSC Recommendation
- The Current Clinical Practice Issues

The SCHARR Report

Overall, the clinical picture provided by the SCHARR report is undermined by a lack of urological input, as evidenced in the Appendices. There is therefore a disconnect from current best practice and an over-dependence on outdated diagnostic practice.

The report does not adequately address the UK's high PCa mortality, late stage of presentation (49%) or the NHS aspiration to achieve the “75% by 2028” early-stage cancer diagnosis target.

Outdated and incorrect stage statistics are presented with little reference to contemporary National Prostate Cancer Audits (NPCA). For instance, the latest NPCA presentation stage statistics for T1 Low Risk disease is 8% and Grade Group 1 is 13% with an over-treatment rate of only 7% (National Prostate Cancer Audit State of the Nation Report October 2025, London). This bias then badly skews the SCHARR cost analysis.

NPCA statistics show that 40% of new diagnoses are in men aged 70-79 and 15% aged ≥80, even men in their 90s, as is permitted by the outdated Prostate Cancer Risk Management Programme (PCRMP) guidelines. This leads to over-diagnosis with no benefit and increases the likelihood of harm as a direct consequence of opportunistic testing under PCRMP's guidelines (www.gov.uk/government/publications/prostate-specific-antigen-testing-explanation-and-implementation/advising-well-men-about-the-psa-test-for-prostate-cancer-information-for-gps; PCRMP12/12/24) that are not addressed by SCHARR. A properly organised age-restricted programme would prevent this and greatly reduce costs.

Currently, 30% of men requesting PSA tests at CHAPS PCa screening events have moderate (25%) or severe (5%) LUTS. These symptoms, together with haematuria, erectile dysfunction and other clinical issues cited by PCRMP are rarely due to PCa and should be excluded from organised testing. Directing them down the appropriate diagnostic pathway would again reduce costs and improve clinical care.

SCHARR makes no reference to correcting the inequity of opportunistic screening. CHAPS statistics in Essex from 2022-2024 show a 3% PCa diagnostic rate in areas of deprivation compared with 1.4% in better off areas and nationally there is a clear north-south divide (<https://prostate-canceruk.org/about-us/news-and-views/2023/01/huge-north-south-divide-in-prostate-cancer-diagnosis>; accessed 10/2/26).

The NSC Recommendation

The recommendation to screen for rare BRCA gene variants affecting 3 in 1,000 men with only 1 in 1,000 developing aggressive PCa compared with PCa developing in 1 in 4 black men and men with a family history, runs counter to the fundamental principle of screening for an important, common health problem, not rarities. This NSC recommendation, if followed, will increase the current social inequity present within the system.

Current Clinical Practice Issues

The NSC recommendation does not address the problems caused by the current inconsistencies prevalent under PCrMP and NICE NG12 guidelines:

- Access to PSA tests is a postcode lottery with many GPs refusing PSA tests or advising to return when symptoms arise – too late if due to cancer!
- Inequity of access to PSA tests favouring the better educated and disadvantaging the socio-economically deprived.
- Opportunistic access to PSA tests has resulted in over-testing of elderly men at little risk and under-testing of younger men at higher risk.
- Over-diagnosis of PCa in elderly men.
- Failure to address lower PCa detection rates in deprived or marginalised groups.

The lack of coherent guidelines and lack of even minimal compliance by many GPs has left a vacuum at national level now being filled by a growing, unregulated market of off-the-shelf PSA tests of questionable quality for anyone to purchase.

All these factors call for the NSC to abandon its isolated, academic approach and provide leadership in turning the UK's disorganised, opportunistic system into an organised programme utilising the entirely adequate tools already at our disposal.

Conclusion

The current NSC proposal is medically, socially and financially unsound. It is based on flawed data and a narrow spectrum of urological opinion. It perpetuates a failed policy (PCrMP) that has been shown to lead to inequity, excess testing and over-diagnosis ([Collins KK et al. Prostate Specific Antigen Retesting Intervals and Trends in England: Population Based Cohort Study, BMJ 2025;391: 083800](#)).

Our recommendation is that the NSC urgently promotes the conversion of current disorganised, opportunistic testing to an organised, programmed screening service whilst supporting further trials and pragmatic, piloted service improvements.

S51	Jamie Hynes, Adrian Hayter	Royal College of General Practitioners	Dear UK NSC Team, Please find attached our comments for the Prostate Cancer Consultation. If you have any questions, feel free to get in touch. Best wishes, Saima

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name:	Dr Jamie Hynes and Dr Adrian Hayter	Email address:	***** & *****
Organisation (if appropriate):	Royal College of General Practitioners		
Role:			
Do you consent to your name being published on the UK NSC website alongside your response?		Yes	
Section and / or page number	Text or issue to which comments relate	Comment <i>Please use a new row for each comment and add extra rows as required.</i>	
5.4.2	Targeted screening	We broadly agree with the modelling assumptions and conclusions presented, with the important caveat that much of the underpinning evidence reflects historical pathways rather than current or evolving diagnostic and treatment approaches. We therefore agree that conclusions should be interpreted cautiously and that further evidence, including from studies such as TRANSFORM, will be important in informing future recommendations. We note that the modelling suggests a favourable risk–benefit balance for targeted screening in men with BRCA1/2 variants, supporting screening in this group between the ages of 45 and 61. In contrast, the benefits of screening men with a strong family history are described as uncertain. We would highlight that a proportion of men with a strong family history are likely to carry BRCA1/2 variants, and if the prevalence of pathogenic variants in this group is high, it is unclear why screening would not also be offered to them. This raises an unresolved question within the modelling and recommendations: whether men with a strong family history should first be offered BRCA1/2 testing, with PSA screening targeted to those who test positive, or whether PSA screening should be offered to this group regardless of genetic testing status. Greater clarity on this point would be helpful, both for clinicians and for men at increased familial risk who may reasonably expect access to screening.	
General		Whilst we have no disagreement with the policy decision, we have concerns that the communication around this has been poor. Men could, and still can, request	

		a PSA test and, following discussion, proceed with testing, leading the risks of poorer individual outcomes from over diagnosis. It remains advisable to offer PSA testing to men with a family history of prostate cancer and to men of Black African or Black Caribbean heritage. This message appears to have been lost in the wider publicity around “not screening”. Furthermore, when a GP sees a patient to discuss or request PSA testing, advising against testing needs to be undertaken carefully and clearly documented. If a person later develops prostate cancer, there may be medicolegal and moral implications. Clearer communication is needed to support informed discussion and appropriate risk-based decision making in primary care, and that there is a need for specific decision support tools related to Prostate cancer screening.
General		We note that the current discussion of family history does not clearly differentiate risk according to the age at which a relative is diagnosed with or dies from prostate cancer. This distinction is clinically important. Prostate cancer diagnosed at a very advanced age, for example in a grandfather living into their 90s, is common and may represent a very different risk profile from prostate cancer occurring at a younger age, such as a father diagnosed or dying at age 50. Earlier-onset disease is more likely to reflect inherited susceptibility and may also be associated with more aggressive, rapidly progressing cancers that contribute to premature mortality, in contrast to more indolent cancers that may never cause symptoms during a person's lifetime. We recommend that the guidance more explicitly reflects this nuance, distinguishing between late-onset and early-onset prostate cancer in relatives, and recognising differences in tumour biology and clinical course. Clarifying how age at diagnosis and cause of death in affected relatives should influence risk stratification and screening decisions would improve clinical applicability and help avoid over- or under-estimation of risk based on family history alone.
General		We note emerging evidence that people with a learning disability experience different cancer epidemiology and outcomes compared with the general population. A recent large UK population-based matched cohort study found that, although overall incidence of some cancers—including prostate cancer—was lower in individuals with a learning disability, those who are diagnosed have substantially poorer survival outcomes, with up to four-fold higher risk of death after diagnosis for melanoma, breast and prostate cancers. People with a learning disability were also more likely to be diagnosed with cancer before age 50 years and less likely to be referred urgently after presenting with possible

		cancer symptoms or to receive treatment within six months of diagnosis. These patterns may indicate under-investigation and inequities in access to timely diagnosis and care for people with a learning disability.

		In light of these findings, we suggest that the Committee consider whether a broader population health approach could be taken when assessing prostate cancer screening and diagnostic pathways. Specifically, there may be value in examining cohorts such as people with a learning disability who present with cancer at younger ages and face barriers to symptom disclosure, investigation and referral, to determine whether tailored approaches to earlier detection and support could improve outcomes for such groups.

Please return your completed form to the UK NSC Inbox UKNSC@dhsc.gov.uk by 11.59pm GMT on 20 February 2026.

S52	Maggie Tween	Norfolk and Waveney ICB	ICBs must consider the needs of their local population, re the average rates for early-stage prostate cancers. Local feasibility studies have been carried out re the best ways of targeting those men at higher risk of prostate cancer (Ie those over 50, family history, black men). Under the proposed recommendations not all of these men would be eligible for testing. We do have a local black Afro-Caribbean community who have greater chance than the average population of developing prostate cancer and live in an area of deprivation. They could be disadvantaged under these proposals, potentially widening the health inequalities gap for early detection of cancers. The proposal is to target men who are known to have the BRCA gene. For those with a family history this would mean that they would need genetic testing. We know that those who experience health inequalities are less likely to be both aware and come forward for testing again widening the gap.
S53		Staffordshire Moorlands District Council	Staffordshire Moorlands District Council welcomes the opportunity to respond to the UK National Screening Committee's (NSC) consultation on prostate cancer screening. We note the NSC's current recommendation to favour a targeted screening programme focused on individuals with particular genetic variants associated with increased risk, and its position not to support a general population screening programme at this time. However, the Council also recognises the significant concerns raised by organisations such as Prostate Cancer Research, which strongly advocate for routine screening for all men over the age of 50. Their position reflects the scale and impact of the disease across the UK. Nationally, around 6 million men are aged over 50; 50,000 men are diagnosed with prostate cancer each year, and 12,200 men die as a result of the disease annually. Within the Staffordshire Moorlands specifically, there are approximately 22,400 men over the age of 50. When extrapolated against national incidence rates, this suggests that more than 200 local men may be living with prostate cancer. Given that early detection significantly improves outcomes, the Council believes that wider access to routine screening could help save lives both locally and nationally. For these reasons, Staffordshire Moorlands District Council supports the stance taken by Prostate Cancer Research in calling for routine population-wide testing for prostate cancer for men over 50, alongside continued targeted approaches for high risk groups. We believe the evidence of prevalence, mortality, and the benefits of early diagnosis justifies reconsideration of the NSC's position on general population screening.

			The Council therefore formally submits its support for routine screening and urges the National Screening Committee to incorporate this perspective as part of its consultation.
S54	Shawn Schwartz	Beckman Coulter	Good morning, Beckman Coulter is pleased to submit the attached Comment form and two associated supporting documents – a value dossier and ISPOR poster presented in 2025. Your thoughtful consideration is appreciated. All the best, Shawn

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name:	Shawn D. Schwartz, MBA	Email address:	*****
Organization (if appropriate):	Beckman Coulter Diagnostics		
Role:	Associate Director, Market Access & Medical Policy		
Do you consent to your name being published on the UK NSC website alongside your response?		☒ Yes	No
Section and / or page number	Text or issue to which comments relate	Comment <i>Please use a new row for each comment and add extra rows as required.</i>	
2 / 11	Key Messages	We support the National Screening Committee (NSC)'s draft recommendation to introduce targeted screening for men with confirmed BRCA1/BRCA2 variants (every 2 years, ages 45–61) and agree that more evidence collection is warranted to evaluate the value of screening programmes for Black men and men with relevant family history. This reflects the Committee's modeling and long-term trial evidence, showing small absolute mortality benefits and substantial overdiagnosis/overtreatment with PSA-based screening alone. [1][2] We agree with the NSC's call for more accurate initial tests than PSA and its openness to multi-step pathways (triage test → mpMRI → targeted biopsy). The Beckman Coulter Prostate Health Index (PHI) test combines PSA, free PSA, and p2PSA into a single, clinically validated score that enhances prostate cancer (PCa) risk assessment and supports more appropriate biopsy decisions. PHI is a practical, low-cost triage tool that improves specificity [EU-validated cut-offs of 89.1% sensitivity / 29.4% specificity] in the PSA "grey zone." It can be utilised immediately by primary care within existing National Health Service (NHS) diagnostic workflows, aiding elective recovery and reducing multiple harms, most notably by lowering false positive (FP) test results that drive avoidable mpMRI use and unnecessary biopsies, along with the associated physical, psychological, and system-level burdens. PHI is therefore the most readily implementable biomarker for NHS prostate diagnostic optimisation. [1][3][6]	

		Performance metrics cited reflect EU-validated cut-offs and population data, consistent with intended NHS application PHI is a guideline-endorsed pre-biopsy blood test, recognised by the National Comprehensive Cancer Network (NCCN) in its Prostate Cancer Early Detection Guidelines as a tool that improves specificity compared with PSA alone and helps reduce unnecessary biopsies. Its diagnostic performance is supported by a substantial body of evidence comprising more than 70 published studies, which consistently demonstrate superior diagnostic accuracy relative to PSA and show that PHI facilitates more efficient biopsy decision-making while mitigating the risk of overdiagnosis. As a result, PHI's market position within the NHS now shifts from "adjunct biomarker" to strategic enabler of a future multi-step diagnostic pathway.
4.1 / 15	Predictions of benefits of screening	Initial test statement: "Pending validation of a more accurate initial test than PSA, the NSC supports evaluation of interim triage pathways (e.g., PSA→PHI→mpMRI/biopsy) that improve specificity, reduce unnecessary imaging/biopsies, and lower costs, with transparent reporting of csPCa detection, harms, and patient-reported outcomes." By improving specificity within the PSA 2–10 ng/mL range, PHI directly reduces the modelled outcomes 'Positive_PSA', 'Invite_MP-MRI', and 'Invite_Biopsy' volumes described in the NSC's Sheffield Centre for Health and Related Research (SCHARR), thereby lowering false positive rates and downstream diagnostic costs, and improving the incremental net monetary benefit at the £20,000/QALY threshold. [1][2]

4.2 / 15-17	Predictions of screening-related harms	The consultation recognises that screening and downstream interventions can cause harm, including urinary incontinence, erectile dysfunction, bowel problems, anxiety, and distress from false positives/overdiagnosis. Patients consistently report the need for clear information on risks/benefits, transparent thresholds, and predictable follow-up timelines to reduce uncertainty. Embedding PHI-led triage can meaningfully address these concerns. [2][5] Reduce unnecessary exposure procedural burden: By decreasing false positives and avoiding potentially low-yield biopsies, PHI lowers the chance of downstream harms and mitigates uncertainty while maintaining clinically significant PCa detection. [2][6] Shorter, clearer journeys: PHI thresholds (e.g., <25 defer; ≥25 proceed to mpMRI; ≥49 recommend biopsy in PIRADS-3) give patients understandable rules and faster access where risk is highest, reducing waiting-list stress. [6][8] Patient-reported outcomes (PROs): Routine collection of decision satisfaction, anxiety scores, and post-biopsy complications should be built into pilots and BRCA pathways to ensure that net benefits are realised from the patient perspective. [2] The SCHARR model explicitly identifies uncertainty around PSA trajectories, mpMRI sensitivity, and opportunistic testing. A biomarker-led triage approach, such as PHI, reduces reliance on PSA alone and mitigates structural uncertainty in the initial test performance parameter.
4.4 / 17-18	Predictions of resource use and costs in screening	As summarized in the PHI Value Dossier Europe pages 11-12, PHI combines p2PSA, free PSA, and total PSA into a single score. It is CE-marked and FDA-approved and is included in major guidelines (NCCN/EAU/AUA/SUO). PHI is intended for use as an aid in distinguishing prostate cancer from benign prostatic conditions, for prostate cancer detection in men aged 50 years and older with total PSA >2.0 to <10.0 ng/mL (EU cutoffs used), and demonstrates superior specificity compared to PSA/%fPSA in the “grey zone” and has a large, consistent evidence base across more than 70 studies. [compiled in 3] UK-based modeling (Bromilow, 2025) and real-world (Kim, 2020) studies indicate that a PHI-based triage can reduce number of false positives by ~25% (Bromilow, 2025), mpMRI use by ~15% (Kim, 2020), reduce unnecessary biopsies by ~15 (Kim et al, 2020) to 25% (Bromilow, 2025) reduce per patient cost by ~10% (Bromilow, 2025; Kim, 2020) than the tested PSA-based standard of

		care strategies, resulting in a per patient net monetary benefit of £100 at a willingness-to-pay threshold of £20,000/QALY (Bromilow, 2025). Decision-curve analyses demonstrate a net clinical benefit across relevant thresholds. [6][9]
6.2 / 24-26	Model Structure	Pre-referral in primary care (PSA → PHI → selective mpMRI/biopsy) using the World Health Organisation (WHO) standard cutoffs. PHI < 25: Consider deferring mpMRI/biopsy and repeating PSA/PHI in 6–12 months unless symptoms or rapid PSA rise. This threshold has been shown to reduce mpMRI demand (~15 to 25%) and unnecessary biopsies (~15 to 25%) while maintaining acceptable miss rates compared to MRI-first pathways. [6][7] PHI ≥ 25: Consider booking mpMRI (and proceed to biopsy if PIRADS 4–5). PHI's AUC for ≥GG2 cancers is ~0.82 across centres and provides cost advantages versus MRI-for-all. [6][7] Local calibration: Systems under pressure may pilot PHI ≥ 25 while tracking csPCa yields and miss rates, per PRIM scenario analyses. [6] Post-mpMRI optimisation (focus on PIRADS-3 “grey-zone”) PIRADS-3 + PHI ≥ 49 → Consider proceeding to biopsy (targeted + systematic). [8] [9] PIRADS-3 + PHI < 49 → Consider deferring biopsy; repeat PSA/PHI and/or mpMRI at 6–12 months. [8] [9]
6.2 / 24-26	Model Structure	Fast-track lane for remarkably high PHI Create expedited slots for PHI ≥ 55 (and/or rapid PHI rise, e.g., >15-point change over 6–12 months), targeting mpMRI within 14 days and biopsy within 21–28 days when indicated; this prioritises capacity where csPCa risk is highest. [1][3] A recent analysis of 2021-2025 NHS England – Hospital Episode Statistics (HES) data of biopsy and mpMRI utilisation and waiting times shows an increasing wait time over the 2021-2025 period for the three OPCS prostate biopsy procedures. Additionally, the percentage of people waiting more than 6 weeks for MRI has ranged from 13.7% to 18.9%.[10]

		Number of patients on MRI waiting on prostate pathway *^a <table><tr><th></th><th>Nov-24</th><th>Dec-24</th><th>Jan-25</th><th>Feb-25</th><th>Mar-25</th><th>Apr-25</th><th>May-25</th><th>Jun-25</th><th>Jul-25</th><th>Aug-25</th><th>Sep-25</th><th>Oct-25</th></tr><tr><td>Total Waiting List</td><td>64,125</td><td>60,194</td><td>64,381</td><td>66,515</td><td>66,256</td><td>64,810</td><td>64,636</td><td>66,984</td><td>67,541</td><td>61,299</td><td>65,993</td><td>72,064</td></tr><tr><td>Number waiting 6+ Weeks</td><td>10,218</td><td>11,400</td><td>12,494</td><td>9,195</td><td>9,106</td><td>10,230</td><td>10,204</td><td>10,434</td><td>11,316</td><td>11,355</td><td>11,436</td><td>12,537</td></tr><tr><td>Number waiting 13+ Weeks</td><td>2,881</td><td>3,324</td><td>2,962</td><td>2,485</td><td>2,104</td><td>2,193</td><td>2,241</td><td>2,557</td><td>2,573</td><td>2,477</td><td>2,747</td><td>2,983</td></tr><tr><td>Percentage waiting 6+ Weeks</td><td>15.94%</td><td>18.94%</td><td>19.41%</td><td>13.82%</td><td>13.74%</td><td>15.78%</td><td>15.79%</td><td>15.58%</td><td>16.75%</td><td>18.52%</td><td>17.33%</td><td>17.40%</td></tr></table> ^aall patients referred with suspected prostate ca require MRI. Standard of Care: The National Institute for Health and Care Excellence (NICE) guidelines, updated in 2019, recommend offering an mpMRI to all men with suspected clinically localised prostate cancer. This approach aims to reduce unnecessary biopsies and improve the detection of clinically significant cancer See Table 1 Below		Nov-24	Dec-24	Jan-25	Feb-25	Mar-25	Apr-25	May-25	Jun-25	Jul-25	Aug-25	Sep-25	Oct-25	Total Waiting List	64,125	60,194	64,381	66,515	66,256	64,810	64,636	66,984	67,541	61,299	65,993	72,064	Number waiting 6+ Weeks	10,218	11,400	12,494	9,195	9,106	10,230	10,204	10,434	11,316	11,355	11,436	12,537	Number waiting 13+ Weeks	2,881	3,324	2,962	2,485	2,104	2,193	2,241	2,557	2,573	2,477	2,747	2,983	Percentage waiting 6+ Weeks	15.94%	18.94%	19.41%	13.82%	13.74%	15.78%	15.79%	15.58%	16.75%	18.52%	17.33%	17.40%
	Nov-24	Dec-24	Jan-25	Feb-25	Mar-25	Apr-25	May-25	Jun-25	Jul-25	Aug-25	Sep-25	Oct-25																																																							
Total Waiting List	64,125	60,194	64,381	66,515	66,256	64,810	64,636	66,984	67,541	61,299	65,993	72,064																																																							
Number waiting 6+ Weeks	10,218	11,400	12,494	9,195	9,106	10,230	10,204	10,434	11,316	11,355	11,436	12,537																																																							
Number waiting 13+ Weeks	2,881	3,324	2,962	2,485	2,104	2,193	2,241	2,557	2,573	2,477	2,747	2,983																																																							
Percentage waiting 6+ Weeks	15.94%	18.94%	19.41%	13.82%	13.74%	15.78%	15.79%	15.58%	16.75%	18.52%	17.33%	17.40%																																																							
6.4.1 / 29-30 6.4.3 / 32-36	Risk Factors for cancer onset – Ethnicity Risk Factors for cancer onset – Family History of prostate, breast, and ovarian cancer	Black men & family history: “Given current uncertainties, the NSC will prioritise rapid subgroup analyses in TRANSFORM and commission pilot evaluations of biomarker-led triage (PHI) plus mpMRI to quantify benefit–harm, cost-effectiveness, and patient-reported outcomes for Black men and men with relevant family history.” [1]																																																																	
8.2 / 106-109	Men of Black ethnicity	Equity and trust: For groups with historically worse outcomes (e.g., black men), using biomarker-led triage plus mpMRI in pilots supports fairer access to accurate diagnosis while evidence matures, reinforcing trust through transparent, data-driven care. [1]																																																																	
8.4 / 136	BRCA carriers	For men with confirmed BRCA1/2 variants—where screening is likely cost-effective—PHI-led prioritisation of mpMRI/biopsy may further enhance pathway efficiency and reduce unnecessary procedures without diluting benefit [1]																																																																	
10.1 / 172-173	General population: Conclusions	PHI provides a practical, evidence-based triage mechanism that the NHS can deploy now to enhance the accuracy, safety, and efficiency of the prostate pathway—aligning with the NSC’s consultation narrative and emphasis on multi-step pathways and improved initial tests over PSA. As TRANSFORM generates definitive answers for broader risk-stratified screening, PHI-led triage can immediately improve the benefit–harm balance, reduce unnecessary procedures, relieve capacity constraints, and deliver a clearer, fairer experience for patients. [1][2][6]																																																																	

10.5 / 184-185	Future modelling work based on additional data	KPIs: mpMRI scans avoided (target $\geq 15\text{--}25\%$), biopsies avoided (target $\geq 15\text{--}25\%$), csPCa detection among biopsied men, missed csPCa within 12 months (benchmarked to PHI ≥ 25 rule-out scenarios), waitlist times to mpMRI/biopsy, post-biopsy complication rates (e.g., sepsis), and patient-reported outcomes (decision satisfaction, anxiety). [2][6] Health Equity audit: Track uptake and outcomes by ethnicity and deprivation quintile, consistent with NSC priorities on health inequalities [1]

- Table 1 (Page 6)
- Decision Tree (Page 7)
- Annex (Page 9-11)

Please return your completed form to the UK NSC Inbox UKNSC@dhsc.gov.uk by 11.59pm GMT on 20 February 2026.

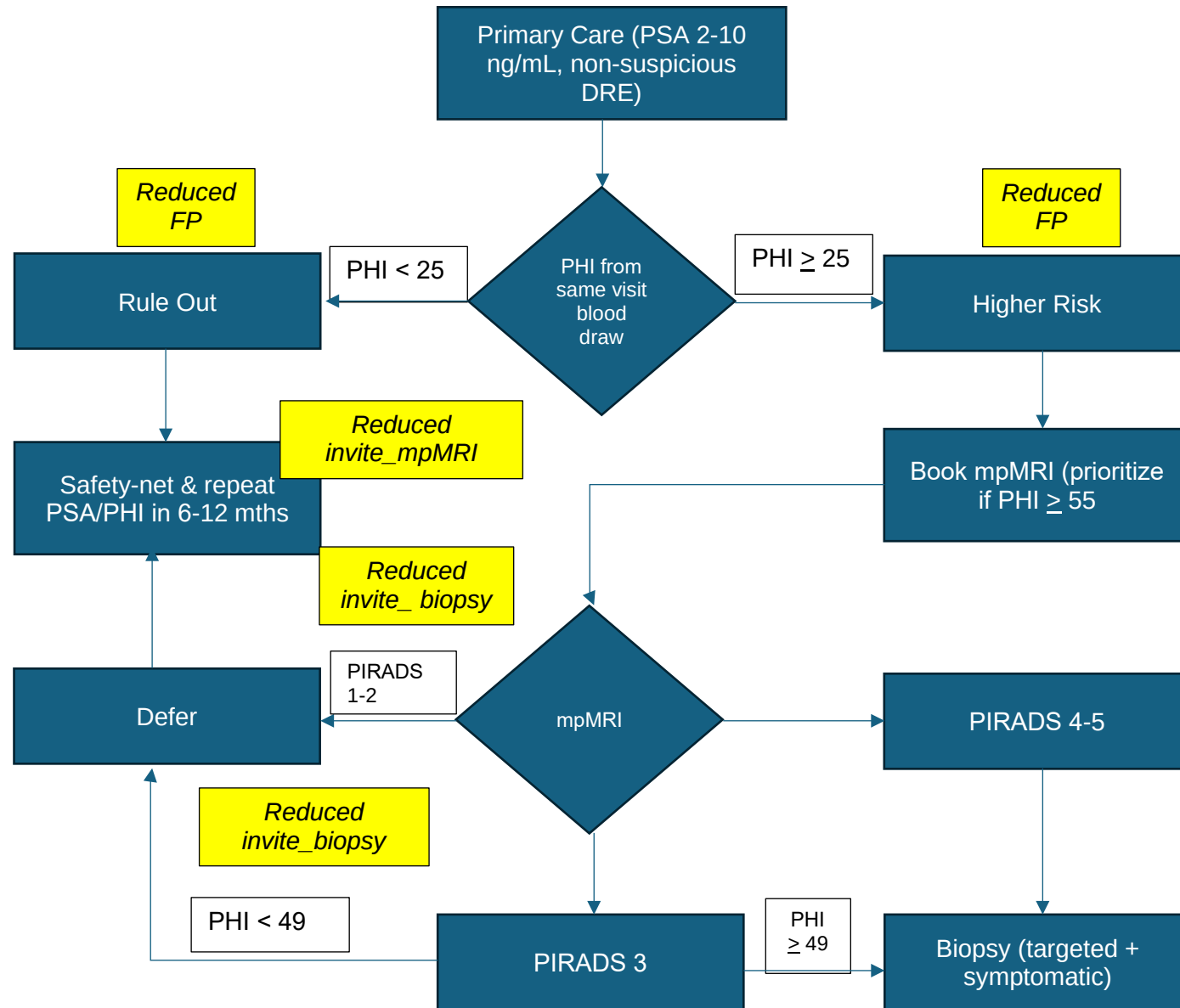
Table 1 – Analysis of NHS England Data – HES 2021 April to 2025 March

Number of patients on MRI waiting on prostate pathway *	Nov-24	Dec-24	Jan-25	Feb-25	Mar-25	Apr-25	May-25	Jun-25	Jul-25	Aug-25	Sep-25	Oct-25
Total Waiting List	64,125	60,194	64,381	66,515	66,256	64,810	64,636	66,984	67,541	61,299	65,993	72,064
Number waiting 6+ Weeks	10,218	11,400	12,494	9,195	9,106	10,230	10,204	10,434	11,316	11,355	11,436	12,537
Number waiting 13+ Weeks	2,881	3,324	2,962	2,485	2,104	2,193	2,241	2,557	2,573	2,477	2,747	2,983
Percentage waiting 6+ Weeks	15.94%	18.94%	19.41%	13.82%	13.74%	15.78%	15.79%	15.58%	16.75%	18.52%	17.33%	17.40%

*all patients referred with suspected prostate ca require MRI. Standard of Care: The National Institute for Health and Care Excellence (NICE) guidelines, updated in 2019, recommend offering an mpMRI to all men with suspected clinically localised prostate cancer. This approach aims to reduce unnecessary biopsies and improve the detection of clinically significant cancer

Decision Tree

This pathway is designed to reduce the screening committee's modelled Positive_PSA, Invite_MP-MRI, Invite_Biopsy and FP volumes while preserving csPCa detection.



References

- [1] UK NSC blog: "UK NSC opens consultation on draft prostate cancer screening recommendation" (28 Nov 2025). <https://nationalscreening.blog.gov.uk/2025/11/28/uk-nsc-opens-consultation-on-draft-prostate-cancer-screening-recommendation/>
- [2] UK NSC Narrative: Prostate Cancer Screening Economic Model: Accompanying Narrative (Nov 2025). https://nationalscreening.blog.gov.uk/wp-content/uploads/sites/254/2025/11/Prostate-Cancer-Screening-Evidence-Review-2025-Narrative_Final.pdf
- [3] PHI Value Dossier Europe
- [4] BMJ News: UK NSC draft—routine NHS screening rejected; targeted BRCA programme proposed (28 Nov 2025). <https://www.bmj.com/content/391/bmj.r2524>
- [5] Cancer Research UK analysis: rationale for targeted programme, balance of harms/benefits, next steps (28 Nov 2025). <https://news.cancerresearchuk.org/2025/11/28/uk-nsc-draft-recommendation-targeted-prostate-cancer-screening-programme/>
- [6] Kim et al. (PRIM) – Clinical utility and cost modelling of PHI to refine mpMRI; BMC Medicine (17 Apr 2020). <https://link.springer.com/article/10.1186/s12916-020-01548-3>
- [7] Cambridge repository copy of PRIM (open access). <https://www.repository.cam.ac.uk/items/c87ad9b3-e843-422f-ae14-77a9bf1575f0>
- [8] Carbutaru et al. – PHI vs PSA density after mpMRI in biopsy-naïve, multiethnic cohort; PIRADS-3 decision support (2021). <https://bjui-journals.onlinelibrary.wiley.com/doi/epdf/10.1002/bco2.91>
- [9] Bromilow T et al. *Cost-Effectiveness Analysis of the Prostate Health Index (PHI) Test After a Prostate-Specific Antigen (PSA) Test in the UK*. Poster Presentation at ISPOR 2025.
- [10] NHS Data Analysis by Device Access – April 2021-March 2025 NHS England Data – HES (Hospital Episode Statistics).

Annex 1

Prostate Health Index (PHI) – Evidence Dossier (Europe)

Indexed Extract for UK NSC Prostate Cancer Screening Consultation

Purpose of this Annex

This annex provides structured signposting to the relevant sections of the **PHI Value Dossier Europe** to support statements made in the consultation response.

It is intended to allow reviewers to efficiently locate clinical performance data, clinical utility evidence, and economic analyses relevant to the modelling framework described in the SCHARR Phase 3 report.

All performance metrics cited in the main submission reflect EU-validated cut-offs and intended NHS population use (men aged ≥50 years with PSA 2–10 ng/mL and non-suspicious DRE).

Section A – Clinical Validity & Intended Use

A1. Indication & Target Population

- Dossier Section 2.1.2 – Indications for Use
- Population: PSA 2–10 ng/mL, non-suspicious DRE
- Intended role: Pre-biopsy risk stratification

A2. Diagnostic Accuracy (EU Data)

- Dossier Section 3.1 – Clinical Validity
- Table 8 – Sensitivity & Specificity by PHI Cut-off
- Table 9 – Pooled Diagnostic Accuracy (Overall PCa)
- Table 10 – Pooled Diagnostic Accuracy (Clinically Significant PCa)

Key relevance to NSC model:

Improves specificity in PSA “grey zone,” reducing downstream Positive_PSA classifications.

Section B – Clinical Utility & MRI Integration

B1. Biopsy Reduction Evidence

- Dossier Section 3.2 – Clinical Utility
- Real-world biopsy reduction studies
- Reduction in low-grade cancer detection

B2. PHI + mpMRI Pathway Evidence

- Dossier Section 3.2 – Imaging-integrated cohorts
- Evidence in PI-RADS 3 populations

Key relevance to NSC model:

Potential reduction in:

- Invite_MP-MRI volumes
- Invite_Biopsy volumes
- False positive (FP) cases

Section C – Economic Evidence

C1. Cost-Effectiveness (UK Perspective)

- Dossier Section 4.2 – Cost-Effectiveness of PHI
- UK modelling summary
- Cost-per-patient estimates
- Table 15 – Cost-Consequence Analysis

C2. Budget Impact & Resource Use

- Dossier Section 4.3 – Budget Impact
- Section 4.5 – Economic Data Summary

Key relevance to NSC model:

Demonstrates reduced diagnostic pathway costs through decreased imaging and biopsy utilisation.

Section D – Additional Supporting Literature

- PRIM Study (Kim et al., 2020) – mpMRI refinement modelling
- Carbutaru et al. – PHI in PI-RADS 3
- UK cost-effectiveness poster (ISPOR 2025)

Relationship to SCHARR Phase 3 Model

The consultation response references the following model variables described in the SCHARR report:

- Positive_PSA
- Invite_MP-MRI
- Invite_Biopsy
- False Positives (FP)
- Incremental Net Monetary Benefit (NMB)

This annex provides evidence relevant to evaluating a potential biomarker-led triage scenario within future modelling updates.

COST-EFFECTIVENESS ANALYSIS OF THE PROSTATE HEALTH INDEX (phi) TEST AFTER A PROSTATE-SPECIFIC ANTIGEN (PSA) TEST IN THE U.K.



Tom Bromilow, MSc,¹ Daniela Afonso, MSc,¹ Reagan Davis, MSc,¹ Stuart Mealing, MSc,¹ Lopamudra Das, PhD²

¹York Health Economics Consortium, York, UK; ²Beckman Coulter Diagnostics, Brea, USA

#EE221

BACKGROUND

- Prostate cancer (PCa) accounted for 23.2% of all new cancer cases (excluding non-melanoma skin cancers) diagnosed in men and for 9.9% of all deaths due to cancer in men in EU-27 countries in 2020.¹
- The total economic cost of PCa in the EU was estimated at €8.43 billion in 2009.²
- In 2006, 106–179 million euros (€) were dedicated to PCa management in the European countries exemplified by the UK, Germany, France, Italy, Spain and the Netherlands with increasing cost expected due to earlier diagnosis and increasing survival.³
- Research indicates that Prostate Health Index (phi) can be used alongside imaging technologies to increase diagnostic accuracy.⁴

STUDY OBJECTIVES

This analysis aimed to determine the clinical and economic consequences of introducing phi into the current diagnostic pathway for clinically significant PCa (csPCa, Gleason Grade ≥7) in the United Kingdom.

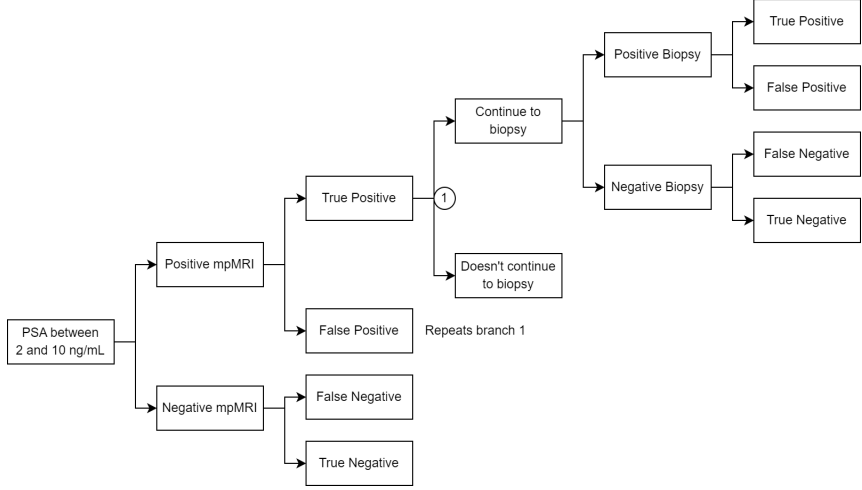
METHODS

A decision-tree-based cost-effectiveness model was developed. Model details:

- The population included men with PSA >2 and <10 and have not yet had a biopsy
- Prevalence of csPCa in the grey zone is 38%⁵
- Hypothetical cohort of 1,000, starting age of 63 years
- Two diagnostic strategies were considered:
 - SoC + phi (phi cutoff 25)
 - SoC
- Outcomes included:
 - Total and incremental costs and quality-adjusted life years (QALYs)
 - Incremental cost-effectiveness ratio (ICER)
 - Net monetary benefit (NMB)
 - Net health benefit (NHB)
 - Total biopsies conducted
 - Total negative biopsies avoided
 - Total csPCa cases missed
- The analysis was performed from the perspective of the UK NHS and personal social services (PSS)
- Time horizon was 1 month to reflect the time it takes to receive a PCa diagnosis in the U.K.
- Disease prevalence, adverse event, health-related quality of life, diagnostic test (phi, mpMRI, TRUS biopsy) accuracy, and associated resource use data were obtained from the published clinical literature.
- Cost information was obtained from National Cost Collection (NCC) and the Personal Social Services Research Unit (PSSRU), and phi test manufacturer
- Analysis was limited to the diagnostic phase; further diagnostics and treatment of PCa were not considered
- Probabilistic sensitivity analyses (PSA) included: PCa prevalence (beta), diagnostic accuracy (beta), unit costs (listed & literature-based, fixed), resource use proportions (beta), population utility norms (beta), and utility decrements (beta)

MODEL STRUCTURE AND INPUTS

Panel A: Standard of Care



Panel B: phi followed by mpMRI

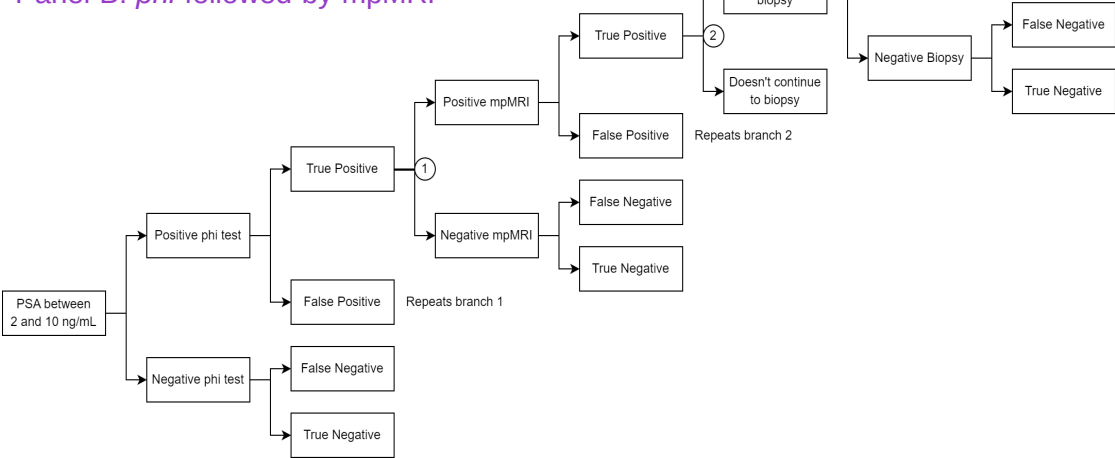


Figure 1. illustrates the decision tree with the current SoC for the UK (Panel A) and phi followed by mpMRI (Panel B)

Diagnostic Clinical Inputs

Input	Sensitivity	Specificity	Source
phi (cut off 25)	96%	25%	Kim et al. (2020)
mpMRI	87%	47%	Ahmed et al. (2017)

Biopsy-Related Adverse Event Inputs

Event	Probability	Source
Urinary infection	1.00%	Nam et al. (2010)
Urinary bleeding	0.27%	Nam et al. (2010)
Urinary obstruction	0.13%	Nam et al. (2010)
Rectal bleeding	0.09%	Rosario et al. (2012)
Monthly utility decrement	0.004	NICE NG131

Biopsy-Related Resource Utilization Inputs

Input	Probability	Source
GP Visit	8.02%	Rosario et al. (2012)
Urology nurse consultation	1.22%	Rosario et al. (2012)

Cost Inputs

Input	Unit Cost	Source
phi test	£30	Beckman Coulter
mp-MRI	£257	NCC 2022/23: RD03Z
TRUS-guided biopsy	£811	NCC 2022/23: LB76Z
Biopsy-related AE treatment		
GP consultation	£42	PSSRU
Urology nurse consultation	£146.23	NCC 2022/23: WF01A
Hospital Admission		
Urinary infection	£422	NCC 2022/23: LA04S
Urinary bleeding	£657	NCC 2022/23: LB18Z
Urinary obstruction	£2,303	NCC 2022/23: LB09D
Rectal bleeding	£173	NCC 2022/23: WF01B

RESULTS

Deterministic Base-Case Results (phi cut off 25)

	phi+mpMRI	SoC	Incremental
Total costs	£709	£801	£92
Total QALYs	0.07	0.07	0.00
ICER	Dominant		
Net Monetary Benefit	£100		
Total biopsies	564	659	-95
Total unnecessary biopsies	246	329	-82
# of csPCa missed	63	49	13
# of True positives	317	331	-13
# of False positives	246	329	-82
# of True negatives	374	291	82
# of False negatives	63	49	13

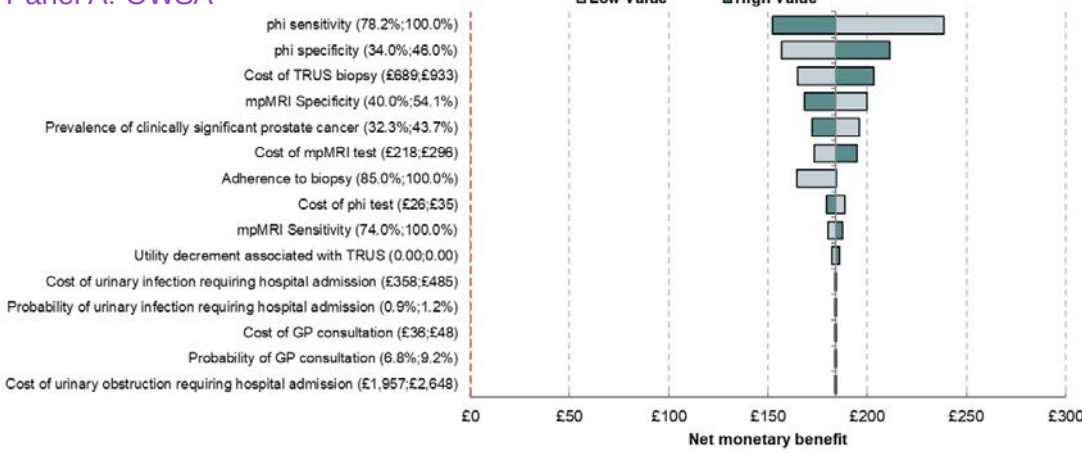
Base Case Cost Breakdown

	phi+mpMRI	SoC	Incremental
phi	£30	--	£30
mpMRI	£213.25	£257.00	-£43.74
TRUS biopsy	£457.26	£534.61	-£77.35
GP consultation	£1.90	£2.22	-£0.32
Nurse consultation	£1.05	£1.23	-£0.18
Urinary infection	£2.38	£2.78	-£0.40
Urinary bleed	£1.00	£1.17	-£0.17
Urinary obstruction	£1.69	£1.97	-£0.29
Rectal bleed	£0.09	£0.10	-£0.01
Total	£708.62	£801.08	-£92.46

- Both the deterministic and probabilistic per-person results showed that for a 30-day time horizon, phi + mpMRI was shown to be a cost-effective option, reducing costs and increasing QALY slightly in the csPCa diagnosis pathway in the UK due to fewer mpMRI and biopsies being conducted in the phi+mpMRI arm
- The phi + mpMRI arm was dominant 100% of iterations of the probabilistic analysis and was cost-effective 100% of iterations at £20,000 per QALY threshold
- There is a trade-off between the cost-effectiveness benefits of phi + mpMRI and the number of cases of csPCa that the arm misses compared with mpMRI

SENSITIVITY ANALYSIS

Panel A: OWSA



Panel B: Cost-effectiveness plane

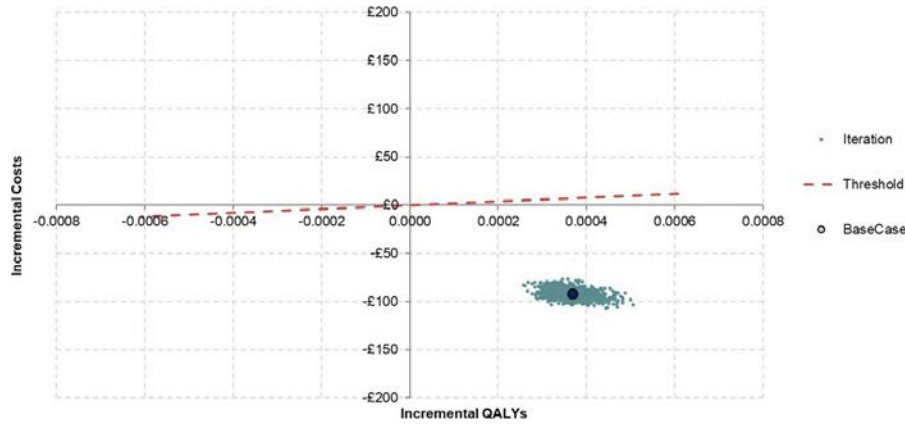


Figure 2. illustrates the one-way sensitivity analyses (Panel A) and the cost-effectiveness plane for phi+mpMRI (Panel B)

- The biggest univariate drivers of the results were the sensitivity and specificity of phi, followed by the cost of the TRUS biopsy and the concentrated cloud of iterations in the south-east quadrant indicates robustness of the results at the NICE threshold of £20,000 per QALY

STUDY LIMITATIONS

- Modeling study might not represent real-world clinical practice
- The effect of a missed csPCa is not captured by the model.
- The study assumed 100% diagnostic accuracy for biopsy, which might not be accurate in the real world
- Simulation does not include other potential comparators of phi.

CONCLUSION

- The use of phi before an mpMRI for men in the PSA 'grey zone' could result in fewer mpMRI and biopsies being conducted. This reduces NHS resource use and prevents unnecessary, risky, and invasive procedures
- The increase in missed csPCa cases can be mitigated if PSA/phi tests are conducted regularly; it is unlikely that a person will not be correctly diagnosed within 6 months of the original test
- Additional research is needed to confirm the benefits in a real-world setting

References

1. Dyls T, Randi G, Bray F, et al. The European cancer burden in 2020: Incidence and mortality estimates for 40 countries and 25 major cancers. Eur J Cancer. 2021;157:308-347. doi:10.1016/j.ejca.2021.07.039

2. Luengo-Fernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. Lancet Oncol. 2013;14(12):1165-1174. doi:10.1016/S1470-2045(13)70442-X

3. Roehrborn CG, Black LK. The economic burden of prostate cancer. BJU Int. 2011;108(6):806-813. doi:10.1111/j.1464-410X.2011.10365.x

4. Ferro M, Crocetto F, Bruzzi D, et al. Prostate health index and multiparametric MRI: partners in crime fighting overdiagnosis and overtreatment in prostate cancer. Cancers (Basel). 2021;13(18). doi:10.3390/cancers13184723

5. 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):815-22.

6. Kim L, Boxall N, George A, Burling K, Acher P, Aning J, et al. Clinical utility and cost modelling of the phi test to triage referrals into image-based diagnostic services for suspected prostate cancer: the PRIM (Phi to Refine MRI) study. BMC Med. 2020;18(1):95.

7. Nam RK, Seshin R, Lee Y, Liu Y, Law C, Klotz LH, et al. Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. J Urol. 2010;183(3):963-8.

8. Rosario DJ, Lane JA, Metcalfe C, Donovan JL, Doble A, Goodwin L, et al. Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen: prospective evaluation within ProtecT study. BMJ. 2012;344:d7894.

9. National Institute of Health and Care Excellence. NICE guideline [NG131]: Recommendations. 2021. [cited April 2024]. Available from: <https://www.nice.org.uk/guidance/ng131/chapter/Recommendations#assessment-and-diagnosis>



Prostate Health Index (*phi*)



Value Dossier Europe

Address: 1000 Lake Hazeltine Drive, Chaska, MN 55318
Website: beckmancoulter.com/en/products/immunoassay/phi



Table of Contents

Overview of the Dossier	4
Glossary	5
1 Executive Summary	6
1.1 Clinical Benefits	6
1.2 Economic Benefits	8
1.3 Conclusions	8
2 Product Information & Disease Description	10
2.1 Product Description	10
2.2 Place of <i>phi</i> in Therapy	14
2.3 Clinical Practice and Guidelines for Testing in PCa	17
3 Clinical Evidence	20
3.1 Clinical Validity of <i>phi</i>	20
3.2 Clinical Utility of <i>phi</i>	25
3.4 Integration of <i>phi</i> in Clinical Risk Calculators	29
4 Economic Value & Modeling Report	36
4.1 Modeling Overview	36
4.2 Cost-Effectiveness of <i>phi</i>	38
4.3 Budget Impact of <i>phi</i>	45
4.4 Other Economic Evidence of <i>phi</i>	46
4.5 Economic Data Summary	47
5 Dossier Appendices	48
5.1 References Contained in Dossier	48
5.2 New references	51
5.3 Coding Information	53

Table of Figures

Figure 1	Five-Year Relative Survival in PCa Patients, by Diagnosis Stage	14
Figure 2	Annualized Mean Net Costs of Care for PCa in the U.S	15
Figure 3	Place of <i>phi</i> in the Diagnostic Considerations for PCa.....	19
Figure 4	ROC Curves for <i>phi</i> , tPSA, %fPSA in the 4-10ng/mL PSA range	21
Figure 5	Real-world Biopsies and Pathological Findings Before and After <i>phi</i>	24
Figure 6	Biopsy Outcomes by <i>phi</i> Testing Status	25
Figure 7	Cost-effectiveness Estimates in Base-case Analysis by Screening Age.....	42
Figure 8	Cost-effectiveness Results with 3% Discounting Rate	43

List of Tables

Table 1	Tests to Improve the Specificity of PCa Detection.....	13
Table 2	Select Commercially Available Tests to Aid the Diagnosis of PCa	13
Table 3	PCa Histologic Grade Group by Gleason Score	16
Table 4	PCa-Specific Survival Rates with 95% CI by Gleason Score	16
Table 5	PCa TNM Prognostic Stage Group, AJCC/UICC	16
Table 6	Key EAU Guidelines for Early Detection.....	17
Table 7	Probability of PCa by Range of <i>phi</i> values.....	21
Table 8	Sensitivity & Specificity PCa Using Various <i>phi</i> Cutoffs in Men with Non-Suspicious DRE.....	21
Table 9	Pooled Diagnostic Accuracy of <i>phi</i> in the detection of PCa.....	23
Table 10	Pooled diagnostic accuracy of <i>phi</i> in detection of clinically significant PCa	29
Table 11	Head-to-head Comparisons of PCA3 and <i>phi</i>	33
Table 12	Glossary of Frequently Encountered Economic Model Terms.....	37
Table 13	Modelling results for a Cohort of 1000 Patients, by Diagnostic strategy.....	39
Table 14	Costs Per Net Cancer Detected, by Risk Threshold.....	40
Table 15	Base Case Cost-Consequence Analysis, by <i>phi</i> Cutoff and Diagnostic Strategy	41
Table 16	Cost-consequence Analysis of Alternative Diagnostic Strategies	45



Overview of the Dossier

The aim of this global value dossier (Europe) is to present the value of the Prostate Health Index (*phi*) as an aid in distinguishing prostate cancer (PCa) from benign prostatic conditions and for prostate cancer detection in men aged 50 years and older with total prostate-specific antigen (tPSA) between 2-10ng/mL and with digital rectal examination (DRE) findings that are not suspicious for cancer or men with no prior biopsy as well men with prior negative biopsy.

The information in this dossier is intended to support pricing and reimbursement negotiations, as well as facilitate payer coverage decisions in Europe.

Beckman Coulter is not promoting any of its products for any purpose other than those expressly approved in the product's labeling and instructions for use.

Glossary

TERM	DESCRIPTION
AJCC	American Joint Commission on Cancer
AUA	American Urological Association
AUC	Area Under the Curve (see ROC)
BPH	Benign Prostatic Hyperplasia
CEA	Cost-Effectiveness Analysis
CUA	Cost-Utility Analysis
CCA	Cost-Consequence Analysis
CI	Confidence Interval
csPCa	Clinically Significant Prostate Cancer
DRE	Digital Rectal Exam
EAU	European Association of Urology
EANM	European Association of Nuclear Medicine, and the
ERSPC	European Randomized Study of Prostate Cancer
ESTRO	European Society for Radiotherapy and Oncology
ESUR	European Society of Urogenital Radiology
FDA	U.S. Food and Drug Administration
fPSA	Free PSA, non-complexed form of PSA
%fPSA	The ratio of fPSA to Total PSA
GG	Group Grade
GS	Gleason Score
HSROC	Hierarchical summary receiver operating characteristic
ICER	Incremental Cost-Effectiveness Ratio
ISUP	International Society of Urological Pathology
IVDMIA	In Vitro Diagnostic Multivariate Index Assay
JHU	Johns Hopkins University
mpMRI	Multiparametric Magnetic Resonance Imaging
NCCN	National Comprehensive Cancer Network
PCa	Prostate Cancer
PCA3	Hologic Gen-Probe PROGENSA® assay
PCPT	Prostate Cancer Prevention Trial
PMPM	Per member per month
<i>phi</i>	Prostate Health Index
PHID	Prostate Health Index Density
PI-RADS	Prostate Imaging–Reporting and Data System
PSA	Prostate-specific antigen
QALY	Quality-adjusted Life Years
ROC	Receiver Operating Characteristic (i.e., ROC Curve; see AUC)
ISOG	International Society of Geriatric Oncology
TNM	Tumor, Nodes, Metastasis system of cancer staging
tPSA	Total PSA
TRUS	Transrectal Ultrasound
UICC	Union for International Cancer Control
WTP	Willingness-To-Pay



1 Executive Summary

Prostate cancer (PCa) is a common malignancy in men, and current PSA-based diagnostic pathways are limited by low specificity, leading to unnecessary imaging, biopsies, and overdiagnosis of indolent disease. There is a need for validated tools that improve risk stratification and identify clinically significant prostate cancer (csPCa) while reducing unnecessary invasive procedures. The Prostate Health Index (phi) is a blood-based biomarker that improves prostate cancer risk assessment beyond PSA alone by combining total PSA, free PSA, and p2PSA into a single score.

1.1 Clinical Benefits

There is a strong relationship between *phi* and the probability of both overall and clinically significant prostate cancer

Clinical validity was demonstrated through a multi-center pivotal trial with 892 men between 50 and 84 years of age with serum total prostate-specific antigen (tPSA) levels ranging from 2–10 ng/mL, inclusive.³⁸ The phi test showed a significant improvement in diagnostic sensitivity and specificity for PCa detection compared to %fPSA. A phi value of 27.0 corresponded to 90% clinical sensitivity and 31.1% clinical specificity. Therefore nearly 1 in 3 men may avoid prostate biopsy while detecting 90% of cancers if their phi value is less than 27.0. The AUC was significantly ($p < 0.001$) higher for phi (0.708, 95% CI 0.668-0.747) than for tPSA (0.516, 95% CI 0.472-0.560) and %fPSA (0.648, 95% CI 0.606-0.690).² A strong

relationship between phi and the probability of PCa was seen with higher phi values indicate a higher likelihood of PCa on biopsy.³⁸

Beyond initial validation, a consistent, graded relationship between increasing phi values and cancer risk has been demonstrated across several studies. Meta-analyses involving more than 29,000 patients report a pooled sensitivity of approximately 0.85 and specificity of 0.52 for detecting clinically significant prostate cancer (csPCa) (Agnello 2022, Kawada 2024). In imaging-integrated cohorts, phi has demonstrated AUCs ranging from 0.78 to >0.84 for csPCa detection, outperforming PSA and PSA derivatives, including in diagnostically challenging PI-RADS 3 populations (Cui 2023, Chung 2024, Huang 2024).

***phi* can reduce biopsies and can help guide patient management for physicians**

Two studies demonstrate the clinical utility of phi in the U.S. clinical practice setting. A prospective observational, multi-center study compared over 500 men tested with phi to a historical control group of similar men who met the same criteria and were seen by the same participating urologists within the previous 24 months, and before the commercial implementation of phi testing in their practice.³ According to the findings, men receiving a phi test showed nearly a 24% reduction in biopsy procedures performed compared to the historical control group with a decrease in the rates of low-grade (Gleason score 6) cancers detected.³ Furthermore, physicians reported that the phi score significantly impacted their patient management plan in over 73% of cases, including biopsy deferrals when the phi score was low, and decisions to perform biopsies when the phi score indicated an intermediate or high probability of PCa ($\text{phi} \geq 36$).³

A similarly designed study was also recently published from a large academic practice at Johns Hopkins University (JHU).⁴ phi was tested in 345 patients presenting for diagnostic evaluation of PCa by their serum tPSA findings. Overall, 39% of men in the prospective registry underwent a biopsy when phi was included in the assessment, representing a 9% reduction in the rate of prostate biopsy compared to historical practice.⁴

More recent studies demonstrate that phi retains clinical utility within contemporary diagnostic pathways that incorporate mpMRI. Multiple studies reported that phi-guided strategies safely avoided approximately 25-50% of prostate biopsies while maintaining high sensitivity for Grade Group ≥ 2 disease (Agnello 2024, Chiu 2023, Esteban 2025). In men with PI-RADS 3 lesions, csPCa rates increased stepwise across phi strata, from approximately 5% at low phi values to >50% at $\text{phi} \geq 55$, demonstrating clinically meaningful risk stratification in this diagnostic grey zone (Leung, 2024).

1.2 Economic Benefits

The use of phi in conjunction with tPSA is a cost-effective option from both a managed care and societal perspectives over the use of tPSA alone

A recent diagnostic pathway modeling study based on Italian data provides quantitative evidence of cost differences across alternative strategies. In a cost-consequence analysis of men with PSA 2-10 ng/mL, total diagnostic costs ranged from approximately €23,964-€29,599 per 100 men for phi-first strategies compared with €31,206 per 100 men for mpMRI alone, demonstrating cost reductions of up to €7,200 per 100 patients evaluated (Borisenko 2024b). Strategies incorporating mpMRI followed by phi achieved maximal detection of clinically significant prostate cancer but at higher total costs (€40,877-€42,338 per 100 men) (Borisenko 2024a, Borisenko 2024b). Complementary UK-based cost-effectiveness modeling from an NHS perspective demonstrated that a phi-before-mpMRI pathway resulted in a per-patient cost saving of £92, with a small gain in QALYs, due to reductions in unnecessary mpMRI scans and prostate biopsies (Bromilow 2025).

Published health economic studies have assessed the budget impact⁵ and cost-effectiveness⁶ of early PCa detection when the phi test is added to current PCa detection strategies. These studies demonstrated that the combination of phi testing with conventional serum tPSA screening is both cost-effective and a better tool for recommendation of a prostate biopsy. The total budgetary impact on the one-year expected total costs for PCa detection was a savings of \$94,219 (\$0.08 PMPM) at a threshold of 4 ng/mL, respectively. In cost-effectiveness studies, the strategy of tPSA plus phi dominated the tPSA-only strategy, resulting in significant cost savings with an expected gain in quality-adjusted life years at a tPSA threshold of 4 ng/mL. It was also noted that the increased cost of adding phi testing to the original cost of tPSA screening could be offset by reducing unnecessary biopsies if it were adopted by insurers.

1.3 Conclusions

The addition of phi testing represents a cost-effective strategy for PCa detection while avoiding unnecessary biopsies. The phi is a clinically validated biomarker that improves prostate cancer risk assessment beyond PSA alone by providing a graded and clinically actionable estimate of cancer risk. Clinical studies demonstrate that phi improves diagnostic accuracy compared with PSA and %fPSA, reduces unnecessary prostate biopsies, and detects clinically significant prostate cancer.

Evidence from several studies and reviews shows that the increasing phi values were consistently associated with graded increases in the probability of clinically significant

prostate cancer, particularly in diagnostically challenging populations such as men with PI-RADS 3 lesions. The findings demonstrate that phi improves risk stratification, informs biopsy decision-making, and increases diagnostic efficiency when used alongside mpMRI.

U.S. budget impact and cost-effectiveness analyses show that phi-based strategies reduce diagnostic costs and outperform PSA-only pathways, delivering cost savings. The findings are supported by recent European modeling studies, which demonstrate that phi-guided diagnostic strategies reduce total diagnostic pathway costs by up to €7,000 per 100 patients evaluated in Italy and achieve per-patient cost savings of approximately £92 in the UK, due to reductions in unnecessary imaging and biopsy procedures.



2 Product Information & Disease Description

2.1 Product Description

2.1.1 Product Name, Code, Manufacturer and Contact

Generic name	Quantitative test for determination of [-2]proPSA levels
Brand name	Access Hybritech p2PSA on the Access Immunoassay Systems
Procode	OYO
Manufacturer	Beckman Coulter, Inc. 1000 Lake Hazeltine Drive. Chaska, MN 55318
Payer contact	Jerry L Garner, MBA-HCA, PAHM Sr. Director, Market Access, Health Economics & Policy Email: jlgarner@beckman.com Phone: +1 (469) 380 8368

Source: FDA Label

2.1.2 Indications for Use

The Access Hybritech p2PSA assay is a paramagnetic particle, chemiluminescent immunoassay for the quantitative determination of [-2] proPSA antigen, an isoform of free PSA, in human serum using the Access Immunoassay Systems. Access Hybritech p2PSA is intended to be used in combination with Access Hybritech total PSA (tPSA) and Access Hybritech free PSA (fPSA) to calculate the Beckman Coulter Prostate Health Index (phi), an In Vitro Diagnostic Multivariate Index Assay (IVDMIA).

Beckman Coulter phi as calculated using the Access Hybritech assays is indicated for use as an aid in distinguishing PCa from benign prostatic conditions, for PCa detection in men aged 50 years and older with total PSA > 2.0 to < 10.0 ng/mL, and with digital rectal examination (DRE) findings that are not suspicious for cancer. A prostatic biopsy is required for the diagnosis of cancer.

2.1.3 About *phi*

The Prostate Health Index (phi) was approved by the FDA on June 14, 2012 and is intended for use as an aid in distinguishing PCa from benign prostatic conditions.² The phi test utilizes a calculation that combines the results of three quantitative blood serum immunoassays (PSA, free PSA, and p2PSA) into a single numerical result (the “phi score”):

$$\mathbf{phi} = \frac{\text{p2PSA}}{\text{free PSA}} \times \sqrt{\text{total PSA}}$$

phi is intended to be used in the same way as %fPSA (= fPSA/tPSA) for assessing the likelihood of PCa in men who meet tPSA standards for consideration of a biopsy. phi is an improved %fPSA test with over 70 published clinical studies demonstrating its benefits and economic value. These studies confirm that phi significantly improves clinical specificity for PCa detection compared to %fPSA and relative to tPSA alone.²

The new p2PSA assay is specific to measuring [-2]proPSA, an isoform of free PSA identified as the most PCa-specific form found in tumor extracts.² The tPSA, free PSA, and p2PSA results are combined in the Beckman Coulter Access instrument to calculate the probability of PCa. This score provides urologists with more accurate information about what an elevated tPSA level might mean and the likelihood of finding PCa with a biopsy.²

Access Hybritech p2PSA is a two-site immunoenzymatic “sandwich” assay. A sample is added to a reaction vessel with mouse monoclonal anti-PSA-alkaline phosphatase conjugate, paramagnetic particles coated with a mouse monoclonal anti-[-2]proPSA

antibody, and a blocking reagent. The [-2] proPSA in the sample binds to the immobilized monoclonal anti- [-2]proPSA on the solid phase while, at the same time, the monoclonal anti-PSA-alkaline phosphatase conjugate reacts with different antigenic sites on the [-2]proPSA molecule. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate Lumi- Phos® 530 is added to the vessel, and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of [-2]proPSA in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

Access Hybritech p2PSA reagents and the Access Immunoassay Analyzers comprise the Access Immunoassay Systems for the quantitative determination of [-2]proPSA levels in human serum using paramagnetic particle solid phase technology and chemiluminescent signal detection. Calibrators, quality controls, and samples containing [-2]proPSA are analyzed in a two-site immunoenzymatic (“sandwich”) assay, using alkaline phosphatase conjugated anti-PSA mouse monoclonal antibody and paramagnetic particles coated with mouse monoclonal anti-[-2]proPSA antibody. Access Hybritech p2PSA consists of reagent packs, calibrators, quality control material, substrate, and wash buffer.

2.1.4 Contraindications for *phi*

None

2.1.5 Potential Adverse Effects of *phi* on Health

Failure of the device to perform as expected may lead to incorrect p2PSA test results and the Beckman Coulter *phi* calculation. A falsely high Beckman Coulter *phi* result (higher Beckman Coulter *phi* is associated with a greater probability of cancer) may lead to a medical decision to perform an unnecessary prostate biopsy. A falsely low Beckman Coulter *phi* result (lower Beckman Coulter *phi* is associated with a lesser probability of cancer) may lead to a medical decision to not perform a prostate biopsy. In addition, there are risks from venipuncture (e.g., hematoma) and complications from biopsy [i.e. infection, fever, rectal bleeding, hematuria and hematospermia (blood in the urine and semen), urinary retention, and hospitalization in some cases] if the Beckman Coulter *phi* result indicated biopsy.

2.1.6 Product Comparison for *phi*

All relevant commercially available tests to aid the diagnosis of PCa are listed in Table 2-1 and Table 2-2 below.

Table 1 Tests to Improve the Specificity of PCa Detection

	<i>phi</i> (Access Hybritech)	%fPSA (Access Hybritech)	tPSA (Access Hybritech)
Manufacturer/ Owner	Beckman Coulter	Beckman Coulter	Beckman Coulter
Description	A blood test that combines the results of tPSA, fPSA, and p2PSA to calculate a probability score	A blood test to detect free/total PSA ratio %fPSA= fPSA/tPSA	A blood test to detect total prostate-specific antigen
FDA Approval	Yes (2012)	Yes (2003)	Yes (1994)
NCCN Guidelines	Yes	Yes	Yes
Biopsy Type	Primary Repeat	Primary Repeat	Primary Repeat
Methodology	Immunoassay	Immunoassay	Immunoassay
Diagnostic Accuracy	90% sensitivity 31.1% specificity	90% sensitivity 19.8% specificity	90% sensitivity 10.8% specificity

Source: FDA product label and product IFU's. PSA, prostate-specific antigen; %fPSA, percent free PSA. All diagnostic accuracy data from phi pivotal trial published in Sanda, 2013.¹

Table 2 Select Commercially Available Tests to Aid the Diagnosis of PCa

	PCA3	4Kscore®	ConfirmMDx®
Manufacturer/ Owner	Multiple labs	OPKO lab	MDxHealth
Description	A urine test that measures PCA3 mRNA. The score correlates with the likelihood of repeat biopsy outcome	A blood test that measures four prostate-specific kallikreins and combines results into an algorithm to produce a score for aggressive PCa	A tissue test that measures hyper methylation of three genes to predict PCa on repeat biopsy
FDA Approval	Yes (2012)	Yes (2021)	No
NCCN Guidelines	Yes	Yes	Yes
Biopsy Type	Repeat	Primary Repeat	Repeat
Methodology	Molecular assay	Multianalyte assay with algorithmic analysis (MAAA)	Multianalyte assay with algorithmic analysis (MAAA); Molecular assay
Diagnostic Accuracy	77.5% sensitivity* 57.1% specificity*	74% sensitivity* 60% specificity*	68% sensitivity* 64% specificity*

*Diagnostic accuracy of PCA3, 4KScore and ConfirmMDx came from different populations compared to *phi*, and thus would not be comparable to the diagnostic accuracies noted in Table 2-1.

Source: U.S. Food and Drug Administration label or product website for non-FDA approved tests, Diagnostic accuracy from PMA P100033 for PCA3, Russo, 2017 (4KScore)⁷; Stewart, 2013 (ConfirmMDx)⁷

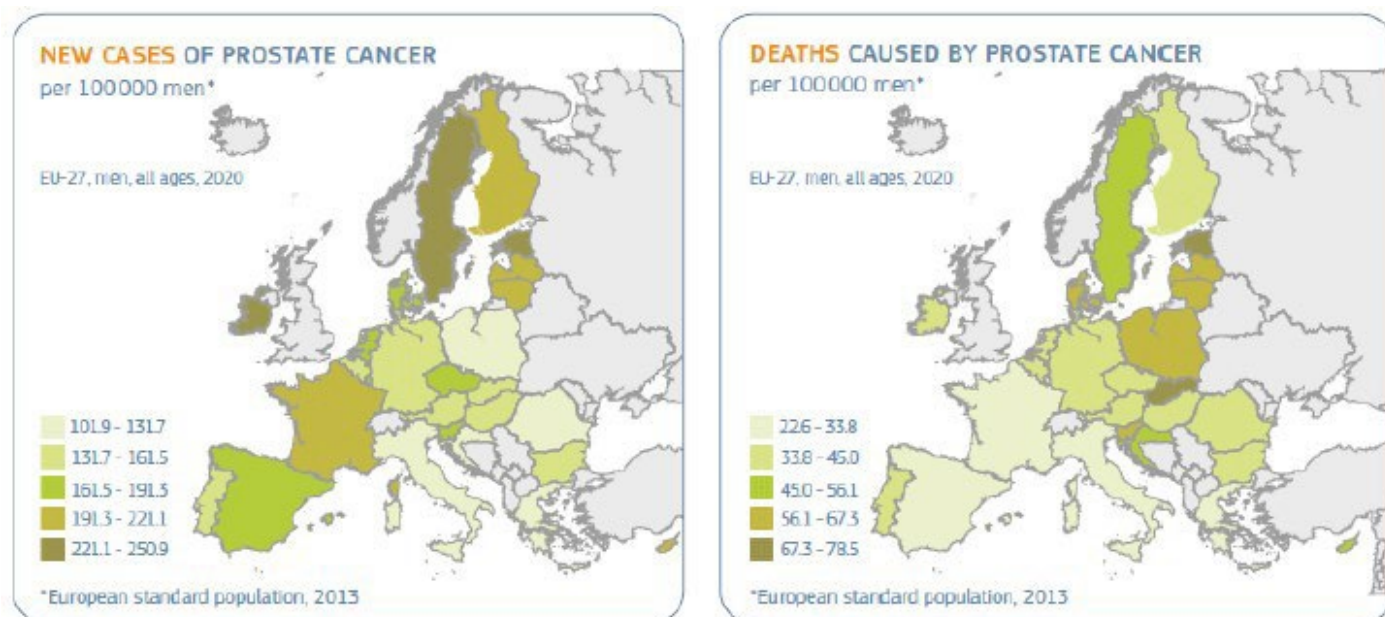
2.2 Place of *phi* in Therapy

2.2.1 Disease Description

2.2.1.1 Epidemiology

Prostate cancer is the second most diagnosed cancer in men, with an estimated 1.4 million diagnoses worldwide in 2020 and is the most frequently diagnosed cancer in 112 countries and the leading cause of cancer death in 48 countries.^{1,2,3} According to the European Cancer Information System (ECIS) data,⁴ it is estimated that, in EU-27 countries in 2020, prostate cancer accounted for 23.2% of all new cancer cases (excluding non-melanoma skin cancers) diagnosed in men and for 9.9% of all deaths due to cancer in men. This made it the most frequently occurring cancer in men and the third cause of cancer death in men, after lung and colorectal cancers.⁴ The variation in the incidence of PCa is driven, in part, by different rates of PSA testing and is influenced by national and international testing guidelines.⁵⁶ While mortality due to PCa has decreased in Europe, the magnitude of reduction varies between countries.

Figure 1 PCa Incidence and Mortality in Europe (per 100,000 men)

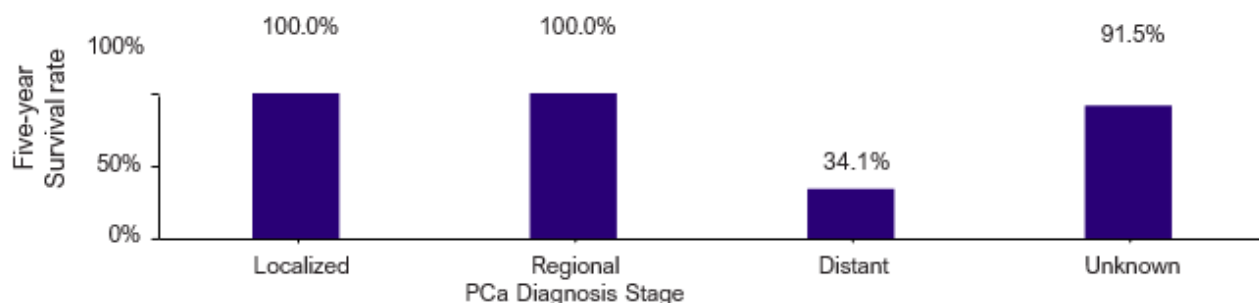


Source: European Cancer Information System Factsheet, 2020

Most prostate cancers in Europe are identified at an early clinical stage, though stage distribution varies by country and registry. While detailed stage-at-diagnosis data across the entire European region are limited, national estimates suggest that metastatic disease at diagnosis comprises a minority of cases (e.g., ~10% in France) (Fizazi 2021). The median age at diagnosis in Europe is around 70 years, consistent with the age-related nature of the disease (Belgian Cancer Registry 2025).

Prostate cancer survival is related to many factors, especially the extent of tumor at the time of diagnosis. The five-year relative survival among men with localized or regional PCa is 100%, compared with 34% among those diagnosed with distant metastases (Figure 2-1).⁹ Thus, an early detection screening program that could accurately identify asymptomatic men with aggressive localized tumors that are then treated appropriately might substantially reduce PCa-related morbidity and mortality.^{10,11}

Figure 2 Five-Year Relative Survival in PCa Patients, by Diagnosis Stage



Source: National Cancer Institute – Cancer State Facts: Prostate Cancer

2.2.1.2 Economic Burden

The total economic cost of prostate cancer in the EU was estimated at €8.43 billion⁷ in 2009 and costs are expected to rise in the future due to increased diagnosis at an earlier stage and increased survival. In 2006, 106-179 million euros (€) were dedicated to PCa management in the European countries exemplified by the UK, Germany, France, Italy, Spain and the Netherlands.⁸ In the same year, for the USA, the total estimated expenditure on prostate cancer was 9.8 billion US dollars, considering \$10,612 versus \$33,691, the mean annual costs per patient in the initial phase after diagnosis versus corresponding costs in the last year of life, respectively.⁸

2.2.1.3 Staging

The most widely used grading scheme for PCa is the Gleason system. The Gleason grade is based solely upon the architectural features of PCa cells and correlates closely with clinical behavior. A higher score indicates a greater likelihood of having a non-organ-confined disease, as well as a worse outcome after treatment of localized disease. The composite Gleason score (GS) is derived by adding together the numerical values for the two most prevalent differentiation patterns (a primary grade and a secondary grade) which is also tied to a histologic grade group classification (Table 2-3).¹⁵ A Gleason score of 6 is low-grade PCa that usually grows slowly; 7 is an intermediate grade; 8 to 10 is high-grade cancer that develops more quickly. Higher Gleason scores are associated with lower five and ten-year survival rates (Table 2-4).¹⁵

Table 3 PCa Histologic Grade Group by Gleason Score

GRADE GROUP	GLEASON SCORE	GLEASON PATTERN
1	≤6	≤3+3
2	7	3+4
3	7	4+3
4	8	4+4, 3+5, 5+3
5	9 or 10	4+5, 5+4, 5+5

Source: AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing. AJCC, American Joint Committee on Cancer; UICC, Union of International Cancer Control

Table 4 PCa-Specific Survival Rates with 95% CI by Gleason Score

GLEASON SCORE	5-YEAR	10-YEAR
2 - 6	99.1 (97.7–99.7)	98.4 (96.7–99.3)
3 + 4	98.9 (95.7–99.7)	92.1 (87.1–95.3)
4 + 3	88.6 (72.3–95.6)	76.5 (58.4–87.5)
8 - 10	86.2 (75.1–92.5)	69.9 (56.9–79.7)

Source: Wright, 2009; CI, confidence interval

The Gleason score has been the preferred system for grading tumors and was incorporated as a critical prognostic factor in the 2010 tumor, nodes, metastasis (TNM) staging system for PCa (Table 2-5).¹⁵

Table 5 PCa TNM Prognostic Stage Group, AJCC/UICC

T	N	M	tPSA	Grade Group	Stage Group
cT1a-c, cT2a	N0	M0	<10	1	I
pT2	N0	M0	<10	1	I
cT1a-c, cT2a, pT2	N0	M0	≥10 <20	1	IIA
cT2b-c	N0	M0	<20	1	IIA
T1-2	N0	M0	<20	2	IIB
T1-2	N0	M0	<20	3	IIC
T1-2	N0	M0	<20	4	IIC
T1-2	N0	M0	≥20	1-4	IIIA
T3-4	N0	M0	Any	1-4	IIIB
Any T	N0	M0	Any	5	IIIC
Any T	N1	M0	Any	Any	IVA
Any T	Any N	M1	Any	Any	IVB

Source: AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing. TNM; tumor, node, metastasis; AJCC, American Joint Committee on Cancer; UICC, Union for International Cancer Control; PSA, Prostate-specific antigen

2.3 Clinical Practice and Guidelines for Testing in PCa

Current clinical practice for PCa detection incorporates serum tPSA testing together with DRE. The main guideline organizations include the National Comprehensive Cancer Network (NCCN), the United States Preventative Services Task Force (USPSTF), the American Urological Association (AUA), and the European Association of Urology (EAU). The relevant guidelines are described below.

The March 2023 European Association of Urology (EAU) guideline⁶ is also endorsed by several other agencies like the European Association of Nuclear Medicine (EANM), European Society for Radiotherapy and Oncology (ESTRO), the European Society of Urogenital Radiology (ESUR), the International Society of Urological Pathology (ISUP), and the International Society of Geriatric Oncology (SIOG).

Table 6 Key EAU Guidelines for Early Detection

Recommendation	Strength rating
Do not subject men to prostate-specific antigen (PSA) testing without counseling them on the potential risks and benefits.	Strong
Offer early PSA testing to well-informed men at elevated risk of having PCa: - men from 50 years of age - men from 45 years of age and a family history of PCa - men of African descent from 45 years of age - men carrying BRCA2 mutations from 40 years of age	Strong
In asymptomatic men with a prostate-specific antigen (PSA) level between 3-10 ng/mL and a normal digital rectal examination (DRE), repeat the PSA test before further investigations	Weak
In asymptomatic men with a PSA level between 3–10 ng/mL and a normal DRE, use one of the following tools for biopsy indication: - risk-calculator, provided it is correctly calibrated to the population prevalence. - magnetic resonance imaging of the prostate	Strong
an additional serum, urine biomarker test.	Weak
Stop early diagnosis of PCa based on life expectancy and performance status; men who have a life-expectancy of < 15 years are unlikely to benefit	Strong

Source: EAU-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on PCa

As per the 2019 NCCN Guidelines,⁹ in cases where biopsies are required to detect prostate cancer, patients and physicians may consider other options to increase the likelihood of cancer detection before proceeding with a biopsy. This is because biopsies pose certain risks. Several biomarker tests are available that can help in this regard. These tests can reduce the need for unnecessary biopsies, improve the accuracy of cancer detection, and ensure that high-grade cancers (Gleason score ≥ 7) are not missed.

The 2023 NCCN PCa Early Detection Guidelines (v1.2023)¹⁰ recommend phi, %fPSA, and 4KScore® for tPSA > 3 ng/mL patients without biopsy. Patients who have negative biopsy results can consider phi, %fPSA, 4KScore, PCA3, and ConfirmMDx. Men with tPSA levels of less than 4 ng/mL have a 15% chance of having prostate cancer, while those with tPSA levels of 4-10 ng/mL have a 25% chance.

2.3.1 Approaches to Diagnosis

There are several alternatives for aiding in the detection of PCa. Each choice has its advantages and disadvantages. A patient should thoroughly discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle. Key alternative practices or procedures used as an aid in the detection of PCa include one or more of the following:

- Physical evaluation and DRE
- Histological examination such as needle biopsy or transurethral resection
- Lymphangiography
- Bone scan
- Serum tPSA and %free PSA (diagnostic biomarker tests)

2.3.1.1 PSA-based biomarkers

Prostate-specific antigen (PSA) is a glycoprotein produced by prostate epithelial cells. PSA exists in blood either in its free form (fPSA) or in a complex with serum protease inhibitors. Free PSA accounts for 5%–35% of total PSA (tPSA) and can occur in three molecular forms: pro-PSA, benign PSA and intact PSA.²⁰

Total PSA levels may be elevated in men with PCa because tPSA production is increased and because tissue barriers between the prostate gland lumen and the capillary are disrupted, releasing more tPSA into the serum.¹⁶ Studies have estimated that tPSA elevations can precede clinical disease by 5 to 10 years^{21,22} or even longer,²³ but the lead-time varies across studies, populations, and screening protocols.¹⁶ However, tPSA is also elevated in some benign conditions like benign prostatic hyperplasia (BPH) and prostatitis.

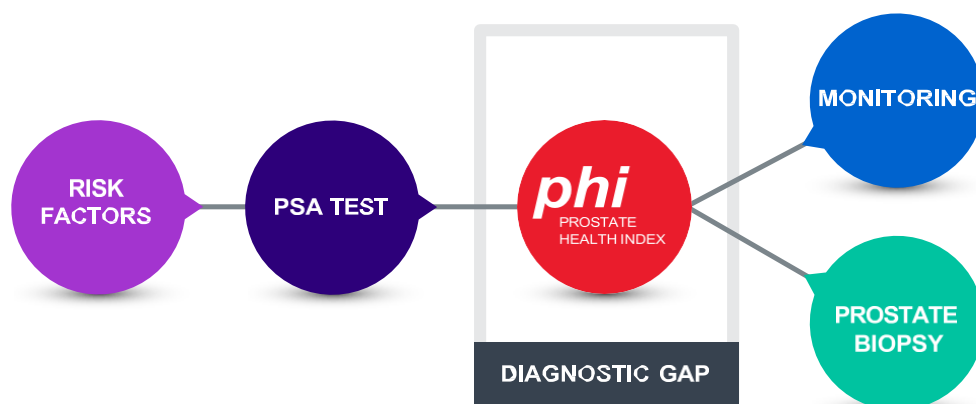
The timing of the tPSA measurement is essential for accurate results. In addition to the tPSA elevations seen with BPH, there are benign transient causes of tPSA elevation.^{24–26} DRE leads to only minimal transient elevations of 0.26 to 0.4 ng/mL, and tPSA can be measured immediately after DRE.^{27,28} Total PSA levels, in conjunction with histologic grade group and TNM information, is used by the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) to determine the prognostic stage group of PCa.¹⁵

2.3.2 Limitations of PSA and %fPSA Biomarkers

PSA is not a cancer-specific marker, and only about 25% of men with tPSA in the 4-10 ng/mL range have a subsequent positive biopsy.^{15,29} Determining the accuracy of PSA testing has been difficult because most men with typical tPSA values will not undergo biopsy unless their DRE is abnormal. This workup bias tends to overestimate the sensitivity and underestimate specificity.³⁰ Performance can also be overestimated because tPSA often detects clinically unimportant cancers. The diagnostic performance of tPSA ideally needs to be calibrated against clinically significant cancers; however, there is no consensus on defining such cancers.³¹ Although many experts consider tumors with Gleason scores ≥ 7 and volumes >0.5 cm³ to have a higher risk for progression, there is no certainty that these cancers will lead to early death or reduce the quality of life.³² Additionally, tPSA has a poor discriminating ability in men with symptomatic BPH.³³

One key limitation of %fPSA is its relatively modest diagnostic specificity, even though it represents an improvement compared to tPSA alone as shown in Table 2-1.³⁴ Furthermore, due to the instability of fPSA compared to complexed PSA, %fPSA exhibits a wide analytical variability limiting its use.^{35,36} These limitations created the need for a more accurate marker than %fPSA or PSA.³⁷

Figure 3 Place of *phi* in the Diagnostic Considerations for PCa





3 Clinical Evidence

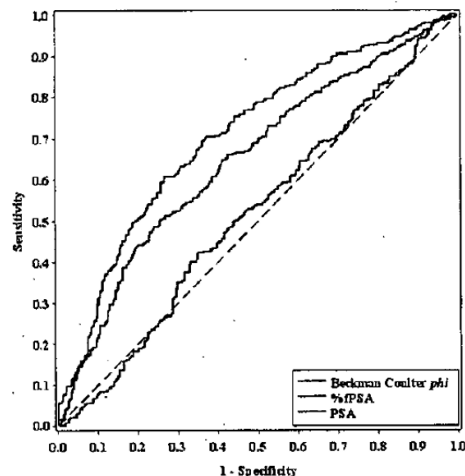
3.1 Clinical Validity of *phi*

The clinical validity of the *phi* has been demonstrated across a substantial body of evidence, including pivotal trials, validation studies, diagnostic studies, systematic reviews and meta-analyses, consistently showing improved discrimination for PCa compared with PSA-based measures alone. The published peer-reviewed evidence consistently demonstrated that *phi* provides improved diagnostic discrimination for PCa, including clinically significant disease, across PSA-based and mpMRI-integrated diagnostic settings, as well as in diagnostically challenging subgroups. These findings were further supported by recent conference abstracts from Italian diagnostic modeling studies, which report high sensitivity for clinically significant PCa detection at commonly evaluated *phi* cut-offs.

Initial clinical validity was demonstrated in a multi-center pivotal trial including 658 men aged 50-84 years with serum tPSA levels of 4-10 ng/mL.^{1,2} In this study, *phi* showed a significant improvement in diagnostic sensitivity and specificity for PCa detection compared with %fPSA (Figure 3-1). At a *phi* cut-off of 27.0, clinical sensitivity was 90% with a specificity of 31.1%, indicating that nearly one in three men could avoid prostate biopsy while maintaining 90% cancer detection.² The area under the ROC curve (AUC) for *phi* (0.708; 95% CI 0.66-0.74) was significantly greater than that for tPSA (0.516; 95% CI 0.47-0.56) and %fPSA (0.648; 95% CI 0.60-0.69; $p < 0.001$).² A strong, graded relationship between increasing *phi* values and the probability of cancer on biopsy was also observed, with cancer risk rising from 9.8%

for $\phi < 27$ to 50.1% for $\phi \geq 55$.²

Figure 4 ROC Curves for ϕ , tPSA, %fPSA in the 4-10ng/mL PSA range



Source: PMA P090026; all cutoffs measured using Hybritech® calibrations

Table 7 Probability of PCa by Range of ϕ values

ϕ RANGE*	PROBABILITY OF CANCER	95% CI
0–26.9	9.8%	5.2%–15.4%
27.0–35.9	16.8%	11.3%–22.2%
36.0–54.9	33.3%	26.8%–39.9%
55.0+	50.1%	39.8%–61.0%

Source: FDA PMA P090026; CI, confidence interval; * ϕ RANGE as calibrated by Beckman Coulter's Hybritech Note: ϕ values should not be interpreted as definitive evidence for the presence or absence of PCa; a prostatic biopsy is required for the diagnosis of cancer.

An expanded multicenter validation study including 892 men with tPSA levels of 2-10 ng/mL further confirmed these findings, demonstrating that increasing ϕ scores were associated with a 4.7-fold increased risk of PCa and a 1.61-fold increased risk of aggressive disease (Gleason score ≥ 7) on biopsy. ϕ outperformed %fPSA in discriminating high-grade disease (AUC 0.724 vs 0.670) and demonstrated superior overall diagnostic accuracy compared with tPSA (AUC 0.703 vs 0.525).³⁸ Investigators concluded that ϕ improves specificity for PCa detection and may reduce unnecessary biopsies in men aged ≥ 50 years with negative DRE findings.³⁸

Table 8 Sensitivity & Specificity PCa Using Various ϕ Cutoffs in Men with Non-Suspicious DRE

% Sensitivity	ϕ Cutoff %	% Specificity (n)
99	17.2	5.2 (24)
98	19.4	8.4 (39)
95	21.3	16.0 (74)
90	24.1dec	26.2 (121)

89.1	25.0	29.4 (136)
85	27.2	39.0 (180)
80	29.3	45.2 (209)
75	31.1	52.6 (243)
70	33.4	60.0 (277)
65	35	65.2 (301)
60	37.5	70.3 (325)
55	39.1	74.2 (343)
50	42.2	79.0 (365)
45	44.3	82.7 (382)
40	46.7	85.7 (396)
35	49.3	87.4 (404)
30	52.6	90.7 (419)
25	55.9	91.8 (424)
20	61.9	93.7 (433)
15	67.6	95.2 (440)
10	78.1	97.6 (451)
5	104.2	100 (462)

More recent diagnostic studies further strengthen the clinical validity of phi, particularly for identifying clinically significant prostate cancer (csPCa) across diagnostically challenging subgroups. In a prospective Italian cohort of 204 men undergoing mpMRI, phi demonstrated superior discrimination for predicting positive imaging findings (PI-RADS ≥ 3), with an AUC of 0.747, outperforming both total PSA and PSA ratio. Importantly, phi remained the only independent predictor of PI-RADS ≥ 3 lesions in multivariable analysis, underscoring its robustness beyond conventional PSA derivatives (Agnello 2024). Consistent findings were reported in a Korean multicenter study of 626 men with PSA levels of 4-10 ng/mL, in which phi-based nomograms achieved AUCs exceeding 0.80 for overall PCa and up to 0.84 for csPCa, confirming high diagnostic accuracy within the PSA grey zone (Chung 2024).

Evidence from diagnostically challenging subgroups further supported the clinical validity of phi. In men with PI-RADS 3 lesions, 24% were diagnosed with PCa on biopsy, of which more than 80% were clinically significant. Mean phi values were significantly higher in men with cancer than in those with benign findings (33.9 vs. 25.8; $p < 0.001$), whereas tPSA and PSA density did not significantly differentiate between the groups. In this cohort, phi achieved an AUC of 0.786 for overall PCa and 0.823 for csPCa, outperforming PSA-based measures (Cui 2023). Similarly, in a large prospective Chinese cohort, phi alone achieved an AUC of 0.779 for PCa detection, comparable to or exceeding the performance of PI-RADS alone and substantially superior to PSA (Huang 2024).

Population-specific analyses highlighted important considerations for interpreting diagnostic performance. In African American men meeting FDA-indicated testing criteria ($n=209$), csPCa prevalence was high (43.5%). In this cohort, phi demonstrated moderate discrimination for csPCa (AUC 0.68; 95% CI 0.61-0.75), suggesting that, while phi retains a prognostic signal, commonly used rule-out thresholds may have limited ability to defer biopsy

in higher-risk populations safely (Morris 2023).

At the evidence-synthesis level, a recent meta-analysis including 49 studies and more than 29,000 patients reported a pooled sensitivity of 0.85 and a specificity of 0.52 for phi in detecting csPCa at representative thresholds, with a diagnostic odds ratio of 6.28. When multiple thresholds were considered, phi achieved higher specificity (~0.72) at the expense of sensitivity (~0.69), highlighting that diagnostic performance is threshold-dependent (Kawada 2024).

More recently, conference abstracts from two Italian diagnostic modeling studies provide supportive evidence consistent with the published literature, reporting high sensitivity for csPCa detection ($\geq 91\%$) at phi cut-offs of 25 and 28 in men with PSA levels of 2-10 ng/mL, with positive phi results confirmed by biopsy (Borisenko 2024a; 2024b).

3.1.1.1 Pooled Data

Eight (Table 3-2) relevant meta-analyses demonstrated the diagnostic accuracy of *phi* in the detection of overall PCa.

Table 9 Pooled Diagnostic Accuracy of *phi* in the detection of PCa

Study ID	Details	Pooled Estimates for <i>phi</i>	Conclusions
Agnello, 2022³⁹	42 studies, 14,255 patients; search up to Jan 2022	PCa: Ss: 0.791 (0.739-0.834); Sp: 0.625 (0.560-0.686)	<i>phi</i> has a high accuracy for detecting PCa and discriminating between aggressive and non-aggressive PCa.
Jia, 2021⁴⁰	20 studies, 10,376 patients; search up to Feb 2020	PCa: Ss: 0.88 (0.86-0.90); Sp: 0.36 (0.34-.0.38); AUC: 0.76	<i>Phi</i> has an acceptable result for the detection of overall and clinically significant PCa. Also analyzed PCA3.
Kawada, 2024	49 studies, 29,000 patients; search up to 2023	PCa: Ss: 0.85 (0.80-0.89); Sp: 0.52 (0.43-0.60); AUC: 0.78	Phi demonstrated moderate diagnostic accuracy in detecting clinically significant prostate cancer (PCa).
Study ID	Details	Pooled Estimates for <i>phi</i>	Conclusions
Zhang, 2019⁴¹	20 studies, 5,543 patients.	PCa: Ss: 0.75 (0.70-0.79); Sp: 0.69 (0.58-.0.83); AUC: 0.78 (0.74-0.81)	Moderate diagnostic accuracy. Asians might have slightly better accuracy (AUC 0.83 vs. 0.76) compared to Caucasians but results not significant.
Russo, 2017⁴²	23 studies, 16,762 patients, search until July 2016	PCa: Ss: 0.89 (0.88-0.90); Sp: 0.34 (0.32-.0.35); AUC: 0.76	phi has moderate accuracy for detecting overall PCa and high-grade PCa. This study also analyzed 4K score.

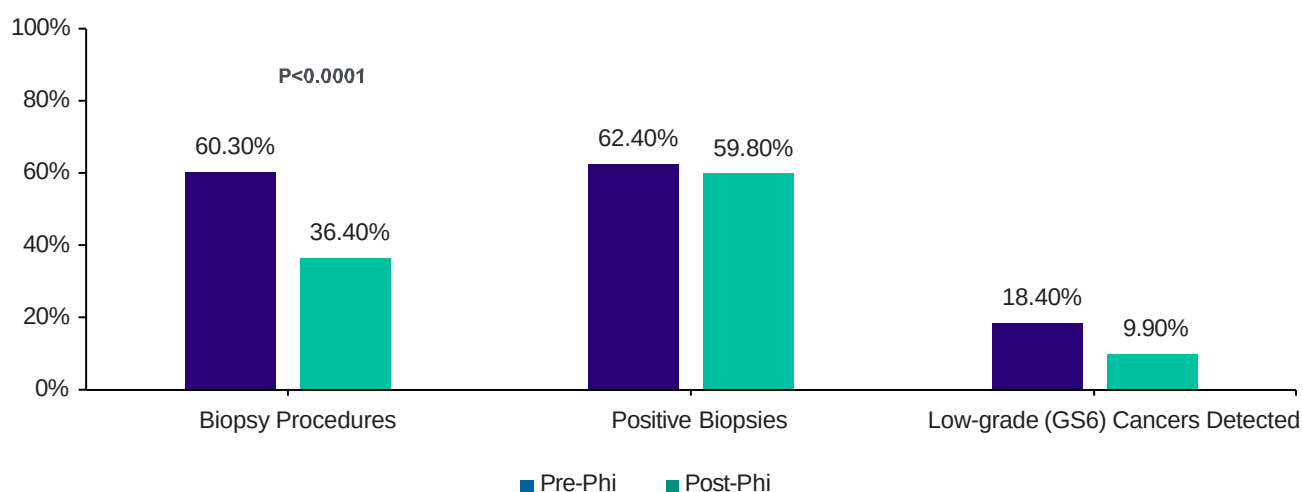
Liu, 201443	12 studies, 1,430 patients with PCa and 2159 benign PCa controls, search up to 2014	PCa: Ss: 0.551 (0.525-0.577); Sp: 0.715 (0.695.-0.734); AUC: 0.757	Study focuses on the ability of phi to predict biopsy results
Bruzzese, 201444	8 studies, 2969 patients, up to Dec 2013	PCa: AUC: 0.74 (0.70-0.77). Does not report pooled Ss and Sp.	This study also analyzed results of %fPSA (fPSA/tPSA*100). Meta-regression analysis confirmed the superiority of phi compared with %fPSA.
Wang, 201445	16 articles, 6,279 patients, search up to March 2014	PCa: Ss: 0.85 (0.83-0.86); Sp: 0.45 (0.44.-0.47); AUC: 0.70 (0.65-0.74)	Study also analyzed %p2PSA (p2PSA/ fPSA*100)
Filella, 201346	8 studies. 2,919 patients, search until December 2011	PCa: Ss: 0.90 (0.83-0.86); Sp: 0.316 (0.292.-0.340); AUC:(0.703-0.77)	phi improves the accuracy of PCa detection in comparison with PSA or %fPSA, particularly in patients with PSA of 2 µ g/L-10 µ g/L. Also analyzed the results for [-2]proPSA.

3.2 Clinical Utility of *phi*

Phi is intended to help physicians make more appropriate biopsy decisions for men presenting with serum tPSA in the 4–10 ng/mL range and non-suspicious DRE findings. These men are often referred to as being in a ‘diagnostic grey zone’ since typically less than 25% of such men who are biopsied are found to be positive for PCa.¹⁶ Appropriate utilization of phi can help reduce the number of unnecessary biopsy procedures performed for men deemed to be at low risk when the phi test result is considered along with other standard clinical risk factors.

A prospective observational study demonstrated this benefit in actual clinical practice.³ The multi-center study compared over 500 men tested with phi to a historical control group of similar men who met the same criteria and were seen by the same participating urologists within the previous 24 months, and before the commercial implementation of phi testing in their practice. According to the findings, men receiving a phi test showed nearly a 24% reduction in biopsy procedures compared to the historical control group, with a decrease in the rate of low-grade (Gleason score 6) cancers detected (Figure 3-3).³

Figure 5 Real-world Biopsies and Pathological Findings Before and After *phi*

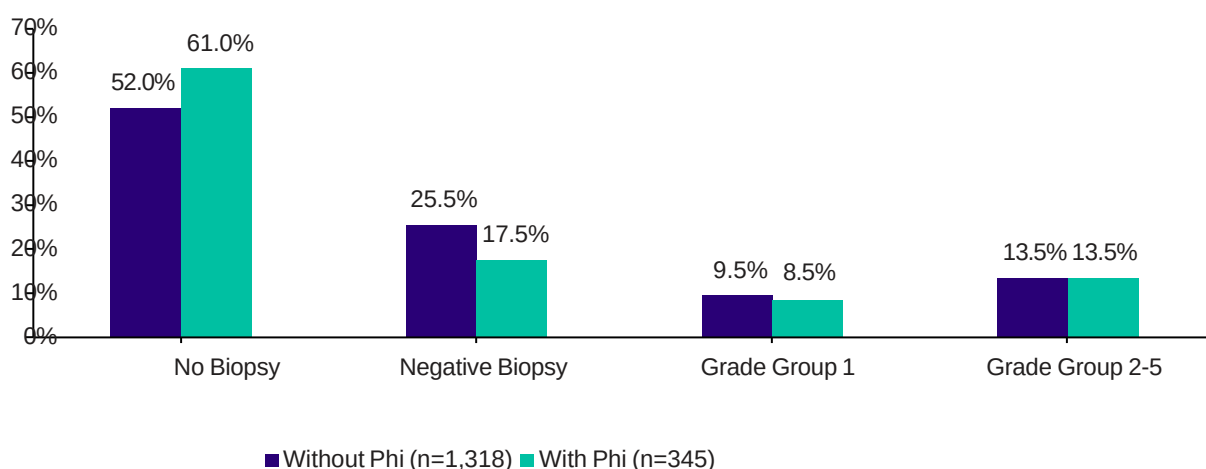


Source: White, 2017

Furthermore, physicians reported that the phi score significantly impacted their patient management plan in over 73% of cases, including biopsy deferrals when the phi score was low, and decisions to perform biopsies when the phi score indicated an intermediate or high probability of PCa (phi ≥ 36).³ The study investigators concluded that phi testing provides valuable information that can significantly modify physician behavior patterns and improve their ability to diagnose and manage their patients.

Consistent findings were reported in an independent prospective registry from a large academic practice at Johns Hopkins University (JHU).⁴ *phi* was tested in 345 patients presenting for the diagnostic evaluation of PCa by their serum tPSA findings. Overall, 39% of men in the prospective registry underwent a biopsy when *phi* was included in the assessment, representing a 9% reduction (Figure 3-4) in the rate of prostate biopsy compared to historical practice.⁴ The *phi* score was further shown to correlate with pathological grading for those men who did undergo a biopsy. For example, 91% of men with *phi*<27 who underwent a biopsy had either a negative biopsy result or low-grade GG1 pathology, whereas 76% of men with *phi* > 55 had GG2 or higher cancers; 8% had GG1 cancer, and 16% had a negative biopsy result.⁴ According to JHU's comparative analysis, *phi* reduced their rate of unnecessary biopsies without changing the frequency of higher-grade cancers detected.⁴

Figure 6 Biopsy Outcomes by *phi* Testing Status



Source: Tosoian, 2017

More recent studies extend this evidence to contemporary, imaging-integrated diagnostic pathways. In a prospective Italian mpMRI triage study, a *phi* cut-off of 30 achieved a sensitivity of approximately 90% for predicting PI-RADS ≥ 3 lesions, supporting the use of *phi* as a pre-imaging triage tool to prioritize mpMRI for men most likely to benefit and to defer imaging in lower-risk individuals (Agnello 2024). In a population-based screening program in Hong Kong, the sequential use of *phi* and mpMRI significantly reduced downstream investigations, with approximately half of men with PSA ≥ 4 ng/mL avoiding biopsy while maintaining clinically meaningful detection of prostate cancer (Chiu 2023).

Clinical utility has also been demonstrated in shared decision-making and combined biomarker strategies. In a US cohort, men with both positive *phi* (≥ 36) and positive ExoDx results had a 75% likelihood of PCa on biopsy, with more than half having Gleason score ≥ 7 disease. In contrast, discordant or double-negative results were associated with significantly lower cancer rates. Although concordance between *phi* and ExoDx was low ($\kappa = 0.19$), *phi* independently influenced biopsy recommendations and patient compliance (Dudinec 2023).

In high-risk populations, Cussenot et al. (2023) demonstrated that phi added value when mpMRI was negative. Among men with hereditary or familial risk, mpMRI alone achieved high sensitivity for csPCa (96% at PI-RADS ≥ 3), but phi and PSA density helped guide biopsy decisions when imaging was negative, improving detection of ISUP grade >1 cancers without reverting to PSA-only strategies (Cussenot 2023).

In the Italian prospective study, phi-based triage identified approximately half of patients with PI-RADS <3 lesions, indicating the potential to reduce unnecessary mpMRI utilization in routine practice significantly (Agnello 2024). In the Hong Kong public healthcare system, a long-term follow-up study of more than 2,800 men demonstrated that the availability of phi led 83% of men with elevated PSA to opt out of immediate biopsy, significantly reducing biopsy volume. Higher baseline phi predicted subsequent detection of clinically significant cancer over a two-year period, suggesting that deferred biopsy decisions were clinically appropriate rather than harmful (Chiu 2025).

In biopsy-naïve European studies, approximately half of biopsies were shown to be safely avoided using phi-integrated models without missing csPCa (Cussenot 2023, Esteban 2025). In Asian (Cui 2023, Huang 2024) and US (Dudinec 2023) settings, phi helped concentrate biopsies in patients at a higher risk, improving biopsy yield and reducing exposure to unnecessary invasive procedures. These reductions translated directly into fewer biopsy-related complications, lower downstream imaging use, and improved efficiency of diagnostic pathways.

The clinical utility of phi was evident in a study of men with equivocal mpMRI findings (Leung 2024). In 747 men who underwent mpMRI, 353 (47.3%) had PI-RADS 3 lesions only, and all underwent phi testing prior to MRI–US fusion biopsy. In this PI-RADS 3-only group, csPCa detection (ISUP grade group ≥ 2) was 15.0% (53/353). Phi meaningfully separated risk: csPCa rates were 5.3% for phi <25 , 7.4% for phi 25–34.9, 17.9% for phi 35–54.9, and 52.6% for phi ≥ 55 ($P < 0.01$). The authors estimated that 26.9% of men could avoid biopsy if a phi <25 threshold were used at the trade-off of a 5.3% csPCa rate in that low-phi group (Leung 2024).

Pathway-level analyses from an Italian diagnostic modeling study indicate that strategies incorporating phi can optimize diagnostic sequencing. Compared with mpMRI alone, mpMRI followed by phi strategies maximized detection of clinically significant disease, while phi-first approaches reduced unnecessary biopsies and imaging utilization (Borisenko 2024b).

3.3 Detection of Clinically Significant PCa using *phi*

Several studies have investigated the accuracy of phi in predicting clinically significant PCa, commonly defined as a biopsy Gleason score of 7 or higher.

Several meta-analyses have evaluated the diagnostic performance of phi for csPCa, consistently demonstrating high sensitivity with moderate specificity. Across five meta-analyses summarized in Table 3-3, pooled sensitivity for csPCa detection generally ranged from approximately 77% to 95%, while pooled specificity ranged from 17% to 64%, depending on the phi cut-off applied. At lower cut-offs (25-30), phi achieved high sensitivity (up to 95%), whereas higher cut-offs (≥ 35 -55) improved specificity (up to 87%) with a corresponding reduction in sensitivity (Pino-Sedeño 2022, Agnello 2022, Jia 2021, Russo 2017, Wang 2014).

Evidence from recent prospective studies further demonstrated that phi meaningfully discriminated risk of csPCa across clinically relevant strata. In a population-based screening cohort, Chiu et al. (2023a) reported that csPCa (ISUP Grade Group ≥ 2) was detected in only 0.7% of men with phi <35, compared with up to 8.6% among those with phi ≥ 35 , representing a more than ten-fold difference in risk. Similarly, in a Taiwanese grey-zone imaging study, phi outperformed PSA and PSA derivatives for csPCa detection, achieving an AUC of 0.85. The incremental diagnostic value of phi was particularly evident in men with PI-RADS 3-4 lesions, where phi significantly improved discrimination of clinically significant disease and reduced diagnostic uncertainty (Chiu 2023b).

Detection of aggressive disease was a consistent strength of phi-based strategies. In the PI-RADS 3 cohort studied by Cui et al., phi and phi density achieved AUCs of 0.823 and 0.796, respectively, for csPCa, significantly higher than PSA (AUC 0.587). Over 80% of detected cancers in this cohort were clinically significant, reinforcing the clinical relevance of PHI-guided biopsy decisions (Cui 2023). Consistent findings were observed in a Spanish prospective study by Esteban et al. (2025), in which a multivariable model integrating phi, PSA density, age, and PI-RADS score achieved an AUC of 0.841 for csPCa prediction. At the selected risk threshold, this model demonstrated 100% sensitivity for csPCa while avoiding approximately half of biopsies (49.4%) (Esteban 2025).

Risk stratification by phi categories has also been shown to be clinically meaningful in real-world settings. In men with PI-RADS 3-only findings, Leung et al. (2024) demonstrated a significant gradient in csPCa probability across phi strata, reaching 52.6% for phi ≥ 55 , compared with 5.3% for phi <25. This risk gradient provides actionable information for clinician–patient counseling in the PI-RADS 3 grey zone (Leung 2024). In contrast, in African American men with a high baseline prevalence of csPCa (43.5%), Morris et al. (2023) reported more modest overall discrimination (AUC 0.68), with only the highest phi category (≥ 55) remaining independently associated with csPCa on multivariable analysis (OR 5.7, $p < 0.01$).

A recent meta-analysis by Kawada et al. (2024), further reinforced the role of phi as a csPCa enrichment tool. The pooled sensitivity and specificity for csPCa detection were 0.85 and 0.52, respectively, with a summary AUC of 0.78. Analyses incorporating multiple thresholds

demonstrated that higher specificity (~0.72) could be achieved at the cost of reduced sensitivity (~0.69) (Kawada 2024).

Findings from an Italian economic analysis were directionally consistent with the clinical literature. In the analyses, mpMRI followed by phi strategies did not miss any csPCa cases per 100 patients modeled, regardless of phi cut-off, whereas mpMRI-only strategies consistently missed at least one csPCa case. Phi-only strategies detected csPCa but showed limited incremental benefit over mpMRI in identifying aggressive disease (Borisenko 2024a).

Table 10 Pooled diagnostic accuracy of *phi* in detection of clinically significant PCa

Study ID	Details	Pooled Estimates for <i>phi</i>	Conclusions
Pino-Sedeno, 2022 ⁴⁷	16 studies, 2,994 patients. Search up to	csPCa: Ss and Sp by cutoff 25-30: Ss 0.95, Sp 0.33, AUC: 0.76 30-35: Ss 0.87, Sp: 0.49, AUC: 0.76 35-40: Ss 0.79, Sp 0.56, AUC: 0.69 55: Ss 0.42, Sp 0.87, AUC: 0.60	<i>phi</i> had higher sensitivity in Asian patients, followed by African American and European patients at cut-offs between 25-35
Agnello, 2022 ³⁹	18 studies, 14,255 patients; search up to Jan 2022	csPCa: Ss 0.874 (0.803–0.923), Sp 0.569 (0.458–0.674)	<i>phi</i> has a high accuracy for detecting PCa and discriminating between aggressive and non-aggressive PCa.
Jia, 2021 ⁴⁰	20 studies, 10,376 patients; search up to Feb 2020	csPCa: Ss 0.77 (0.71–0.82), Sp 0.64 (0.61–0.67); AUC: 0.77	<i>phi</i> has an acceptable result for the detection of overall and clinically significant PCa. Also analyzed PCA3.
Russo, 2017 ⁴²	23 studies, 16,762 patients, search until July 2016	csPCa: Ss 0.93 (0.90–0.95), Sp 0.26 (0.26–0.28); AUC: 0.82	<i>phi</i> has moderate accuracy for detecting overall PCa and high-grade PCa. This study also analyzed 4K score.
Wang, 2014 ⁴⁵	16 articles, 6,279 patients, search up to March 2014	csPCa: Ss 0.90 (0.87–0.92), Sp 0.17 (0.14–0.19); AUC: 0.67 (0.57-0.77)	Study also analyzed %p2PSA (p2PSA/fPSA*100)

3.4 Integration of *phi* in Clinical Risk Calculators

Evidence from multiple studies supports integrating the phi into multivariable clinical risk calculators to improve individualized risk prediction and guide diagnostic decision-making.

Several published studies, predominantly conducted in non-US populations, have evaluated the incremental contribution of phi when added to clinical risk models that incorporate age, PSA, prostate volume, and biopsy history.⁴⁸⁻⁵³ Across these studies, incorporation of phi consistently improved model discrimination for PCa and csPCa compared with models based on clinical variables alone, supporting its role as a complementary biomarker within multivariable prediction tools.

More robust prospective evidence was provided by a Beckman Coulter–sponsored multicenter study conducted in the US, which evaluated the impact of incorporating phi into a clinical risk model in men with tPSA values of 2-10 ng/mL and non-suspicious DRE. In this cohort of 892 men, 79.2% were biopsy-naïve, 17.8% had undergone a prior biopsy, and 3% had an unknown biopsy history. All participants underwent prostate biopsy irrespective of phi value, and both investigators and participants were blinded to phi results. The primary endpoint was the detection of aggressive prostate cancer, defined as a biopsy Gleason score ≥ 7 . A multivariable model including age, prior biopsy status, prostate volume, PSA, and phi demonstrated significantly improved discrimination with inclusion of phi, increasing the AUC from 0.695 to 0.746 ($p = 0.005$). This performance was superior to that of the modified Prostate Cancer Prevention Trial (PCPT) risk calculator (AUC 0.577; $P < 0.001$) and the European Randomized Study of Prostate Cancer (ERSPC) risk calculator (AUC 0.650; $P < 0.001$), highlighting the added predictive value of phi within established risk frameworks.⁵⁴

Beyond formal risk calculators, multiple studies supported the integration of phi at key decision points within imaging-integrated diagnostic pathways. Evidence from Italy (Agnello 2024) and Hong Kong (Chiu 2025) indicated that phi can be effectively positioned before mpMRI to prioritize imaging resources for men at higher risk, while studies from Taiwan (Chiu 2023b) and South Korea (Chung 2024) support its use alongside mpMRI to refine biopsy decisions in patients with equivocal imaging findings. In the Taiwanese cohort, adding phi to mpMRI significantly improved diagnostic accuracy for csPCa and enabled biopsy avoidance in approximately 35% of patients without compromising detection of aggressive disease (Chiu 2023b). Similar conclusions were drawn in the South Korean study evaluating combined phi-mpMRI nomograms (Chung 2024).

Risk-calculator-based stratification using phi has shown value in clinically challenging imaging scenarios. In men with PI-RADS 3 lesions, phi provided a clear gradient of csPCa risk, increasing from single-digit percentages at $\phi < 35$ to approximately 18% at $\phi 35-54.9$ and exceeding 50% at $\phi \geq 55$, enabling more nuanced biopsy decisions within this equivocal group (Leung 2024). Conversely, in men with negative mpMRI findings or prior negative targeted biopsy, phi contributed additional risk information, with prostate cancer detected in 25.2% of men without an MRI index lesion (Jeon 2025).

Meta-analytic evidence supported the need for integrated decision-making strategies. Kawada et al. (2024) concluded that optimal diagnostic performance was unlikely to be achieved with liquid or imaging biomarkers in isolation, and that combination strategies were required to balance sensitivity for csPCa detection with avoidance of unnecessary biopsy (Kawada 2024).

Subgroup-specific analyses further indicated that integration of phi into risk calculators may require contextual calibration. In African American men, where baseline csPCa prevalence is

high, commonly applied low phi thresholds provided limited biopsy reduction despite high sensitivity, suggesting that risk-calculator thresholds incorporating phi may need adjustment in higher-risk populations (Morris 2023).

Evidence from recent conference abstracts using modeled diagnostic pathways demonstrated that phi can be flexibly integrated either before or after mpMRI within risk-based strategies. Phi-first approaches act as an effective triage tool to reduce mpMRI utilization, whereas mpMRI-first strategies with reflex phi testing maximize clinical sensitivity for csPCa at a higher cost. These findings align with real-world diagnostic decision points and reinforce the role of phi as a component of integrated risk-based pathways rather than a replacement for existing modalities (Borisenko 2024b, Bromilow 2025).

3.5 Integration of *phi* with other detection technologies

3.5.1 Multiparametric MRI

Three studies were conducted to evaluate the diagnostic ability of phi and mpMRI in detecting prostate cancer. Across multiple studies, combining phi with mpMRI metrics has been shown to improve diagnostic performance and/or reduce unnecessary biopsies compared with reliance on imaging or PSA-derived measures alone. The first study conducted in the U.S. revealed that phi and PSA density can improve the detection of prostate cancer, and phi may be superior to PSA density in moderate-risk lesions.⁵⁵ The second study conducted in Italy found that phi was more effective than PIRADS in predicting positive biopsy results, while both had comparable effectiveness in identifying pathological clinically significant prostate cancer.⁵⁶ The third study conducted in the Czech Republic showed that phi had a better accuracy in predicting clinically significant prostate cancer compared to PIRADS.⁵⁷

The US study⁵⁵ compared the effectiveness of phi and PSA density as secondary tests after multiparametric magnetic resonance imaging (mpMRI) to detect prostate cancer in a multiethnic biopsy-naïve population. The study included 143 men, of whom 65 (45.5%) were Black. Results showed that a Phi score of ≥ 49 prevented unnecessary biopsies in 55% of men with no missed cancer.⁵⁵ Findings suggested that phi may be superior to PSA density in PIRADS 3 lesions by avoiding 55% of unnecessary biopsies.⁵⁵

A study conducted in Italy by Ferro et al.⁵⁶ aimed to evaluate the effectiveness of phi and mpMRI in predicting the likelihood of positive biopsy results and high-grade prostate cancer (PCa) during radical prostatectomy (RP). The study involved 196 individuals who had never undergone a biopsy before and had an mpMRI. Of these, 116 subjects who were confirmed to have PCa through biopsy underwent surgery. The study found that the phi was significantly more effective than both PI-RADS score and phi density in predicting positive biopsy results, with a cut-off value of 43 being the best threshold for phi. In contrast, when it

came to identifying clinically significant prostate cancer (csPCa) during RP, both $\phi \geq 61$ and PI- RADS score ≥ 4 were effective in identifying csPCa (Gleason score ≥ 7 (3 + 4)) either on their own or when added to a base model which included factors such as age, PSA, fPSA-to-tPSA ratio, and prostate volume.⁵⁶ In conclusion, the study found that ϕ had a better ability to predict positive biopsy results compared to PI-RADS score, whereas they had comparable effectiveness in identifying pathological csPCa.⁵⁶

A study conducted in the Czech Republic by Stejskal and colleagues⁵⁷ compared the diagnostic ability of ϕ and mpMRI for detecting clinically significant prostate cancer (csPCa). The study was conducted on 395 men who were scheduled for a prostate biopsy. Before the biopsy, the men underwent an mpMRI of the prostate using PIRADS v1 criteria, and ϕ was measured. Suspicious lesions were then examined using software fusion-guided biopsy with 12-core systematic biopsy in all patients. The study evaluated PCa detection using total PSA, PSA density, PIRADS score, and ϕ . The AUC was calculated for all criteria and a combination of PIRADS score and ϕ . Sub-analyses were performed on patients undergoing their first and repeat biopsies. The results showed that ϕ had an AUC of 69.7 for predicting the presence of csPCa in all patients, while PIRADS had an AUC of 62.5. In patients who had not undergone a biopsy before, the AUC for ϕ was 68.9, and for PIRADS it was 63.1.⁵⁷ In patients with a previous negative biopsy, the AUC for ϕ and PIRADS was 71.2 and 69.3, respectively.⁵⁷ The study found that adding ϕ to PIRADS significantly increased the accuracy for predicting csPCa ($p = 0.007$).⁵⁷ There is additional published evidence (including Asian population) that suggests that combining ϕ with mpMRI improves diagnostic performance in prostate cancer detection.⁵⁸⁻⁵⁹

More recent evidence highlighted the value of combining ϕ with quantitative imaging parameters and multivariable prediction models. Huang et al. (2024) showed that a nomogram integrating ϕ with ADC improved diagnostic accuracy beyond either parameter alone. In men with PI-RADS 3 lesions, the combined model achieved AUCs of 0.817-0.904 for overall prostate cancer and 0.856-0.871 for csPCa across training and validation cohorts. Applying this strategy was estimated to avoid ~50% of biopsies, at the cost of missing ~7% of csPCa (Huang 2024). Similarly, Esteban et al. (2025) reported that ϕ -mpMRI models outperformed simplified sequential strategies (e.g., ϕ -only or PI-RADS-only), particularly in balancing biopsy avoidance with maintenance of sensitivity for aggressive disease, supporting the positioning of ϕ as a tool that refines equivocal imaging rather than replacing mpMRI (Esteban 2025).

3.6 Comparison of *ϕ* with Other PCa Biomarkers

Several head-to-head studies comparing ϕ to PCA3 and 4Kscore were identified. Comparative evidence assessing the performance of the ϕ relative to other PCa biomarkers is based on a combination of direct head-to-head studies conducted within the same patient cohorts and systematic reviews and meta-analyses. While true head-to-head

comparisons remain limited for many biomarkers, the available evidence indicated that phi performed at least as well as other established serum- and urine-based PCa biomarkers for the detection of clinically significant disease. Differences between biomarkers were driven by threshold selection and the relative emphasis on sensitivity versus specificity, rather than by large differences in overall discriminatory ability. Recent meta-analytic evidence positioned phi among the better-performing commercial biomarkers for csPCa detection, with a favorable balance between sensitivity and specificity that supports its use as part of integrated, risk-based diagnostic pathways.

3.6.1 PCA3

Many same-study comparisons of phi with PCA3 have been published (Table 3-4); all studies reported phi and PCA3 had a statistically similar diagnostic performance for predicting biopsy outcome. Several studies directly compared phi with the PCA3 test, primarily in repeat-biopsy or mixed-biopsy populations. Results across these studies have been variable. In some cohorts, PCA3 demonstrated numerically higher discrimination for overall biopsy outcome, while in others, phi showed comparable or superior performance. For example, Seisen et al. (2015) reported higher AUC values for PCA3 than phi in predicting biopsy outcome (0.71 vs 0.65; $p=0.03$), whereas Scattoni et al. (2013) reported higher AUCs for phi than PCA3 in a repeat biopsy setting (0.73 vs 0.63; $p=ns$). Overall, these studies suggested similar performance for phi and PCA3, with no consistent advantage across populations or clinical settings.

In a more recent multiple-threshold diagnostic meta-analysis comparing commercial PCa biomarkers, PCA3 demonstrated the lowest overall performance for csPCa detection among included tests, with a summary AUC of approximately 0.73. The authors concluded that PCA3 was generally less performant than newer liquid biomarkers, including phi, for identifying clinically significant disease (Kawada 2024).

Table 11 Head-to-head Comparisons of PCA3 and *phi*

	POPULATION & GEOGRAPHY	DIAGNOSTIC ACCURACY (AUC)
Seisen, 2015 ⁶⁰ (n=138)	>50y, initial biopsy, tPSA 4-20 ng/ml or abnormal DRE, no 5- α reductase or invasive treatment, prostatitis, renal failure or hemophilia (France)	PCA3: 0.71 vs. <i>Phi</i> : 0.65 $p=0.03$
Stephan, 2013 ⁶¹ (n=246)	tPSA 0.5-20 ng/ml scheduled for biopsy due to suspicious DRE or ultrasound findings, no UTIs or no 5- α reductase treatment (Germany)	PCA3: 0.74 vs. <i>Phi</i> : 0.68, $p=ns$
Scattoni, 2013 ⁶² (n=211)	tPSA 2-15ng/ml and/or positive DRE scheduled for an initial or repeat biopsy (Italy)	<u>Initial biopsy</u> PCA3: 0.59 vs. <i>Phi</i> : 0.70, $p=ns$ <u>Repeat biopsy</u> PCA3: 0.63 vs. <i>Phi</i> : 0.73, $p=ns$
Ferro, 2013 ⁶² (n=300)	>50y, tPSA 2-20ng/ml, negative DRE, with no prior history of prostate surgery or biopsy, no prostatitis, no 5- α -reductase inhibitor use in the previous six months (Italy)	PCA3: 0.73 vs. <i>Phi</i> : 0.77, $p=ns$

Perdona, 2012 ⁶³ (n=160)		PCA3: 0.66 vs. <i>Phi</i> : 0.71, p=ns
Ferro, 2012 ⁶⁴ (n=251)		PCA3: 0.71 vs. <i>Phi</i> : 0.77, p=ns

Note: AUC, area under the curve; PCA, prostate cancer antigen, UTI, urinary tract infection; DRE, digital rectal examination; ns, not significant

A 2015 review of the literature by the UK NICE concluded that the implications of adding the PCA3 (10 studies) or the *phi* (4 studies) biomarker to clinical assessment remained unclear and could not identify a single threshold value for use in a clinical setting.⁶⁵

3.6.2 4KScore

Comparative evidence between *phi* and 4Kscore is more extensive, including both head-to-head studies and meta-analyses. A large meta-analysis including 28 studies and 16,762 patients reported comparable overall diagnostic accuracy for *phi* and 4Kscore.⁴² Derived HSROC AUCs were 0.76 for *phi* and 0.72 for 4Kscore for overall PCa detection, and 0.82 and 0.81, respectively, for detection of high-grade PCa. For high-grade disease, pooled sensitivity was higher for *phi* (0.93 vs. 0.87 for 4Kscore), whereas pooled specificity was higher for 4Kscore (0.61 vs 0.34).⁴² These findings were supported by a Swedish head-to-head cohort study of 531 men, in which AUCs for overall PCa detection were similar for *phi* and 4Kscore (0.704 vs 0.690), as were AUCs for high-grade disease (0.711 vs 0.718).⁶⁶

More recent comparative evidence was provided by Kawada et al. (2024), who synthesized performance across multiple commercial biomarkers using both representative thresholds and multiple-threshold approaches. Using representative thresholds, pooled sensitivity and specificity for csPCa detection were 0.85 and 0.52 for *phi* and 0.87 and 0.58 for 4Kscore, respectively, with 4Kscore demonstrating the highest diagnostic odds ratio. In the multiple-threshold analysis, 4Kscore showed the highest sensitivity, whereas *phi* demonstrated the highest specificity among the compared biomarkers, reinforcing that relative performance depends on whether a diagnostic pathway prioritizes minimizing missed csPCa or avoiding unnecessary biopsy (Kawada 2024).

3.6.3 Prostate Health Index Density

Several studies have examined the effectiveness of *phi* and Phi density (PhiD) in diagnosing prostate cancer, but the evidence for PhiD is mixed. Four studies, conducted in Lithuania⁶⁷, Spain,⁶⁹ Portugal,⁶⁹ and China,⁷⁰ found that both *phi* and PhiD were useful in predicting clinically significant prostate cancer, but *phi* was the most accurate predictor. However, two studies carried out in Germany⁷¹ and Singapore⁷² concluded that PhiD did not offer significant incremental benefits over *phi*. On the other hand, a study from the US⁷³ found that PhiD was superior to *phi* alone in terms of its discriminative ability for clinically significant disease. A systematic review of nine studies⁷⁴ comparing PhiD to *phi* that aimed to evaluate the diagnostic accuracy of both assays in the detection of csPCa concluded that PhiD did not consistently outperform *phi* and had lower clinical utility in the diagnosis of PCa.

3.6.4 Comparison with Other Molecular Biomarkers (SelectMDx, ExoDx, MPS)

Direct head-to-head studies comparing phi with newer molecular tests such as SelectMDx, ExoDx, and MyProstateScore (MPS) remain limited. However, indirect comparative evidence from recent meta-analyses provided some additional context. In the meta-analysis by Kawada et al. (2024), pooled sensitivity and specificity for csPCa detection at representative thresholds were 0.82/0.56 for SelectMDx, 0.85/0.54 for ExoDx, and 0.82/0.59 for MPS, compared with 0.85/0.52 for phi (Kawada 2024). These findings indicate broadly similar diagnostic performance across several modern biomarkers, with differences reflecting threshold selection and the balance between sensitivity and specificity rather than a clear superiority of one test across all settings.



4 Economic Value & Modeling Report

4.1 Modeling Overview

4.1.1 Use of Modeling for Decision-Making

A model is a structured representation of real-world healthcare activities, incorporating event probabilities, resource utilization, costs, and patient outcomes.⁷⁵ Economic models are used to evaluate the impact of an intervention on costs and other outcomes under conditions of uncertainty.⁷⁵ In the absence of empirical data, economic models can allow decision-makers to define treatment options and likely outcomes associated with each healthcare decision. The quantification of healthcare decisions can also facilitate communication between patients and healthcare providers.⁷⁵ A table of key economic modeling terms is described below in Table 4-1.

Three recent conference abstracts employed decision-tree models limited to the diagnostic phase of the PCa pathway. Analyses were conducted from payer perspectives (Italian healthcare system; UK NHS/PSS), using hypothetical cohorts (100-1,000 men) with PSA 2-10 ng/mL and no prior biopsy. Sensitivity, specificity, prevalence, adverse events, and costs were sourced from published literature and national tariffs (Borisenko 2024a and 2024b, Bromilow 2025).

Table 12 Glossary of Frequently Encountered Economic Model Terms

TERM	DESCRIPTION
Cost-effectiveness	The point at which the minimum amount of input (and therefore cost) is used to achieve a given output.
TERM	DESCRIPTION
Cost-effectiveness analysis (CEA)	An economic evaluation in which the costs and consequences of alternative interventions are expressed cost per unit of health outcome. CEA is used to determine technical efficiency, i.e., comparison of costs and consequences of competing interventions for a given patient group within a given budget.
Cost-consequence analysis (CCA)	This compares the costs (such as treatment and hospital care) and the consequences (such as health outcomes) of a test or treatment with a suitable alternative. Unlike cost-benefit analysis or cost effectiveness analysis, CCA does not attempt to summarize outcomes in a single measure (such as the quality-adjusted life year) or in financial terms. Instead, outcomes are shown in their natural units (some of which may be monetary) and it is left to decision-makers to determine whether, overall, the treatment is worth carrying out.
Cost-utility analysis (CUA)	A form of economic study design in which interventions that produce different consequences, in terms of both quantity and quality of life, are expressed as 'utilities'. These are measures that comprise both length of life and subjective levels of wellbeing. The best-known utility measure is the 'quality-adjusted life year' or QALY. In this case, competing interventions are compared in terms of cost per utility (cost per QALY).
Cost analysis	Absolute, comparative, or differential costs pertaining to services, institutions, resources, etc., or the analysis and study of these costs.
Discounting	A technique that allows the calculation of present values of inputs and benefits that accrue in the future. Discounting is based on a time preference that assumes that individuals prefer to forego a part of the benefits if they accrue it now, rather than fully in the uncertain future. By the same reasoning, individuals prefer to delay costs rather than incur them in the present. The strength of this preference is expressed by the discount rate, which is inserted in economic evaluations.

Dominant (ICER)	When a new intervention is both clinically superior and cost saving, it is referred to as an economically “dominant” strategy. A dominant ICER is the opposite is a “dominated” strategy.
TERM	DESCRIPTION
Quality-adjusted-life-year (QALY)	Units of utility, which combine life years gained because of health interventions/health care programs with a judgment about the quality of these life years. QALY is a common measure of health improvement used in the cost-utility analyses; it measures life expectancy adjusted for quality of life.
Sensitivity analysis	A technique that repeats the comparison between inputs and consequences, varying the assumptions underlying the estimates. In so doing, sensitivity analysis tests the robustness of the conclusions by varying the items around which there is uncertainty.
Willingness-to-pay (WTP)	A technique that aims to assign a value to health benefits by directly eliciting individual preferences in the views of samples of the general public who are asked how much they would be prepared to pay to accrue a benefit or to avoid certain events.
Incremental cost-effectiveness ratio (ICER)	The incremental cost-effectiveness ratio (ICER) is a statistic used in cost-effectiveness analysis to summarize the cost-effectiveness of a health care intervention. It is defined by the difference in cost between two possible interventions, divided by the difference in their effect. It represents the average incremental cost associated with one additional unit of the measure of effect.

Source: National Information Center on Health Services Research and Health Care Technology. Health Economics Information Resources: A Self Study Course. Accessed on 24th May 2019 from <https://www.nlm.nih.gov/nichsr/edu/healthecon/glossary.html> and NICE Glossary. Accessed 13th Jun 2019 from <https://www.nice.org.uk/Glossary?letter=C>

4.2 Cost-Effectiveness of *phi*

Four cost-effectiveness models evaluating *phi* were identified. Two studies^{6,76} were from a U.S. perspective, and five studies were conducted in ex-U.S. settings like The Netherlands,⁷⁷ United Kingdom,^{67,78} Italy,⁷⁹ and Hong Kong.⁸⁰

4.2.1 European studies

A study from The Netherlands that assessed the cost-effectiveness of adding *phi* testing to improve PCa detection was investigated in a micro-simulation model based on the results of the European Randomized Study of Screening for Prostate Cancer trial.⁷⁷ This study focused on men with serum tPSA ranging between 3-10 ng/mL. When the *phi* test was added to the PSA screening, the model predicted a 23% reduction in negative biopsies. This would lead to a 17% reduction in costs for PCa detection and 1% overall reduction in total costs for PCa

treatment.⁷⁷

A study from the U.K. built an economic model to assess the cost-effectiveness of two detection biomarkers, including phi, in helping clinicians decide whether or not to recommend a repeat biopsy.⁶⁵ The cost-effectiveness assessment included two components: a systematic review of existing full economic evaluations and the development of a de novo health economic model. The economic model was constructed using data from the clinical validity review. The model used values for derived specificities at defined sensitivity levels. By modeling defined sensitivities, the only difference between testing strategies was the number of biopsies required to identify a given number of cancers.

The cost-effectiveness results were, therefore, driven by the differences in costs and QALYs losses that accrued in the different testing strategies (as a result of differences in numbers of biopsies performed); ICERs were also presented. Model input values for resource use, costs, and utility values were extracted from published sources. The time horizon, in the base case, was three years (extended to six years in the scenario analysis), the model perspective was that of the UK National Health Services (NHS), and costs and benefits were discounted at a rate of 3.5%. The model found no clear evidence that either biomarker worked better than the standard of care (biopsies) and did not represent value for money in deciding whether or not to recommend a repeat biopsy from the perspective of the U.K. National Health Services (NHS).⁶⁵

Another UK-based study by Kim et al.⁷⁸ tested the use of the phi assay in clinical practice to refine the use of mpMRI and biopsies for men at high risk of prostate cancer. The study compared several testing strategies and costs. The study focused on two important types of cancer and used the proportion of men with positive test results to determine the number of cancers detected or missed under each pathway. The cost inputs included the price of the phi test, the cost of the mpMRI scan (including the outpatient appointment), the expense of the biopsy, and the cost of sepsis treatment per case. The base case strategy (Table 4-2) of mpMRI and biopsy for all men detected every cancer but led to unnecessary biopsies for 53% of men. Strategies to biopsy only positive mpMRI (M3–5) or only men with a phi of ≥ 30 reduced unnecessary biopsy procedures by 23% and 25%, respectively. The phi ≥ 30 option achieved a 25% reduction in mpMRI usage and missed 8% of $\geq$ GG2 cancers. The phi ≥ 25 option missed only 4% of $\geq$ GG2 cancers but reduced unnecessary biopsies by only 25%.

Table 13 Modelling results for a Cohort of 1000 Patients by Diagnostic Strategy

	MRI + Biopsy all (Base case)	MRI all + biopsy if M3-5	MRI + biopsy only if $\phi \geq 25$	MRI + biopsy only if $\phi \geq 30$
No. of MRI scans (% lower)	1000	1000 (0%)	850 (-15%)	750 (-25%)
No. of biopsies needed (% lower*)	1000	772 (-23%)	850 (-15%)	750 (-25%)
No. of $\geq$ GG2 cancers identified (% lower)	100%	91% (-9%)	96% (-4%)	92% (-8%)

No. of unnecessary biopsies (% lower)	527	343 (-35%)	396 (-25%)	314 (-40%)
Cost/patient (% lower)	£965	£796 (-18%)	£869 (-10%)	£774 (-20%)

Source: Kim, 2020

At very low values of the risk threshold, biopsy all is the optimal strategy because these values represent a belief that there is little to no harm associated with an unnecessary biopsy. For risk thresholds 0.2–0.5 (the estimated range of uncertainty in clinical practice), the net benefit is highest under the $\phi \geq 30$ pathway. Since this is also the cheapest option (Table 9), this appears to be the optimal testing strategy representing a cost/cancer detected of between £2,120 and £5,860 depending on the risk threshold. This cost modelling suggests that a ϕ -based triage pathway may be less costly than other existing strategies.

Table 14 Costs Per Net Cancer Detected, by Risk Threshold

Risk threshold	Cost per net cancer detected. under $\phi \geq 30$ pathway	Additional cost per additional net cancer detected under biopsy all pathway*
0.5	£5860	NA
0.4	£3280	NA
0.3	£2500	NA
0.2	£2120	NA
0.1	£1890	NA
0.05	£1810	£7600
0	£1750	£5280

Source: Kim, 2020

In the UK NHS setting, the introduction of ϕ prior to mpMRI was shown to be economically dominant compared with standard diagnostic care over a one-month diagnostic horizon. For a hypothetical cohort of 1,000 men, the ϕ -followed-by-mpMRI strategy resulted in a mean per-patient diagnostic cost of £709 compared with £801 under standard care, corresponding to a cost saving of £92 per patient. This reduction in costs was mainly due to fewer mpMRI scans and fewer biopsies being performed (Bromilow 2025).

Total biopsies were reduced from 659 under standard care to 564 with ϕ triage, corresponding to 95 fewer biopsies per 1,000 men, while unnecessary biopsies were reduced by 82 procedures. Despite these reductions in invasive procedures, total QALYs were maintained at 0.07 per patient in both arms, resulting in dominance of the ϕ -based strategy. Probabilistic sensitivity analysis demonstrated that the ϕ -first strategy was cost-

effective in 100% of simulations at the NICE willingness-to-pay threshold of £20,000 per QALY, with diagnostic accuracy of phi and the cost of biopsy identified as the key drivers of results (Bromilow 2025).

In a more recent clinical study, (Data on File),⁶⁷ the clinical effectiveness of several diagnostic strategies was measured in terms of PCa cases identified and PCa cases missed. The resources use included the total number of biopsies performed and the number of unnecessary biopsies. The differences between total costs and effects assuming mpMRI alone as the reference strategy were also calculated, healthcare resource, and cost consequences of different diagnostic strategies for diagnosing prostate cancer (PCa) in Italy. The population assessed in the model included men aged ≥ 50 years with normal or suspicious digital rectal examination (DRE) and/or prostate-specific antigen (PSA) levels between 2–10 ng/ml. The diagnosis of PCa was confirmed by transrectal, ultrasound guided (TRUS) prostate biopsy. The following diagnostic strategies were evaluated in the model:

1. mpMRI all, followed by biopsy (PIRADS 3-5)
2. mpMRI all, followed by phi (PIRADS 1-3) + biopsy or biopsy (PIRADS 4-5)
3. phi all followed by mpMRI (if phi positive) + biopsy (PIRADS 3-5)
4. phi all followed by biopsy (if phi positive)

All clinical and resource use inputs were obtained from peer-reviewed publications. Cost inputs were obtained from the Italian government tariff lists. The clinical effectiveness of the diagnostic strategies was measured in terms of PCa cases identified and missed PCa cases. The resources use included the total number of biopsies performed and the number of unnecessary biopsies. The differences between total costs and effects assuming mpMRI alone as the reference strategy were also calculated. The study found that mpMRI followed by phi was associated with additional benefits in identifying all PCa cases but also increased total costs (Tables 4-5). At phi cutoff points 25 and 28, the phi stand-alone strategy was associated with lower costs and higher benefits in terms of PCa cases identified compared to the mpMRI stand-alone strategy. However, there were no benefits in the number of identified csPCa cases. The findings support the idea that phi cutoffs between 25 to 30 may add value as triage for mpMRI based diagnostic pathways as found by another study.⁷⁸

Table 15 Base Case Cost-Consequence Analysis, by *phi* Cutoff and Diagnostic Strategy

Diagnostic strategy	Total costs	Total biopsies	Unnecessary biopsies	All PCa cases identified	PCa cases missed	csPCa cases identified	csPCa cases missed
<i>Phi</i> cutoff 25							
mpMRI stand-alone	€ 31,206	51	14	36	12	18	1
mpMRI followed by <i>Phi</i>	€ 42,338	84	38	46	2	19	0

<i>Phi</i> followed by mpMRI	€ 29,599	41	9	32	16	17	3
<i>Phi</i> stand-alone	€ 23,964	77	35	42	6	18	2
<i>Phi</i> cutoff 28							
mpMRI stand-alone	€ 31,206	51	14	36	12	18	1
mpMRI followed by <i>Phi</i>	€ 40,877	78	33	45	3	19	0
<i>Phi</i> followed by mpMRI	€ 26,639	37	8	29	19	17	3
<i>Phi</i> stand-alone	€ 21,538	67	29	38	10	18	2

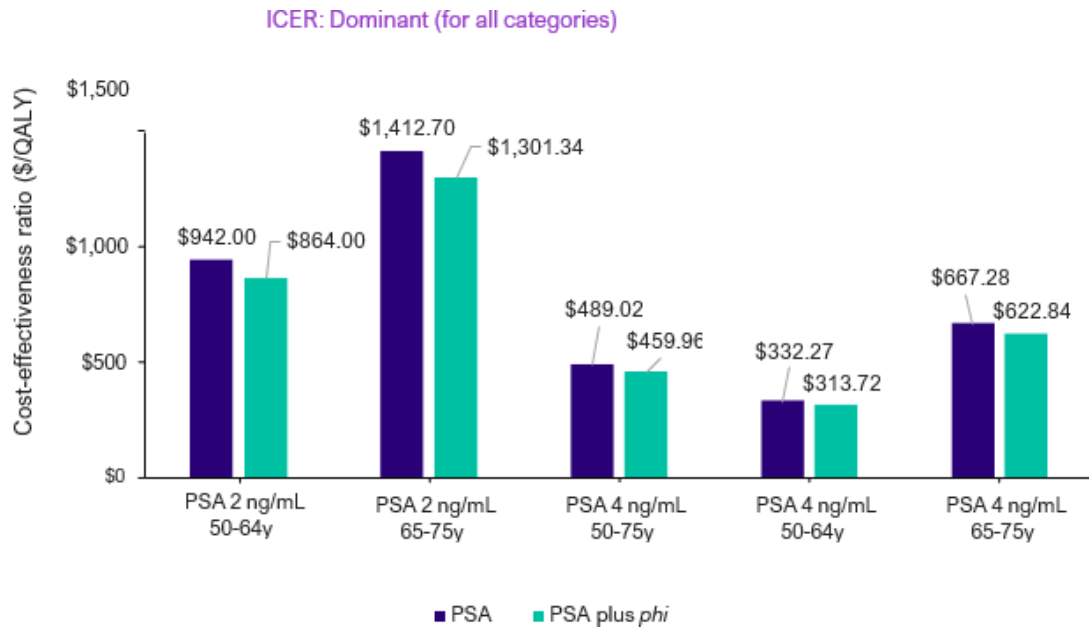
Source: Beckman Coulter DOF (2024)

4.2.2 U.S. Studies

Nichol et al. evaluated the cost-effectiveness of early PCa detection with phi used in conjunction with the PSA test compared with the PSA test alone from the U.S. societal perspective.⁶ This study constructed a Markov model to estimate the expected costs and utilities of PCa detection and following treatment for the annual PCa screening in the 50-75-year-old male population over 25 annual screening cycles, representing 25 years of PSA screening for a man. The transition probabilities, health state utilities, and PCa treatment costs were derived from the published literature. The diagnostic performance of phi was obtained from a multicenter study. Diagnostic-related costs were obtained from the 2009 Medicare Fee Schedule.

The strategy of tPSA plus phi dominated (Figure 4-1) the tPSA-only strategy, resulting in significant cost savings with an expected gain in quality-adjusted life years at both tPSA thresholds of 2 ng/mL and 4 ng/mL.⁶ It was also noted that the increased cost of adding phi testing to the original cost of PSA screening could be offset by reducing unnecessary biopsies if it were adopted by insurers.⁶

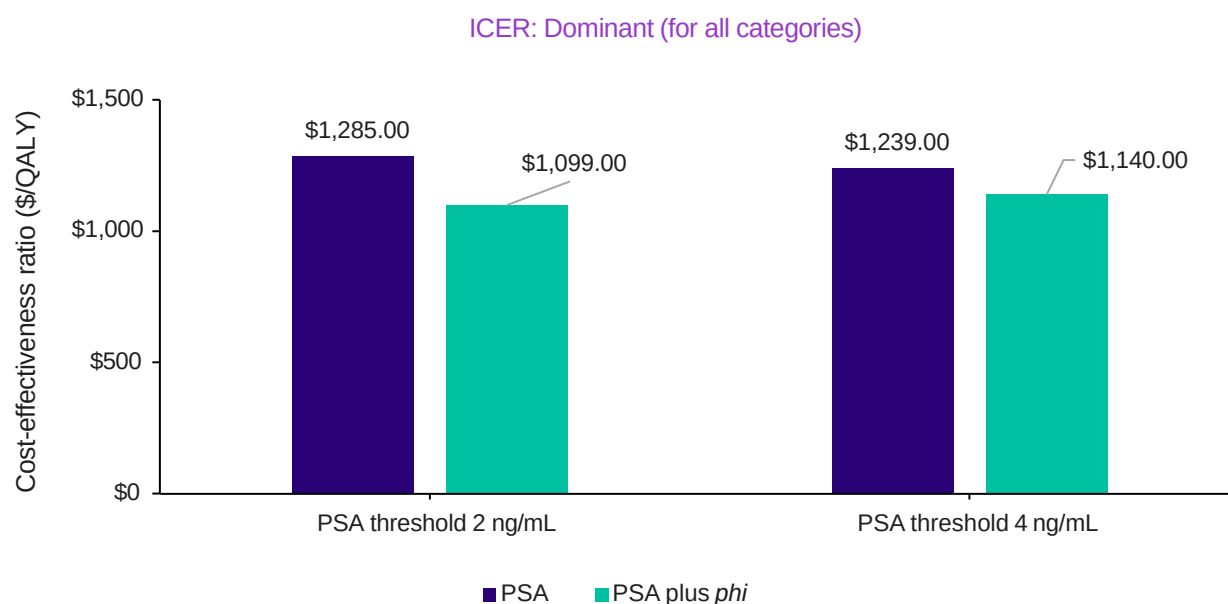
Figure 7 Cost-effectiveness Estimates in Base-case Analysis by Screening Age



Source: Nichol, 2011. Costs in 2009 USD, NMB, net monetary benefit; INMB, incremental net monetary benefit, ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year

In yet another study, Nichol et al. assessed the cost-effectiveness of early PCa detection with phi plus PSA compared to PSA test alone from a managed care perspective.⁷⁶ A Markov model was used to estimate the expected costs and utilities of PCa detection and consequent treatment using four strategies in men aged 50–75 years. The treatment strategies differed by PSA test thresholds (≥ 2 or ≥ 4 ng/mL) and diagnostic methods (PSA alone vs. PSA plus phi) to determine the need for a prostate biopsy. The transition probabilities were derived from the electronic medical records of males in Kaiser Permanente Southern California during 1998–2007. Health state utilities and PCa-related treatment costs were obtained from the published literature. With 10,000 samples simulated from age 50–75y under a 3% discount rate the most cost-effective strategy (Figure 4-2) used the PSA plus phi at PSA 2–10 ng/mL (\$1,099/QALY) followed by PSA plus phi at PSA 4–10 ng/mL (\$1,140/QALY) and PSA test at threshold ≥ 4 ng/mL (\$1,240/QALY).⁷⁶

Figure 8 Cost-effectiveness Results with 3% Discounting Rate



Source: Nichol, 2015. QALY, quality-adjusted life years; ICER, incremental cost-effectiveness ratio (\$/QALY); PSA, prostate-specific antigen; *phi* strategy2, PSA plus *phi* at PSA 2 to 10 ng/mL; *phi* strategy4, PSA plus *phi* at PSA 4 to 10 ng/mL; PSA strategy2, the PSA alone test using PSA threshold ≥ 2 ng/mL; PSA strategy4, PSA alone test using PSA threshold ≥ 4 ng/mL

PSA plus *phi* at tPSA 2-10 ng/mL displayed a 74% to 86% probability of being cost-effective at a willingness-to-pay range of 0 to \$150,000/QALY gained.⁷⁶ The PSA test alone at the threshold of ≥ 2 ng/mL was the least effective testing strategy. The differences between the most and least effective testing strategies were \$2,139 in costs and 0.129 QALY in effectiveness but ranged from \$1,552 to \$2,810 in costs, and 0.084 to 0.18 QALY in effectiveness, depending on the discount rate.⁷⁶

This cost-effectiveness analysis⁷⁶ based on a managed care payer's perspective on PSA test for PCa detection produced three major findings, 1) using *phi* at tPSA 2-10 ng/mL or 4-10 ng/mL were the dominant strategies compared to using the PSA test alone; 2) using *phi* at tPSA 2-10 ng/mL is the optimal strategy among all four PSA testing strategies across a range of willingness-to-pay (WTP) from \$0 to \$150,000/QALY gained; 3) without adding *phi*, the PSA test alone using tPSA threshold ≥ 2 ng/mL to recommend a prostate biopsy was the most costly and least effective strategy in PCa detection and consequent treatment.

4.2.3 Asian studies

A cost consequence analysis from Hong Kong evaluated the impact of adopting *phi* in the Hong Kong public health service perspective.⁸⁰ The model was set up as a decision tree and compared the current diagnostic pathway with a proposed diagnostic pathway using *phi*, in men with normal DRE and PSA result between 4–10 ng/mL. In the current strategy under which all patients undergo transrectal ultrasound (TRUS) biopsy and the proposed testing strategy. In the proposed pathway, all patients are tested using *phi*. Those with a positive result undergo TRUS biopsy. Those with *phi* scores under the threshold (negative result) do not undergo biopsy. In both positive and negative test result arms, there is the possibility of

the test result being correct or incorrect resulting in missed cases of cancer as well as a proportion of unnecessary biopsies. The model time horizon covered the diagnostic process up to biopsy. Costs and consequences were estimated for three different cut-off levels (25, 35, and 55 ng/mL) of the test. Data for the model was taken from a prospective cohort study recruited at a single institution and micro-costing studies. Any accident and emergency attendances and length of hospital stay, where appropriate, following biopsy were recorded. This resource usage was valued using costs from the Hospital Authority Annual Report for 2016/17.

Table 16 Cost-consequence Analysis of Alternative Diagnostic Strategies

Strategy, cut off	Biopsy rate	Cost of biopsies	Cost of phi	Cost of AE's	Total cost	Cost savings*	Missed cancer cases – all	Missed high-grade cancer cases
Biopsy all	100%	10,900	0	698	11,598	-	-	-
<i>phi</i> all (25)	66.26%	7,222	3,000	463	10,685	914	1.23%	0.18%
<i>phi</i> all (35)	26.71%	2,912	3,000	187	6,098	5,550	4.22%	0.53%
<i>phi</i> all (55)	3.69%	402	3,000	26	3,428	8,170	9.49%	2.11%

Source: Bouttell, 2019. *Compared to biopsy for all; all costs in Hong Kong dollars. The base case is the strategy of *phi* for all with cut off 35.

Using a cut off phi score of 35 to avoid biopsy would cost HK\$3,000 and save HK\$7,988 per patient in biopsy costs and HK\$511 from a reduction in biopsy-related adverse events.⁸⁰ The net cost impact of the change was estimated to be HK\$5,500 under base case assumptions (Table 4-4). The base case sensitivity and specificity for all grades of cancer was 61.3% and 77.5%, respectively. At the base cutoff of 35, cancer in 4.22% of the population (including 0.53% with high-grade cancers) may be missed. The study concluded that the introduction of phi into the diagnostic pathway for prostate cancer in Hong Kong had the potential to reduce biopsies, biopsy costs and biopsy-related adverse events.⁸⁰

4.3 Budget Impact of *phi*

One study evaluating the budget impact of phi from a U.S. perspective was identified.⁵ Nichol et al. evaluated the total budgetary impact of phi on the one-year expected total costs for PCa detection. The model was calculated using a hypothetical health plan with 100,000 male members aged 50–75 years old.⁵ Three PSA testing strategies, based on the most recent AUA recommendation for PCa screening, were compared: 1) PSA, 2) tPSA plus %fPSA, and 3) phi. Probabilities of positive PSA test results and cancer detection were derived from the published literature, where available. Base case costs were obtained from the 2009 Medicare national fee schedule. Base case market share for the PSA strategy was estimated as 90, and 10% for the %fPSA strategy. In the new scenario, we assumed a 10% market share for the index strategy and maintenance of 10% for the %fPSA strategy, and 80% for the PSA strategy. Assuming that at least 10% of eligible men for phi testing would receive the test, the one-year cost savings were \$356,647 (or \$0.30 per member per month, PMPM) or \$94,219 (\$0.08 PMPM), depending on whether serum tPSA was used at a threshold of 2

ng/mL or 4 ng/mL, respectively.⁵

Italian cost-consequence analyses demonstrated that diagnostic strategies incorporating phi were associated with substantial reductions in total diagnostic costs compared with mpMRI-only pathways. At a phi cut-off of 25, the total diagnostic cost per 100 patients was €31,206 for mpMRI alone, compared with €29,599 for phi followed by mpMRI and €23,964 for phi as a stand-alone strategy. This corresponds to cost savings of approximately €7,201 per 100 patients when phi alone was used instead of mpMRI alone (Borisenko 2024a).

At a higher phi cut-off of 28, the economic advantage of phi-based strategies was further amplified. Total diagnostic costs per 100 patients were €31,206 for mpMRI alone, €26,639 for phi followed by mpMRI, and €21,538 for phi alone. Across both cut-offs, reductions in total cost were mainly due to fewer mpMRI scans and lower biopsy-related resource use, including management of biopsy-related complications (Borisenko 2024a).

4.4 Other Economic Evidence of *phi*

A cost analysis study from France assessed the economic impact of introducing phi for PCa detection.⁸¹ A decision tree modeling was used to describe the patient's diagnostic pathway with phi or PSA strategies. A PSA value ≥ 4 ng/mL and a phi value ≥ 43 were used to define respective test positivity and derived the corresponding positive and negative predictive values. Both phi and PSA have a similar sensitivity of 69% at the chosen thresholds. For each branch of the decision tree, a probability and a cost were estimated using data from a study of 177 patients (male >50 y with tPSA 2–10 ng/mL and undergoing transrectal ultrasound guided prostate biopsy within 6 months of referral) who were prospectively identified between June 2009 and October 2010 in a single academic institution. The mean cost was assessed with Monte Carlo simulations. With a similar sensitivity, the phi strategy increased positive predictive value by 13.9 points and negative predictive value by 31.6 points in comparison to PSA strategy. Mean costs per patient with PSA and phi strategies were €514 and €528, respectively, for a phi test price at €50.⁸¹ One-way sensitivity analysis showed that phi strategy was less expensive (€508/patient) than PSA strategy with a phi test price below €30.⁸¹ Thus the introduction of phi in PCa detection could result in a significant clinical benefit with only a slight increase in expenditure.

In the Italian analyses, differences in cost outcomes were associated with clinical trade-offs between diagnostic efficiency and detection of clinically significant disease. The mpMRI-followed-by-phi strategy consistently achieved the highest level of clinical benefit, identifying all csPCa cases per 100 patients at both phi cut-offs, but was associated with the highest total diagnostic cost, exceeding mpMRI alone by approximately €9,700–€11,100 per 100 patients depending on cut-off. In contrast, phi-only and phi-first strategies achieved lower total costs while maintaining comparable detection of overall PCa, although without incremental gains in csPCa detection relative to mpMRI. For example, at a phi cut-off of 25, phi alone detected 42 PCa cases and 18 csPCa cases per 100 patients, compared with 36 PCa cases and 18 csPCa cases detected by mpMRI alone, while reducing total costs by more than €7,000 (Borisenko 2024a and 2024b).

4.5 Economic Data Summary

Published health economic studies have assessed the budget impact and cost-effectiveness of early PCa detection when the phi test is added to current PCa detection strategies. These studies demonstrated that the combination of phi testing with conventional serumPSA screening is both cost-effective and a better tool for a recommendation of a prostate biopsy. The total budgetary impact on the one-year expected total costs for PCa detection was a savings of \$356,647 (or \$0.30 per member per month, PMPM) or \$94,219 (\$0.08 PMPM), depending on whether serum tPSA was used at a threshold of 2 ng/mL or 4 ng/mL, respectively. In cost-effectiveness studies, the strategy of PSA plus phi dominated the PSA-only strategy, resulting in significant cost savings with an expected gain in quality-adjusted life years at both PSA thresholds of 2 ng/mL and 4 ng/mL. It was also noted that the increased cost of adding phi testing to the original cost of PSA screening could be offset by reducing unnecessary biopsies if it were adopted by insurers. Studies also support the value of using phi cutoff below 30 in conjunction with mpMRI to decide on biopsy.

Economic evidence from conference abstracts demonstrated that incorporating phi into prostate cancer diagnostic pathways can result in cost savings and reductions in invasive procedures at the healthcare system level. In Italy, phi-based strategies reduced diagnostic costs by €7,000-€9,700 per 100 patients compared with mpMRI-only pathways, while in the UK, phi triage reduced per-patient costs by £92 and avoided up to 95 biopsies per 1,000 men. While mpMRI followed by phi maximized csPCa detection at higher cost, phi-first strategies consistently improved diagnostic efficiency and budget impact without materially compromising overall clinical outcomes.

5 Dossier Appendices

5.1 References Contained in Dossier

1. Sanda M, Wei J, Broyles DL, et al. Prostate Health Index (*phi*) for reducing overdetection of indolent prostate cancer and unnecessary biopsy while improving detection of aggressive cancers (#2055). In: ; 2013.
2. IVDR. UDI (01)08720938015007(8012)v1.0(4326)250212(240)10531: CE Device Label . 2012.
3. White J, Shenoy BV, Tutrone RF, et al. Clinical utility of the Prostate Health Index (*phi*) for biopsy decision management in a large group urology practice setting. *Prostate Cancer Prostatic Dis.* 2018;21(1):78-84. doi:10.1038/s41391-017-0008-7
4. Tosoian JJ, Druskin SC, Andreas D, et al. Use of the Prostate Health Index for detection of prostate cancer: results from a large academic practice. *Prostate Cancer Prostatic Dis.* 2017;20(2):228-233. doi:10.1038/pcan.2016.72
5. Nichol MB, Wu J, An JJ, et al. Budget impact analysis of a new prostate cancer risk index for prostate cancer detection. *Prostate Cancer Prostatic Dis.* 2011;14(3):253-261. doi:10.1038/pcan.2011.16
6. Nichol MB, Wu J, Huang J, Denham D, Frencher SK, Jacobsen SJ. Cost-effectiveness of Prostate Health Index for prostate cancer detection. *BJU Int.* 2012;110(3):353-362. doi:10.1111/j.1464-410X.2011.10751.x
7. Stewart GD, Van Neste L, Delvenne P, et al. Clinical utility of an epigenetic assay to detect occult prostate cancer in histopathologically negative biopsies: results of the MATLOC study. *J Urol.* 2013;189(3):1110-1116. doi:10.1016/j.juro.2012.08.219
8. American Cancer Society ACS. Cancer Facts for Men | Common Cancers in Men | American Cancer Society. Cancer Facts for Men. Accessed March 4, 2024. <https://www.cancer.org/cancer/risk-prevention/understanding-cancer-risk/cancer-facts/cancer-facts-for-men.html>
9. NCI. Cancer Stat Facts: Prostate Cancer. Reports on Cancer. 2024. Accessed March 6, 2024. <https://seer.cancer.gov/statfacts/html/prost.html>
10. Roobol MJ. Screening for prostate cancer: are organized screening programs necessary? *Transl Androl Urol.* 2018;7(1):4-11. doi:10.21037/tau.2017.12.10
11. Vickers AJ, Roobol MJ, Lilja H. Screening for prostate cancer: early detection or overdetection? *Annu Rev Med.* 2012;63:161-170. doi:10.1146/annurev-med-050710-134421
12. Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, Brown ML. Projections of the cost of cancer care in the United States: 2010-2020. *J Natl Cancer Inst.* 2011;103(2):117-128. doi:10.1093/jnci/djq495
13. Roehrborn CG, Black LK. The economic burden of prostate cancer. *BJU Int.* 2011;108(6):806-813. doi:10.1111/j.1464-410X.2011.10365.x
14. Sun M, Marchese M, Friedlander DF, et al. Health care spending in prostate cancer: An assessment of characteristics and health care utilization of high resource-patients. *Urol Oncol.* 2021;39(2):130.e17-130.e24. doi:10.1016/j.urolonc.2020.09.033
15. Amin MB, Greene FL, Edge SB, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more “personalized” approach to cancer staging. *CA Cancer J Clin.* 2017;67(2):93-99. doi:10.3322/caac.21388
16. NCCN. *Prostate Cancer - Prostate Cancer Early Detection Version 2.2024; 2024.*
17. United States Preventative Services Task Force U. Screening for Prostate Cancer Recommendation Statement. 2012. 2012. Accessed March 6, 2024. <http://www.uspreventiveservicestaskforce.org/prostatecancerscreening/prostatefinalrs.htm>
18. United States Preventative Services Task Force U. Final Recommendation Statement: Screening for Prostate Cancer . 2018. Accessed March 6, 2024. <https://www.uspreventiveservicestaskforce.org/uspstf/announcements/final-recommendation-statement-screening-prostate-cancer>
19. Wei JT, Barocas D, Carlsson S, et al. Early detection of prostate cancer: AUA/SUO guideline part I: prostate cancer screening. *J Urol.* 2023; 210(1): 45-53.
20. Romero Otero J, Garcia Gomez B, Campos Juanatey F, Touijer KA. Prostate cancer biomarkers: an update. *Urol Oncol.* 2014;32(3):252-260. doi:10.1016/j.urolonc.2013.09.017
21. Gann PH, Hennekens CH, Stampfer MJ. A prospective evaluation of plasma prostate-specific antigen for detection of prostatic cancer. *JAMA.* 1995;273(4):289-294.

22. Draisma G, Boer R, Otto SJ, et al. Lead times and overdiagnosis due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer. *J Natl Cancer Inst.* 2003;95(12):868-878. doi:10.1093/jnci/95.12.868
23. Whittemore AS, Cirillo PM, Feldman D, Cohn BA. Prostate specific antigen levels in young adulthood predict prostate cancer risk: results from a cohort of Black and White Americans. *J Urol.* 2005;174(3):872-876; discussion 876. doi:10.1097/01.ju.0000169262.18000.8a
24. Tchetgen MB, Oesterling JE. The effect of prostatitis, urinary retention, ejaculation, and ambulation on the serum prostate-specific antigen concentration. *Urol Clin North Am.* 1997;24(2):283-291. doi:10.1016/s0094-0143(05)70374-8
25. Yuan JJ, Coplen DE, Petros JA, et al. Effects of rectal examination, prostatic massage, ultrasonography and needle biopsy on serum prostate specific antigen levels. *J Urol.* 1992;147(3 Pt 2):810-814. doi:10.1016/s0022-5347(17)37392-5
26. Nadler RB, Humphrey PA, Smith DS, Catalona WJ, Ratliff TL. Effect of inflammation and benign prostatic hyperplasia on elevated serum prostate specific antigen levels. *J Urol.* 1995;154(2 Pt 1):407-413. doi:10.1097/00005392-199508000-00023
27. Chybowski FM, Bergstralh EJ, Oesterling JE. The effect of digital rectal examination on the serum prostate specific antigen concentration: results of a randomized study. *J Urol.* 1992;148(1):83-86. doi:10.1016/s0022-5347(17)36517-5
28. The Internal Medicine Clinic Research Consortium. I. Effect of digital rectal examination on serum prostate-specific antigen in a primary care setting. *Arch Intern Med.* 1995;155(4):389-392.
29. Draisma G, Etzioni R, Tsodikov A, et al. Lead time and overdiagnosis in prostate-specific antigen screening: importance of methods and context. *J Natl Cancer Inst.* 2009;101(6):374-383. doi:10.1093/jnci/djp001
30. Punglia RS, D'Amico AV, Catalona WJ, Roehl KA, Kuntz KM. Effect of verification bias on screening for prostate cancer by measurement of prostate-specific antigen. *N Engl J Med.* 2003;349(4):335-342. doi:10.1056/NEJMoa021659
31. Hoffman RM. Clinical practice. Screening for prostate cancer. *N Engl J Med.* 2011;365(21):2013-2019. doi:10.1056/NEJMcp1103642
32. Carroll P, Coley C, McLeod D, et al. Prostate-specific antigen best practice policy—part I: early detection and diagnosis of prostate cancer. *Urology.* 2001;57(2):217-224. doi:10.1016/s0090-4295(00)00993-6
33. Meigs JB, Barry MJ, Oesterling JE, Jacobsen SJ. Interpreting results of prostate-specific antigen testing for early detection of prostate cancer. *J Gen Intern Med.* 1996;11(9):505-512. doi:10.1007/BF02599596
34. Catalona WJ, Partin AW, Slawin KM, et al. Use of the percentage of free prostate-specific antigen to enhance differentiation of prostate cancer from benign prostatic disease: a prospective multicenter clinical trial. *JAMA.* 1998;279(19):1542-1547. doi:10.1001/jama.279.19.1542
35. Cary KC, Cooperberg MR. Biomarkers in prostate cancer surveillance and screening: past, present, and future. *Ther Adv Urol.* 2013;5(6):318-329. doi:10.1177/1756287213495915
36. Khan MA, Sokoll LJ, Chan DW, et al. Clinical utility of proPSA and "benign" PSA when percent free PSA is less than 15%. *Urology.* 2004;64(6):1160-1164. doi:10.1016/j.urol.2004.06.033
37. Adhyam M, Gupta AK. A review on the clinical utility of PSA in cancer prostate. *Indian J Surg Oncol.* 2012;3(2):120-129. doi:10.1007/s13193-012-0142-6
38. Catalona WJ, Partin AW, Sanda MG, et al. A multicenter study of [-2]pro-prostate specific antigen combined with prostate specific antigen and free prostate specific antigen for prostate cancer detection in the 2.0 to 10.0 ng/ml prostate specific antigen range. *J Urol.* 2011;185(5):1650-1655. doi:10.1016/j.juro.2010.12.032
39. Agnello L, Vidali M, Giglio RV, et al. Prostate health index (*Phi*) as a reliable biomarker for prostate cancer: a systematic review and meta-analysis. *Clin Chem Lab Med.* 2022;60(8):1261-1277. doi:10.1515/cclm-2022-0354
40. Jia W, Wu B, Shao Y, Cao X, Wang D. Diagnostic performance of prostate cancer antigen 3 and the Prostate Health Index in detecting overall and clinically significant prostate cancer in men at first biopsy: A meta-analysis. *Int J Urol.* 2021;28(3):315-325. doi:10.1111/iju.14464
41. Zhang G, Li Y, Li C, Li N, Li Z, Zhou Q. Assessment on clinical value of prostate health index in the diagnosis of prostate cancer. *Cancer Med.* 2019;8(11):5089-5096. doi:10.1002/cam4.2376
42. Russo GI, Regis F, Castelli T, et al. A Systematic Review and Meta-analysis of the Diagnostic Accuracy of Prostate Health Index and 4-Kallikrein Panel Score in Predicting Overall and High-grade Prostate Cancer. *Clin Genitourin Cancer.* 2017;15(4):429-439.e1. doi:10.1016/j.clgc.2016.12.022
43. Liu Y, Xu Y, Zhang Z-H, Yang K. [Prostate health index in predicting the results of prostate biopsy for prostate cancer: a meta-analysis]. *Zhonghua Nan Ke Xue.* 2014;20(8):723-729.

44. Bruzzese D, Mazzearella C, Ferro M, et al. Prostate health index vs percent free prostate-specific antigen for prostate cancer detection in men with “gray” prostate-specific antigen levels at first biopsy: systematic review and meta-analysis. *Transl Res*. 2014;164(6):444-451. doi:10.1016/j.trsl.2014.06.006
45. Wang W, Wang M, Wang L, Adams TS, Tian Y, Xu J. Diagnostic ability of %p2PSA and prostate health index for aggressive prostate cancer: a meta-analysis. *Sci Rep*. 2014;4:5012. doi:10.1038/srep05012
46. Filella X, Giménez N. Evaluation of [-2] proPSA and Prostate Health Index (*phi*) for the detection of prostate cancer: a systematic review and meta-analysis. *Clin Chem Lab Med*. 2013;51(4):729-739. doi:10.1515/ccim-2012-0410
47. Del Pino-Sedeño T, Infante-Ventura D, de Armas Castellano A, et al. Molecular Biomarkers for the Detection of Clinically Significant Prostate Cancer: A Systematic Review and Meta-analysis. *European Urology Open Science*. 2022;46:105-127. doi:10.1016/j.euros.2022.10.017
48. Sanchís-Bonet A, Barrionuevo-González M, Bajo-Chueca AM, et al. Validation of the prostate health index in a predictive model of prostate cancer. *Actas Urol Esp*. 2018;42(1):25-32. doi:10.1016/j.acuro.2017.06.003
49. Foley RW, Gorman L, Sharifi N, et al. Improving multivariable prostate cancer risk assessment using the Prostate Health Index. *BJU Int*. 2016;117(3):409-417. doi:10.1111/bju.13143
50. Cantiello F, Russo GI, Cicione A, et al. *Phi* and PCA3 improve the prognostic performance of PRIAS and Epstein criteria in predicting insignificant prostate cancer in men eligible for active surveillance. *World J Urol*. 2016;34(4):485-493. doi:10.1007/s00345-015-1643-z
51. Zhu Y, Han C-T, Zhang G-M, et al. Development and external validation of a prostate health index-based nomogram for predicting prostate cancer. *Sci Rep*. 2015;5:15341. doi:10.1038/srep15341
52. Roobol MJ, Vedder MM, Nieboer D, et al. Comparison of Two Prostate Cancer Risk Calculators that Include the Prostate Health Index. *Eur Urol Focus*. 2015;1(2):185-190. doi:10.1016/j.euf.2015.06.004
53. Lughezzani G, Lazzeri M, Haese A, et al. Multicenter European external validation of a prostate health index-based nomogram for predicting prostate cancer at extended biopsy. *Eur Urol*. 2014;66(5):906-912. doi:10.1016/j.eururo.2013.12.005
54. Loeb S, Shin SS, Broyles DL, et al. Prostate Health Index improves multivariable risk prediction of aggressive prostate cancer. *BJU Int*. 2017;120(1):61-68. doi:10.1111/bju.13676
55. Carbutaru S, Stinson J, Babajide R, et al. Performance of prostate health index and PSA density in a diverse biopsy-naïve cohort with mpMRI for detecting significant prostate cancer. *BJUI Compass*. 2021;2(6):370-376. doi:10.1002/bco2.91
56. Ferro M, Crocetto F, Bruzzese D, et al. Prostate health index and multiparametric MRI: partners in crime fighting overdiagnosis and overtreatment in prostate cancer. *Cancers (Basel)*. 2021;13(18). doi:10.3390/cancers13184723
57. Stejskal J, Adamcová V, Záleský M, et al. The predictive value of the prostate health index vs. multiparametric magnetic resonance imaging for prostate cancer diagnosis in prostate biopsy. *World J Urol*. 2021;39(6):1889-1895. doi:10.1007/s00345-020-03397-4
58. Ye C, Ho J-N, Kim DH, et al. The Prostate Health Index and multi-parametric MRI improve diagnostic accuracy of detecting prostate cancer in Asian populations. *Investig Clin Urol*. 2022;63(6):631-638. doi:10.4111/icu.20220056
59. Hsieh P-F, Li T-R, Lin W-C, et al. Combining prostate health index and multiparametric magnetic resonance imaging in estimating the histological diameter of prostate cancer. *BMC Urol*. 2021;21(1):161. doi:10.1186/s12894-021-00928-y
60. Seisen T, Rouprêt M, Brault D, et al. Accuracy of the prostate health index versus the urinary prostate cancer antigen 3 score to predict overall and significant prostate cancer at initial biopsy. *Prostate*. 2015;75(1):103-111. doi:10.1002/pros.22898
61. Stephan C, Jung K, Semjonow A, et al. Comparative assessment of urinary prostate cancer antigen 3 and TMPRSS2:ERG gene fusion with the serum [-2]prostate-specific antigen-based prostate health index for detection of prostate cancer. *Clin Chem*. 2013;59(1):280-288. doi:10.1373/clinchem.2012.195560
62. Scattoni V, Lazzeri M, Lughezzani G, et al. Head-to-head comparison of prostate health index and urinary PCA3 for predicting cancer at initial or repeat biopsy. *J Urol*. 2013;190(2):496-501. doi:10.1016/j.juro.2013.02.3184
63. Ferro M, Bruzzese D, Perdonà S, et al. Prostate Health Index (*Phi*) and Prostate Cancer Antigen 3 (PCA3) significantly improve prostate cancer detection at initial biopsy in a total PSA range of 2-10 ng/ml. *PLoS ONE*. 2013;8(7):e67687. doi:10.1371/journal.pone.0067687
64. Ferro M, Bruzzese D, Perdonà S, et al. Predicting prostate biopsy outcome: prostate health index (*phi*) and prostate cancer antigen 3 (PCA3) are useful biomarkers. *Clin Chim Acta*. 2012;413(15-16):1274-1278. doi:10.1016/j.cca.2012.04.017

65. Nicholson A, Mahon J, Boland A, et al. The clinical effectiveness and cost-effectiveness of the PROGENSA® prostate cancer antigen 3 assay and the Prostate Health Index in the diagnosis of prostate cancer: a systematic review and economic evaluation. *Health Technol Assess*. 2015;19(87):i-xxxi, 1. doi:10.3310/hta19870
66. Nordström T, Vickers A, Assel M, Lilja H, Grönberg H, Eklund M. Comparison Between the Four-kallikrein Panel and Prostate Health Index for Predicting Prostate Cancer. *Eur Urol*. 2015;68(1):139-146. doi:10.1016/j.eururo.2014.08.010
67. Barisiene M, Bakavicius A, Stanciute D, et al. Prostate health index and prostate health index density as diagnostic tools for improved prostate cancer detection. *Biomed Res Int*. 2020;2020:9872146. doi:10.1155/2020/9872146
68. Filella X, Foj L, Wijngaard R, Luque P. Value of *Phi* and *Phi*D in the detection of intermediate- and high-risk prostate cancer. *Clin Chim Acta*. 2022;531:277-282. doi:10.1016/j.cca.2022.04.992
69. Garrido MM, Ribeiro RM, Pinheiro LC, Holdenrieder S, Guimarães JT. The prostate health index (*Phi*) density: Are there advantages over *Phi* or over the prostate-specific antigen density? *Clin Chim Acta*. 2021;520:133-138. doi:10.1016/j.cca.2021.06.006
70. Chen H, Shi B, Wu Y, et al. The modified prostate health index (*Phi*) outperforms *Phi* density in the detection of clinical prostate cancer within the PSA grey zone. *Int Urol Nephrol*. 2022;54(4):749-756. doi:10.1007/s11255-022-03113-8
71. Peters R, Stephan C, Jung K, Lein M, Friedersdorff F, Maxeiner A. Comparison of *Phi* and *Phi* density for prostate cancer detection in a large retrospective caucasian cohort. *Urol Int*. 2022;106(9):878-883. doi:10.1159/000517891
72. Tan TW, Png KS, Lee CH, et al. MRI Fusion-Targeted Transrectal Prostate Biopsy and the Role of Prostate-Specific Antigen Density and Prostate Health Index for the Detection of Clinically Significant Prostate Cancer in Southeast Asian Men. *J Endourol*. 2017;31(11):1111-1116. doi:10.1089/end.2017.0485
73. Druskin SC, Tosoian JJ, Young A, et al. Combining Prostate Health Index density, magnetic resonance imaging and prior negative biopsy status to improve the detection of clinically significant prostate cancer. *BJU Int*. 2018;121(4):619-626. doi:10.1111/bju.14098
74. Tezcan E, Abdalla O. 1226 the clinical utility of prostate health index density in the diagnosis of clinically significant prostate cancer: A systematic review. *British Journal of surgery*. 2021;108(Supplement_6). doi:10.1093/bjs/znab259.825
75. Halpern MT, Luce BR, Brown RE, Geneste B. Health and economic outcomes modeling practices: a suggested framework. *Value Health*. 1998;1(2):131-147. doi:10.1046/j.1524-4733.1998.120131.x
76. Nichol MB, Wu J, Denham D, et al. Cost-Effectiveness of Prostate Health Index from a Managed Care Payer Perspective. *Medical Research Archives*. 2015;2(12):17-23.
77. Heijnsdijk EAM, Denham D, de Koning HJ. The Cost-Effectiveness of Prostate Cancer Detection with the Use of Prostate Health Index. *Value Health*. 2016;19(2):153-157. doi:10.1016/j.jval.2015.12.002
78. Kim L, Boxall N, George A, et al. Clinical utility and cost modelling of the *phi* test to triage referrals into image-based diagnostic services for suspected prostate cancer: the PRIM (*Phi* to Refine Mri) study. *BMC Med*. 2020;18(1):95. doi:10.1186/s12916-020-01548-3
79. Data on File. Diagnostic pathways for prostate cancer in Italy: a cost-consequences analysis. 2024.
80. Bouttell J, Teoh J, Chiu PK, et al. Economic evaluation of the introduction of the Prostate Health Index as a rule-out test to avoid unnecessary biopsies in men with prostate specific antigen levels of 4-10 in Hong Kong. *PLoS ONE*. 2019;14(4):e0215279. doi:10.1371/journal.pone.0215279
81. Mathieu R, Castelli C, Fardoun T, et al. Cost analysis of prostate cancer detection including the prostate health index (*phi*). *World J Urol*. 2019;37(3):481-487. doi:10.1007/s00345-018-2362-z

5.2 New references

Agnello L, Vidali M, Salvaggio G, et al. Prostate Health Index (PHI) as a triage tool for reducing unnecessary magnetic resonance imaging (MRI) in patients at risk of prostate cancer. *Clin Biochem*. 2024;127-128:110759. doi:10.1016/j.clinbiochem.2024.110759

Borisenko O, Maslov A, Baka A, Das L, Anelli MC, Terracciano D. Diagnostic pathways for prostate cancer in Italy: a cost-consequence analysis. *Value Health*. 2024;27(Suppl 1):S-. Presented at: ISPOR Europe 2024; November 2024; Barcelona, Spain. Poster #140786

Borisenko O, Maslov A, Baka A, Das L, Anelli MC, Terracciano D. Utility of multiparametric MRI and prostate health index (*phi*) in the detection of prostate cancer in Italy: a decision analytic model. *Eur Urol Open Sci*. 2024; (Suppl):. Presented at: Italian National Urology Congress; 2024; Italy. Poster #66

Bromilow T, Afonso D, Davis R, Mealing S, Das L. Cost-effectiveness analysis of the prostate health index (phi) test after a prostate-specific antigen test in the United Kingdom. *Value Health*. 2025;28(Suppl 1):S-. Presented at: ISPOR Europe 2025; November 2025; Glasgow, United Kingdom. Poster #EE221

Chiu PK, Lam TY, Ng CF, et al. The combined role of MRI prostate and prostate health index in improving detection of significant prostate cancer in a screening population of Chinese men. *Asian J Androl*. 2023;25(6):674-679. doi:10.4103/aja20239.

Chiu ST, Chen YC, Huang CY, et al. Prostate biopsy strategy integrating prostate health index and multiparametric magnetic resonance imaging optimizes the predictive value of clinically significant prostate cancer in Prostate Imaging Reporting and Data System gray-zone imaging. *Urol Sci*. 2023;34(2):86-92.

Chiu PK, Liu AQ, Lau SY, et al. A 2-year prospective evaluation of the Prostate Health Index in guiding biopsy decisions in a large cohort. *BJU Int*. 2025;135(1):71-77. doi:10.1111/bju.16457.

Chung JH, Kim JH, Lee SW, et al. Nomogram Using Prostate Health Index for Predicting Prostate Cancer in the Gray Zone: Prospective, Multicenter Study. *World J Mens Health*. 2024;42(1):168-177. doi:10.5534/wjmh.220223

Cui Y, Zhao J, Sun Y. The Value of the Prostate Health Index and Derived Indexes in the Diagnosis of Prostate Cancer with PI-RADS-3 Lesions. *Urol Int*. 2023;107(10-12):959-964. doi:10.1159/000534597

Cussenot O, Renard-Penna R, Montagne S, et al. Clinical performance of magnetic resonance imaging and biomarkers for prostate cancer diagnosis in men at high genetic risk. *BJU Int*. 2023;131(6):745-754. doi:10.1111/bju.15968

Dudinec JV, Wang SM, Kotamarti S, Morris KE, Polascik TJ, Moul JW. Clinical utility of multiple secondary combined tests in prostate cancer screening. *Can J Urol*. 2023;30(3):11538-11544

Esteban MD, Guzman EF, Barselo ER, et al. Multivariable model integrating PHI and mpMRI for detecting csPCa in biopsy-naïve men. *BJUI Compass*. 2025;6(12):e70101. Published 2025 Dec 2. doi:10.1002/bco2.70101

European Cancer Organisation. Improving Prostate Cancer Screening Across Europe. 17 Nov 2025. Available from: <https://www.europeancancer.org/next-level-prostate-cancer-screening.html>

Fizazi K. ASCO 2021 Conference Coverage. Prostate Cancer with Metastases at the Time of Diagnosis. 8 Jun 2021. Available from: <https://www.gustaveroussy.fr/en/asco-2021-prostate-cancer-metastases-time-diagnosis-combination-two-hormone-therapies-and-single>

Huang H, Liu Z, Ma Y, et al. Based on PI-RADS v2.1 combining PHI and ADC values to guide prostate biopsy in patients with PSA 4-20 ng/mL. *Prostate*. 2024;84(4):376-388. doi:10.1002/pros.24658

Jeon SS, Song W, Kang M, et al. Diagnostic value of prostate health index in patients with no index lesion on mpMRI or negative previous combined biopsy. *Investig Clin Urol*. 2025;66(2):124-129. doi:10.4111/icu.20250007

Kawada T, Shim SR, Quhal F, et al. Diagnostic Accuracy of Liquid Biomarkers for Clinically Significant Prostate Cancer Detection: A Systematic Review and Diagnostic Meta-analysis of Multiple Thresholds. *Eur Urol Oncol*. 2024;7(4):649-662. doi:10.1016/j.euo.2023.10.029

Leung JS, Ma WK, Ho BS, et al. Prostate health index can stratify patients with Prostate Imaging Reporting and Data System score 3 lesions on magnetic resonance imaging to reduce prostate biopsies. *Asian J Androl*. 2024;26(1):20-24. doi:10.4103/aja202332

Morris KE, Kotamarti S, Polascik TJ, Moul JW. Re-thinking How We Use Prostate Health Index for African American Men. *Urology*. 2023;175:144-150. doi:10.1016/j.urology.2022.12.057

5.3 Coding Information

Current Procedural Terminology® (CPT) coding for reporting the calculation of *phi* is similar to coding for reporting the calculation of %free PSA. For %free PSA, laboratories have billed for both the total PSA and free PSA tests when reporting %free PSA results. National Government Services (NGS), a Medicare Administrative Contractor (MAC), has a Biomarker Testing for Prostate Cancer Diagnosis Local Coverage Article (LCA), that is designed to guide the correct reporting of prostate biomarker testing. For *phi*, the article recommends that laboratories should bill for the total PSA (CPT 84153), free PSA (CPT 84154), and p2PSA (CPT 86316) tests. All three CPT codes within the recommendation are listed on the Medicare Clinical Lab Fee Schedule (MCLFS).

CPT codes are copyright 2023 American Medical Association. All rights reserved. CPT® is a registered trademark of the American Medical Association (AMA).

Coding References

1. National Government Services (NGS). Biomarker Testing for Prostate Cancer Diagnosis (A56609). March 1, 2024. <https://www.cms.gov/medicare-coverage-database/search.aspx>



© 2024 Beckman Coulter, Inc. All rights reserved. Beckman Coulter, the stylized logo, and the Beckman Coulter product and service marks mentioned herein are trademarks or registered trademarks of Beckman Coulter, Inc. in the United States and other countries. All other trademarks are the property of their respective owners.

For Beckman Coulter's worldwide office locations and phone numbers, please visit www.beckmancoulter.com/contact

2024-12736



S55	Akshay Mody	Antegenes Ltd.	Submitted by: Antegenes Ltd Focus: Risk-stratified clinical guidance and personalised cancer prevention 1. Introduction and stakeholder position Antegenes welcomes the opportunity to respond to the UK National Screening Committee's consultation on the draft prostate cancer screening recommendation. We support the UK NSC's evidence-based mandate and recognise the long-standing challenges associated with prostate cancer screening, including the limitations of PSA-based approaches and the risks of overdiagnosis and overtreatment. Antegenes provides regulated, clinically validated risk-stratification tools to support personalised cancer prevention and screening decisions. Our comments are therefore focused on responsible clinical guidance and implementation considerations, rather than on population screening programme design. 1. Support for the draft recommendation We agree with the UK NSC's conclusion that population-wide prostate cancer screening is not currently justified, and we support the Committee's cautious and proportionate approach. In particular, we support: The decision not to introduce population screening at this time. The recognition of the limitations of PSA as a stand-alone screening tool. The proposal for highly targeted screening in clearly defined high-risk groups, while recognising that such highly targeted approaches are complex to implement consistently in routine practice. This last point is important: while narrowly targeted screening is conceptually sound from an evidence perspective, it is operationally challenging in real-world clinical settings and reinforces the need for clear, practical guidance to support clinicians and patients. 1. Support for TRANSFORM and the need for definitive evidence We strongly support the objectives and design of the TRANSFORM trial and agree that robust trial evidence should underpin any future national screening recommendation. TRANSFORM is well positioned to address key evidence gaps identified by the UK NSC, including:

			How best to combine genetic, clinical, and demographic risk factors Outcomes in men of African and Caribbean ancestry The performance of multi-factor approaches beyond PSA alone. We fully support the Committee's decision to await these results before making broader or more prescriptive screening recommendations. 1. The interim clinical guidance gap While supporting the need to await definitive trial outcomes, we wish to highlight an interim gap in current clinical practice. Men with recognised risk factors for prostate cancer (such as family history or ancestry) currently receive limited, inconsistent, or non-specific guidance on how to approach screening decisions. In practice, opportunistic PSA testing continues in the absence of a structured framework for risk assessment and shared decision-making. This creates variability in care and uncertainty for both clinicians and patients, despite the availability of validated tools that can inform risk discussions. 1. What is reasonable now: PRS as adjunctive decision support In this interim period, we suggest that polygenic risk scores (PRS), when clinically validated and appropriately governed, represent a reasonable adjunctive tool to support clinician-led discussions for men with recognised risk factors. At present, PRS can reasonably be used to: Support shared decision-making, not to mandate screening Help contextualise PSA testing within an individual's broader risk profile Inform discussions alongside age, family history, ancestry, and clinical judgement This reflects current clinical reality and does not pre-empt the outcomes of TRANSFORM. 1. What TRANSFORM is expected to confirm We recognise that key questions remain unresolved and are appropriately the focus of TRANSFORM, including: The optimal composition and weighting of multi-factor risk algorithms

		Clinical outcomes associated with different risk-stratification thresholds How such approaches might be translated into equitable, scalable NHS pathways The role of PRS and other risk-stratification tools in any future national screening approach should be determined on the basis of this evidence. 1. Consideration of interim, principles-based guidance In light of the above, we respectfully suggest that the UK NSC may wish to consider whether high-level, principles-based guidance could be issued to support current practice while awaiting trial outcomes. Such guidance could: Acknowledge what is reasonable and evidence-aligned now Clarify appropriate use of risk-stratification tools in higher-risk men Reinforce clinician oversight and shared decision-making Avoid endorsement of specific technologies or algorithms This would not constitute a screening programme, but would improve consistency and quality of care in the interim. 1. Conclusion Antegenes supports the draft recommendation and the decision not to introduce population-wide prostate cancer screening. We support TRANSFORM as the appropriate mechanism to confirm how genetic and multi-factor risk stratification should inform future screening policy. In the meantime, we encourage consideration of principles-based guidance that reflects current clinical realities and supports informed decision-making for men at increased risk. Clarification of what Antegenes is not proposing To avoid ambiguity, Antegenes wishes to clarify that, in relation to population-wide screening, this submission does not advocate for: The introduction of population-wide prostate cancer screening The use of PRS as a population-level screening test Automatic or algorithm-driven screening invitations without clinical oversight This submission does not preclude the use of validated risk-stratification tools, including PRS, to support clinician-led guidance

			and shared decision-making for men with recognised risk factors while awaiting the outcomes of TRANSFORM.
S56	Professor Alan McNeill	Prostate Scotland	Prostate Scotland has consistently sought to raise awareness of the familial risk of prostate cancer and promote early testing in these men. We also encourage all men aged >50 years to discuss PSA testing with their GPs irrespective of whether they have symptoms, which is in line with the UK Government Prostate Cancer Risk Management Guideline. [https://www.gov.uk/government/publications/prostate-specific-antigen-testing-description-in-brief/psa-testing-and-prostate-cancer-advice-for-men-without-symptoms-of-prostate-disease-aged-50-and-over] Whilst we are aware that the Scottish Government do not hold data regarding the number of men with a family history of prostate cancer [Communication by Neil Gray, Cab Sec for Health in Scotland at the Cross Party Group on Cancer, 2/12/25], which means a formal screening programme for men with a family history would be difficult to implement, we were disappointed with the SCHARR modelling used for the NSC recommendations as we do not believe this adequately highlighted the increased risk in these men. The SCHARR model [https://nationalscreening.blog.gov.uk/wp-content/uploads/sites/254/2025/11/SCHARR-Report-Phase-3-Prostate-Cancer-Modelling_FINAL.pdf] used a definition of family history of one relative affected by prostate, breast or ovarian cancer, which appears to have been based on the Canrisk risk calculator, which includes the same definition of a family history [https://ascopubs.org/doi/10.1200/JCO.22.01453], and concluded that screening based on this would not be cost effective. We wish to raise a couple of issues with regard to this – 1. One of the clinical advisers to the SCHARR team is also one of the leads for the TRANSFORM study of screening for prostate cancer and therefore had a potential conflict of interest. 2. We feel that a better definition to have used for the modelling would have been that described in the European Association of Urology Guidelines on Prostate Cancer [https://uroweb.org/guidelines/prostate-cancer/chapter/epidemiology-and-aetiology] and would suggest that the SCHARR team be asked to remodel the benefits of screening based on this definition of family history. Whilst we acknowledge that the healthcare system does not currently hold data regarding men with a family history, it would help encourage such men to come forward for testing if their increased risk was acknowledged by the NSC. Formal recognition of the increased risk conferred through a family or racial history would help facilitate a testing programme for men

			in these groups who could be encouraged to self-present until our healthcare systems develop the data systems that allow them to be invited for testing (screening). Finally, whilst we welcome the recommendation for biennial screening of men who carry the BRCA 1 and 2 genes we believe that this will have little impact on the number of men currently affected by or dying of prostate cancer in Scotland as only men who have a female family member known to be BRCA +ive or who are known to have metastatic hormone resistant prostate cancer are currently eligible for BRCA testing. We have been advised by Professor Zosia Miedzybrodzka OBE, MB ChB, PhD, FRCP Edin, FRCOG, Honorary Consultant Clinical Geneticist & Service Clinical Director-Genetics, NHS Grampian and having reviewed available literature understand that – 1. The BRCA 2 gene confers an increased risk of prostate cancer of 27%. 2. The BRCA 1 gene confers an increased risk of prostate cancer of 1% 3. The prevalence of the BRCA 2 gene in the general male population is up to 1 in 277. 4. The prevalence of the BRCA 1 gene in the general male population is in the region of 1 in 1,100. 5. There are approximately 715,000 men aged 45-64 in Scotland, of which 2,581 are likely to carry the BRCA 2 gene. 6. Professor Miedzybrodzka estimates that in Scotland approximately 570 men aged 45-75 are currently known to carry the BRCA 2 gene. These men are already advised to seek regular PSA tests. We therefore request that the NSC review the SCHARR modelling that was used as a basis for their recommendations and after further evidence has been assessed they could then support a targeted testing programme for men at risk, which is already in place in Australia [https://www.cancer.org.au/clinical-guidelines/prostate-cancer/psa-testing] and several countries in Europe. These countries have adopted a different strategy than that currently recommended by the NSC but presumably have done so because of different interpretation of the same evidence.
S57	Anjali Behal, Sophie Brooks, Sowmiya Moorthie, Claire	Cancer Research UK	Hello, I hope you are well. Please see the attached document for Cancer Research UK's response to the prostate cancer screening consultation. Do get in touch if you have any questions or concerns.

	Knight, Samantha Harrison, Fiona Osgun, Naser Turabi, Jo Harby		Thank you and best wishes, Anjali Behal

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name:	Anjali Behal, Sophie Brooks, Sowmiya Moorthie, Claire Knight, Samantha Harrison, Fiona Osgun, Naser Turabi, Jo Harby		Email address:	*****
Organisation (if appropriate):	Cancer Research UK			
Role:	Strategic Evidence & Health Information Teams			
Do you consent to your name being published on the UK NSC website alongside your response?				Yes No
Section and / or page number	Text or issue to which comments relate	Comment <i>Please use a new row for each comment and add extra rows as required.</i>		
	Introduction:	Each year in the UK there are around 55,300 cases of prostate cancer and over 12,000 men* lose their lives to the disease.¹ To improve outcomes, it is crucial that we find accurate ways to detect and treat prostate cancers that do need treatment, while avoiding unnecessary diagnosis and treatment of cancers that are unlikely to cause harm. More research is needed to detect aggressive cancers earlier and develop treatments that are more precise and more effective. If implemented, a targeted prostate screening programme for men with a pathogenic variant in BRCA1 or BRCA2 could be an important step forward in saving more lives, but we must also accelerate research into earlier detection of aggressive disease, develop more precise diagnostic tools, and reduce unwarranted variation in access to treatment and help-seeking to enable men with aggressive prostate cancer live longer, better lives.		

Prostate cancer affects men, trans women and non-binary people with a prostate. We have used the term men throughout this consultation to reflect the evidence and statistics available. The recommendations of this consultation should be applied to other genders where relevant, and access to screening for prostate cancer must be inclusive.

	To support its review of evidence on prostate cancer screening, the UK National Screening Committee (UK NSC) commissioned an independent modelling study from the Sheffield Centre for Health and Related Research (SCHARR). The modelling was commissioned to help predict the impact that different screening approaches could have, particularly in regard to the potential benefits, harms, and costs, so that the UK NSC could make an informed recommendation on the best screening strategy. The screening approaches that were modelled included population-wide screening and targeted screening of groups with higher incidence of prostate cancer – namely those with a relevant family history of cancer (defined as a first-degree relative with breast, ovarian, or prostate cancer), Black men, and men with a BRCA1 or BRCA2 pathogenic variant. For each approach, different age ranges and screening intervals were modelled. • Cancer Research UK (CRUK) agrees that current evidence does not support recommending a population-wide prostate cancer screening programme using the Prostate-Specific Antigen (PSA) test. Current evidence suggests that population-wide screening of asymptomatic men using a PSA test would result in a very small reduction of mortality but a significant increase in overdiagnosis and overtreatment. The SCHARR modelling confirms this by indicating that population-wide PSA screening is unlikely to achieve a favourable balance of benefits and harms. CRUK recommends investment in improving earlier diagnosis of aggressive prostate cancer, including strengthening current diagnostic tools in the short term and advancing scientific understanding of markers that distinguish aggressive disease, to support the development of more effective screening approaches in the future. • CRUK agrees that due to evidence gaps relating to Black men, including clear definition of the group, disease aggressiveness, and prostate cancer progression, targeted screening for Black men should not be introduced at this stage. Current evidence from the SCHARR report shows that there is significant uncertainty on whether the benefits would outweigh the harms for this cohort, largely driven by limitations in the underlying evidence base. This limits what the model can confidently predict for this cohort. • CRUK agrees that due to important evidence gaps around how relevant family history is defined, and ongoing uncertainty about disease aggressiveness and the underlying drivers of increased risk in this group, targeted screening for this cohort should not be introduced at this stage. For men with a relevant family history of cancer, overall findings from the SCHARR modelling were similar to the population-wide screening scenario i.e., screening would be unlikely to achieve a favourable balance of benefits and harms. This finding was associated with a large amount of uncertainty due to evidence gaps which limits what the model can confidently predict.

		• For both Black men and men with a relevant family history, CRUK recommends further research to clarify the drivers of risk and disease aggressiveness in these groups, and to develop better, more accurate tests, to inform future policy. The TRANSFORM trial will be particularly useful in building the evidence base for Black men, and the PROFILE study will provide more evidence to explain genetic drivers of risk in both Black men and men with a family history. We support the UK NSC working closely with these research teams to ensure findings inform future policy decisions. The UK NSC should also continue collaborating with researchers to revisit the definition of family history and Black men, and to ensure specific ethnicity data, including men from mixed ethnicity, is collected in trials and included in future modelling to enable a more accurate assessment of the benefit and harms. • While CRUK supports introducing screening with the PSA test every two years for men aged 45-61 with a confirmed BRCA1 or BRCA2 pathogenic variant, we urge the Committee to review the evidence regarding the most optimal age-range as well as prostate cancer risk associated with Lynch syndrome. We also call for enhanced evaluation and close monitoring of outcomes amongst BRCA1 carriers and suggest consideration of whether this programme would be better suited as a surveillance programme rather than a targeted screening programme. The SCHARR report grouped together BRCA1 and BRCA2 variants into one model. Overall, for men with a pathogenic variant in BRCA1 or BRCA2, the model predicted that screening would have a more favourable benefit-harm balance and likely be cost-effective. The report notes that this is likely because those with a BRCA1 or BRCA2 pathogenic variant may develop more aggressive prostate cancers, which reduces the risk of overdiagnosis. However, for BRCA1 carriers, current data shows a small increase in incidence of prostate cancer, with less consistent evidence around carriers being at higher risk of developing aggressive forms of the disease. The lower rates of aggressive disease in this group could impact the benefit-harm ratio by potentially increasing the risk of screening-related harms, such as overdiagnosis, and reducing the benefits, including mortality impact. Because the report grouped BRCA1 and BRCA2 variants into one model, it is difficult to determine whether screening BRCA1 carriers actually results in a favourable balance of benefits to harms. The UK NSC should re-run BRCA1 and BRCA2 in two separate models to reflect the different levels of evidence. The Committee should also consider whether screening for men with a BRCA1 pathogenic variant should take place as a surveillance programme with enhanced data collection and monitoring instead of a targeted screening programme in order to allow for a more risk-adapted approach to screening this cohort. This will also allow the evidence base to be strengthened to inform future screening policy.

Across each of the screening approaches assessed, the balance of benefits and harms is shaped by the performance of the PSA test, which has important limitations that must be acknowledged. The PSA test is associated with a high rate of false positives and screening can therefore result in harm. For example, NICE cites that 75% of men with a raised PSA level (more than 3ng/mL) will have a negative prostate biopsy.² *(note: it is not clear whether the numbers NICE cites are for asymptomatic men, symptomatic men, or both, and other diagnostic accuracy studies for PSA in asymptomatic populations are lacking).*

Harms also include **unnecessary further investigations** (e.g., MRI or invasive biopsies) and **overdiagnosis**. Estimates of overdiagnosis from prostate cancer screening across research studies vary due to differences in methods of calculation, or length of follow-up and age of participants, but overall estimates are between 15-65%.³⁻⁸ UK data also shows that since the early 1990s, which is when PSA testing started to be used more regularly in the UK, prostate cancer incidence rates have increased by 55% in males but mortality has decreased by approximately 25% which may be indicative of overdiagnosis.⁹

Overdiagnosis can result in **overtreatment** which is associated with long term side effects such as **urine leakage** and **erectile dysfunction, as well as psychological impacts**. For example, the ProtecT trial found:

- 24% of participants receiving prostatectomy reported urine leakage (measured by wearing one pad or more per day) at 12 years post-treatment compared with 11% in the active monitoring group and 8% in the radiotherapy group.¹⁰
- 18% of participants receiving prostatectomy reported erections firm enough for intercourse compared to 30% in the active monitoring group and 27% in the radiotherapy group.¹⁰

While pre-biopsy MRI can reduce some harm from unnecessary biopsies, it remains unclear whether it reduces overdiagnosis and overtreatment in the real-world setting. There is also evidence of variation in how pre-biopsy MRI has been implemented across the UK, including limitations such as poor image quality and lack of reporting expertise. It is important that instances of unnecessary investigations, overdiagnosis, and overtreatment of prostate cancer are limited to ensure that men are not harmed from the introduction of a screening programme.

To support the Committee's review, our consultation response is organised around the key aspects of the draft recommendation and the evidence informing it. We have set out our consultation response as follows:

- [Our feedback on the recommendation against a population-wide screening programme](#)
- [Our feedback on the recommendation against introducing a targeted screening programme for Black men](#)
- [Our feedback on the recommendation against introducing a targeted screening programme for men with a family history](#)

		• Our feedback on the recommendation for introducing a targeted screening programme for BRCA1 and BRCA2 pathogenic variant carriers, including implementation considerations • Identified limitations and concerns from the SCHARR modelling (relevant across scenarios) • Reflections on the wider landscape and implications • Concluding thoughts
	CRUK feedback on the recommendation against a population wide prostate screening programme	Evidence currently shows that the harms outweigh the benefits of PSA-based screening for the general public. Therefore, CRUK agrees with the UK National Screening Committee’s recommendation against introducing a population-wide prostate cancer screening programme using the PSA test. Evidence from large screening trials (CAP, ERSPC, PLCO) suggests very small or no impact on prostate-specific mortality, but trials and other analyses consistently demonstrate high rates of overdiagnosis: • The UK-based Cluster Randomised Trial for PSA testing for Prostate Cancer (CAP trial) found that after 15 years of follow-up, those screened had a 0.09% lower risk of death compared to the unscreened control group, whereas around 15% of men diagnosed through screening were likely to have been overdiagnosed. It should be noted that this is likely an underestimate given that a large proportion of men in the control group were likely to have gotten a PSA test over 15 years.⁷ • The European Randomised Study for Prostate Screening (ERSPC) found that after 23 years of follow-up, those screened had a 0.22% lower risk of death from prostate cancer compared to those in the control group. The study found an excess incidence of prostate cancer (which is a common way of estimating overdiagnosis) to be around 30% at 23-year follow-up.⁸ • The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) showed no significant difference in mortality amongst those screened compared to the unscreened control group.¹¹ Estimates of overdiagnosis from prostate cancer screening across research studies and analyses vary due to differences in methods of calculation, or length of follow-up and age of participants, but overall estimates are between 15-65%.^{3,4,6–8} It should be noted that these trials are not without limitations. The CAP trial only explored one-off PSA testing and compliance with the screening intervention was only 36%.⁷ The ERSPC trial conducted repeat PSA testing, though screening intervals varied across centres, mortality reduction was driven by only a few countries, and contamination rates (i.e., the number of men in the control group who received a PSA test) were between 7-40% depending on centre, with Finland having the highest rate of 63% contamination.^{12,13} In the PLCO trial, an analysis showed that contamination rates are likely to be as high as 90%.¹⁴ All of these trials were

		also conducted before multiparametric MRI (mpMRI) was included as part of the diagnostic pathway for prostate cancer. Therefore, these trials should be interpreted with some caution. The SCHARR modelling reinforces the evidence from the CAP, ERSPC, and PLCO trials, showing that screening all men with a PSA test would generate more harms than benefits, regardless of the age range assessed. These findings reflect both the limitations of the PSA test and the risk of detecting many slow-growing cancers due to prostate cancer's long sojourn time. There is an urgent need to improve earlier diagnosis of aggressive prostate cancer. In the short-term, there needs to be increased focus on improving current diagnostic tools and approaches, and in the long-term, new markers of aggressive disease need to be uncovered by discovery science, which should aid the development of new, more accurate technologies.
	CRUK feedback on the recommendation against introducing a targeted screening programme for Black men	Given the significant evidence gaps around cohort definition, disease aggressiveness, and screening outcomes in Black men, as well as the current potential for harm, CRUK currently agrees with the UK NSC's recommendation against targeted screening for Black men. There is limited understanding of prostate cancer disease progression and screening outcomes in Black men. The SCHARR modelling was limited due to these fundamental gaps in the evidence as well as limited data available for this cohort. Ongoing research, including the TRANSFORM trial, aims to build the evidence base needed to inform future screening recommendations for this cohort. In the interim, to ensure the Committee has the right information to inform future recommendations, additional points for their consideration are highlighted below: <u>Definition of Black men</u> The SCHARR model utilises broad ethnicity categories (i.e., "Black Caribbean" and "Black African") drawn from the Health Survey for England. While this is a reasonable data source given that more granular data on ethnicity is not currently available, it is important to note that these broad categories do not capture the substantial diversity within these groups. Men of mixed Black ethnicity were also not included in the SCHARR modelling due to data limitations. Applying a single average risk estimate to such heterogeneous populations may obscure important differences, reducing the precision and reliability of the modelled outcomes. The UK NSC should continue collaborating with researchers, including the TRANSFORM trial team, to ensure specific ethnicity data is collected in trials and data from men of mixed ethnicity are captured and included in future modelling so that future screening recommendations can be based on stronger evidence.

Assumption that Black men have more aggressive disease

Gleason Grade Group (GGG) measures prostate cancer disease aggressiveness with more specificity than stage. While a lower GGG often corresponds to earlier stage disease, and a higher GGG is more frequently associated with advanced stage disease, the correlation is not perfect. We agree with the SCHARR report using GGG when discussing risk of aggressive prostate cancer and believe that GGG should be used over stage when assessing whether a tool detects aggressive prostate cancer.

However, the SCHARR model assumes, based on US data,¹⁵ that Black men have a higher risk of being diagnosed with a higher GGG. **Most of the available research from the UK looks at stage and ethnicity rather than GGG and ethnicity. These studies have mixed findings with respect to whether Black men have a higher likelihood of being diagnosed with later stage cancer:**

- A retrospective study using registry data from England showed that Black African (odds ratio 0.79, 95% CI 0.71-0.88) and Black Caribbean (odds ratio 0.74, 95% CI 0.68-0.80) men have a lower likelihood of being diagnosed with late-stage prostate cancer than White men.¹⁶
- Another study using UK data found similar advanced stage incidence rates between Black and White men (7.5% for White men, 95% CI 7.3-7.8 versus 7.0 for Black men, 95% CI 6.1-7.8).¹⁷
- A study focused on a multi-ethnic area in London found no significant difference in risk of disease progression amongst ethnic groups.¹⁸
- The 2025 National Prostate Cancer Audit reported that Black African and Black Caribbean men aged 65-84 with a recorded stage at diagnosis had a greater number of diagnoses per 1,000 across all stages, including stage 3 and 4, compared to White men.¹⁹

Although these studies use stage rather than GGG, they highlight the uncertainty in whether Black men truly are at higher risk of being diagnosed with more aggressive prostate cancer. By assuming that Black men in the UK do have a higher risk of being diagnosed with a higher GGG cancer, the SCHARR model may overestimate the cost-effectiveness of screening in men of Black ethnicity. There is also some evidence to suggest Black men may be at greater risk of overdiagnosis, driven by both biological (e.g., higher baseline levels of PSA²⁰) and social factors (e.g., higher likelihood of getting a PSA test^{21,22}). This further casts doubt on benefits versus harms achieved for this group of men.

		It should also be noted that there is still a lack of consensus on what “clinically significant prostate cancer” or “aggressive prostate cancer” (i.e., prostate cancers that need treatment) should be defined as with respect to GGG.²³ While many define clinically significant disease as GGG 2 or higher, this is not robustly supported by current evidence. For example, many GGG 2 cancers do not require treatment and may not progress further. Therefore, there is a need to improve our understanding of the natural history of prostate cancer and its disease progression to better understand which tumours need to be diagnosed and treated, and which are likely to be overdiagnosed. CRUK recommends that more research be completed that explores disease aggressiveness in Black men in the UK. The TRANSFORM trial will also be valuable in evaluating screening in this population. Once the evidence base is stronger, the Committee should re-run the model to more robustly assess the balance of benefits and harms. <u>Concluding thoughts</u> The SCHARR modelling is limited due to the lack of more granular data on ethnicity as well as a lack of UK-based evidence linking disease aggressiveness and ethnicity. This creates significant uncertainty in whether the benefits would outweigh the harms of targeted screening for Black men. CRUK believes that any future consideration of screening in this group must be underpinned by stronger evidence, and we urge continued investment in research to address these gaps, including close collaboration with the TRANSFORM trial team to allow trial results to feed into future decisions.
	CRUK feedback on the recommendation against introducing a targeted screening programme for men with a family history	Given the lack of data and high-quality evidence, unfavourable benefit to harm balance, and varying definitions of family history, CRUK agrees with the UK NSC’s recommendation against introducing a targeted screening programme for men with a family history. Below we outline our main points of feedback on the SCHARR modelling relating to this group, alongside our recommendations. <u>Definition of men with a family history</u>

In the SCHARR modelling, familial risk is defined broadly as having a first-degree relative diagnosed with breast, ovarian, or prostate cancer at any age or stage. This definition could result in a wider range of individuals being considered to be at risk. It is generally accepted that familial risk is based on consideration of age that relatives were diagnosed, stage of disease and number and pattern of affected relatives. The evidence for this is outlined below:

- A systematic review and meta-analysis reported a relative risk (RR) of 2.22 (95% CI 2.06-2.40) for a first-degree relative with prostate cancer and a RR of 1.88 (95% CI 1.54-2.30) second-degree relative with prostate cancer. Risk was higher for a brother with prostate cancer compared to a father with prostate cancer (RR=2.87 compared to 2.12 respectively).²⁴
- Another systematic review and meta-analysis reported a pooled RR of 2.5 (95% CI 2.2-2.8) for a first-degree relative with prostate cancer. The RR increased in studies that looked at cases diagnosed before the age of 60, and in men with two affected relatives compared to one.²⁵
- A large international cohort study found an interaction between age and first-degree prostate cancer family history. Family history was more strongly associated with high-grade prostate cancer in younger ages.²⁶
- A US-based study found that men with a father or brother diagnosed with prostate cancer before the age of 60 had a RR of 2.16 compared to RR of 1.95 if diagnosed at or after age 60.²⁷
- The UK Genetic Prostate Cancer Study found that age at diagnosis was strongly correlated with a first-degree relatives age at diagnosis. This association was not found for second-degree relatives.²⁸
- A US-based study found that those with a first-degree family history of breast cancer had a 21% greater risk of prostate cancer diagnosis (95% CI 1.10-1.34) and 34% greater risk of lethal disease (defined as cases who were diagnosed with metastasis or developed metastasis throughout follow-up, or who died of prostate cancer) though this was not clinically significant (95% CI 0.96–1.89). The study also found that those with a first-degree family history of prostate cancer had a 68% increased risk of prostate cancer diagnosis (95% CI 1.53–1.83) and a 72% increased risk of lethal disease (95% CI 1.25–2.38).²⁹
- Evidence is lacking for the association between family history of ovarian cancer and risk of prostate cancer diagnosis.

Overall, the SCHARR model's broad definition of family history creates a highly heterogeneous group with wide variation in underlying risk. For example, if the cohort includes many men with only modest or negligible risk, the potential benefits of screening are diluted, while the potential harms, such as unnecessary investigations and overdiagnosis, increase. **CRUK recommends reviewing the evidence on what types of family history and what degree of family history is most relevant to prostate cancer risk to enable a more accurate assessment of the benefit and harms in future modelling.**

Assumption that men with a family history have more aggressive disease

The SCHARR model assumes that men with a relevant family history are more likely to have aggressive disease. However, evidence to support this assumption is conflicting:

- A large international cohort study found that those with a first-degree relative with prostate cancer have an increased risk of GGG 2 or higher prostate cancer compared with men who do not have a first-degree relative with prostate cancer (rate ratio=1.40, 95% CI 1.57-2.00). The trial did not consider age or stage of relatives in the family history definition.²⁶
- A large US based study that analysed data from an active surveillance cohort found that a family history of breast, ovarian, or pancreatic cancer alone was not associated with disease progression (defined as grade reclassification to GGG ≥ 2). Findings did show an association between family history of prostate cancer and grade reclassification to GGG ≥ 2 , however there was no significant association between this and adverse pathological features, and long-term outcomes after treatment were not worse compared to those without a family history.³⁰
- An analysis of those with metastatic castration-resistant prostate cancer (mCRPC) found that patients with a family history of prostate cancer have similar disease progression, but a significantly lower risk of death than those without a family history (hazard ratio: 0.66, $p=0.003$).³¹
- Results from the UK Genetic Prostate Cancer Study showed no evidence to suggest an interaction between Gleason score and family history. The study also notes that the stronger the family history of prostate cancer (measured as number of relatives and degree of relationship), the better overall survival after diagnosis.²⁸ This means that a lower mortality has been shown for those with a family history of prostate cancer. The researchers largely attribute this to awareness of prostate cancer and potentially increased PSA testing, which has been shown in other studies.^{21,29}

Overall, it is unclear whether those with a family history of prostate, breast or ovarian cancer have a higher risk of more aggressive disease and whether they experience worse outcomes. This is further complicated by varying definitions of family history included within studies, so it is also unclear how differing patterns of family history (e.g., age and stage that relatives were diagnosed at, or degree and number of relatives affected) impacts disease aggressiveness. The role of overdiagnosis in this group also remains poorly understood. **By including the assumption that all those with a relevant family history (as described in the SCHARR report) have a greater likelihood of aggressive disease, the model risks overstating the benefits of screening and understating the potential harms.**

		CRUK recommends investment in more research to give a clearer understanding of the underlying drivers of risk including genetic, environmental and behavioural factors (i.e., awareness and PSA testing), before screening can be meaningfully considered for this population. Studies like the PROFILE study will be valuable in building up this evidence base. <u>Concluding thoughts</u> Overall, the broad definition of family history and the assumptions made in the SCHARR modelling introduce substantial uncertainty into the projected benefits of targeted screening for this group. Any future consideration of screening based on familial risk must be underpinned by stronger, more granular evidence that considers the underlying factors that drive risk and disease severity in men with a family history of prostate, breast, or ovarian cancer. We encourage continued investment in research in these areas, including studies such as the ongoing PROFILE study which will help to build up the evidence to inform future screening decisions. More immediate efforts should instead be made to improve how those with a relevant family history are identified and supported, including strengthening existing clinical guidance on when to refer those with a family history of prostate cancer to specialist services.
	CRUK feedback on the recommendation to introduce a targeted screening programme for BRCA1 and BRCA2 carriers	CRUK supports introducing screening for men with a confirmed BRCA1 or BRCA2 pathogenic variant, with the PSA test every two years, however, we suggest: • Reviewing evidence to assess the risk of aggressive prostate cancer in those with BRCA1 pathogenic variants before implementation, as well as reviewing evidence for men with Lynch syndrome • Consideration of whether a surveillance programme for BRCA1 pathogenic variant carriers would be more appropriate than a targeted screening programme, given the need for more tailored risk assessment, enhanced evaluation, and close monitoring of outcomes due to evidence limitations • Reviewing evidence from the IMPACT trial to ensure the most optimal age-range is included for both BRCA1 and BRCA2 pathogenic variant carriers to maximise benefits and minimise harms To support these recommendations, important evidence gaps and limitations are highlighted below that the Committee should note, especially regarding BRCA1. There are also important implementation considerations highlighted below that will be important to consider to support effective and equitable implementation of a screening programme.

Evidence gaps and limitations

In this section, we discuss the following topics:

- [Mixed evidence showing the link between BRCA1 pathogenic variants and aggressive prostate cancer](#)
- [The exclusion of Lynch Syndrome](#)
- [The eligible age range](#)
- [Considerations of trials](#)

Mixed evidence showing the link between BRCA1 pathogenic variants and aggressive prostate cancer:

The SCHARR modelling groups BRCA1 and BRCA2 into one model and assumes that pathogenic variants in both genes are associated with more aggressive prostate cancer. This assumption may impact the modelled benefit–harm estimates for BRCA1 screening in comparison to BRCA2. **While current research clearly shows that men with pathogenic variants in BRCA2 gene have a higher risk of aggressive prostate cancer,^{32,33} this is not as clear for BRCA1 pathogenic variant carriers.**

There is more evidence looking at BRCA1 carriers and the association between prostate cancer incidence rather than the association between aggressive disease. While incidence is important to consider, for prostate cancer, aggressive disease is the more important factor when determining whether the benefit-harms ratio is likely to be more favourable. Evidence on both incidence and aggressiveness of disease is outlined below.

Studies showing a small association between BRCA1 pathogenic variants and higher incidence of prostate cancer diagnosis:

- A systematic review and meta-analysis published in 2021 showed that BRCA1 carriers had a pooled relative risk for being diagnosed with prostate cancer of 1.18 (95% CI 0.95-1.47). The pooled relative risk estimates were higher when looking at BRCA1 carriers with a family history of prostate cancer specifically (RR=2.79 95% CI 1.33-5.88) which indicates this could be an important factor to consider, though the study did not provide more information on how family history of prostate cancer was defined across studies.³⁴

- Another meta-analysis showed that BRCA1 carriers have increased odds of developing prostate cancer (Odds Ratio = 1.35, 95% CI = 1.03-1.76), but overall survival and cancer specific survival was not different between carriers and non-carriers.³⁵
- A cohort study conducted in the UK and Ireland showed a weak association for BRCA1 carriers and prostate cancer diagnosis, though the population was small (n=16 BRCA1 carriers).³⁶

Studies that show no association between BRCA1 pathogenic variants and incidence of prostate cancer diagnosis.

- An international study found no association between BRCA1 and prostate cancer diagnosis.³⁷
- Interim results from the IMPACT trial, which assesses the impact of prostate screening on those with a pathogenic variant in BRCA1/2, also showed no significant differences between men who carry a BRCA1 pathogenic variant and non-carriers, including no differences in age at diagnosis or tumour characteristics.³³
- The latest 5-year findings from the IMPACT study (reported at ESMO in October 2025, yet to be fully published) reinforce the above finding by still showing no increased incidence of prostate cancer in BRCA1 pathogenic variant carriers compared to non-carriers.³⁸

Studies that explore disease aggressiveness amongst BRCA1 pathogenic variant carriers diagnosed with prostate cancer:

- A systematic review, also noted above, found the pooled relative risk for aggressive prostate cancer (defined as Gleason Score ≥ 7) to be 1.59 (95% CI 1.02-2.49) for BRCA1 carriers. Notably, this was much lower than what was found for BRCA2 carriers (RR=4.94 95% CI 3.51-6.96).³⁴
- A UK-based study found that BRCA1 pathogenic variants were very rare and the contribution of BRCA1 to metastatic prostate cancers found in the study was <1%, though the study only included 2 BRCA1 pathogenic variant carriers given how rare it was.³⁹
- The latest findings of the IMPACT trial (reported at ESMO in October 2025, yet to be fully published) do suggest that those with a pathogenic variant in BRCA1 who are diagnosed with prostate cancer through screening have a higher proportion of 'higher-risk' disease using the [NCCN classification](#).³⁸

Note: we acknowledge definitions of classifying prostate cancer disease aggressiveness differ across research.

The evidence base linking a pathogenic variant in BRCA1 to a higher incidence of prostate cancer or, more importantly, to more aggressive disease is conflicting. **It is not clear whether BRCA1 pathogenic variant carriers will develop more aggressive prostate cancer, meaning the assumption made in the SCHARR model may not be appropriate. This limits confidence in the SCHARR model's predictions for this group. If BRCA1 is not linked with aggressive disease, screening these men could do more harm than good, and could lead to greater overdiagnosis and unnecessary tests and treatments.**

CRUK recommends more research and longer-term follow-up to understand if BRCA1 pathogenic variant carriers are at increased risk of developing aggressive disease. We recognise that this group is clinically well defined and already managed by specialist services, so for this reason, we support the inclusion of men with a BRCA1 pathogenic variant within this recommendation, but **recommend that UK NSC consider whether targeted screening for men with a BRCA1 pathogenic variant should take place as a surveillance programme with enhanced data collection and monitoring instead of a targeted screening programme.**

A surveillance programme would allow more personalised risk-adapted screening protocols and ongoing monitoring as part of a wider clinical risk-management plan. The intensity of screening would be dependent on individual risk and involve a more nuanced consideration of family history and patterns of disease. This approach may be more suitable for BRCA1 pathogenic variant carriers in the absence of stronger evidence.

The exclusion of Lynch syndrome:

It is unclear if Lynch syndrome was taken into consideration by the UK NSC, as we note this potential risk factor is not included in the modelling or evidence review that informed the proposed recommendation. Evidence suggests that there may be an association between germline pathogenic variants in one of the mismatch repair genes *MLH1*, *MSH2*, *MSH6*, or *PMS2* and risk of prostate cancer diagnosis, and in some studies, aggressive disease:

- Studies from Denmark⁴⁰, Norway⁴¹, Australia⁴² and the US^{43,44} show that those with Lynch syndrome have a higher risk of being diagnosed with prostate cancer, comparable to the risk that BRCA2 carriers have.
- A systematic review and meta-analysis showed that, across studies, there was a 2.13-fold increased risk of prostate cancer diagnosis (95% CI, 1.45–2.80) for those with Lynch syndrome.⁴⁵

- Many of these studies^{40,41,46} also suggest that the diagnosis of prostate cancer for those with Lynch syndrome occurs at a younger age and is more commonly aggressive (i.e., higher Gleason scores), though there is still conflicting evidence^{42,44} suggesting this may not be the case. More research is needed to clarify this.

The IMPACT trial published initial results on targeted PSA-based screening of men with Lynch syndrome in 2021.⁴⁷ Findings showed that prostate cancer incidence was higher in *MSH2* carriers and *MSH6* carriers compared to non-carriers. Further follow-up is required to confirm these findings and understand whether screening is useful in detecting more aggressive cancers.

CRUK urges the Committee to consider the evidence on Lynch syndrome and prostate cancer, especially given that the risk of diagnosing aggressive prostate cancer for those with Lynch syndrome may be higher than BRCA1 carriers and more comparable to BRCA2 carriers. We also encourage the Committee to work closely with the IMPACT trial team to ensure the trial findings are considered in future policy decisions. In the absence of a targeted screening programme for this cohort, clinical management guidance needs to be clarified and strengthened to ensure men with Lynch syndrome are supported.

Eligible age range:

The IMPACT trial included men aged 40-69 with a BRCA1 or BRCA2 pathogenic variant to be screened for prostate cancer using the PSA test. The interim results of the trial found that aggressive prostate cancers were more common in BRCA2 pathogenic variant carriers in this age group than in non-carriers.³³ Furthermore, over 50% of prostate cancers diagnosed in BRCA1 or BRCA2 carriers were in men over the age of 61, and of these, half were considered “intermediate” or “high-risk” tumours, as per the [NCCN classification](#) (note: we acknowledge definitions of classifying prostate cancer disease aggressiveness differ across research). The trial also found that clinically significant disease was diagnosed as young as 41 in BRCA2 carriers and 43 for BRCA1 carriers.

The UK NSC recommendation specifies an age range of 45-61 for targeted screening of men with a BRCA1 or BRCA2 pathogenic variant. Started screening at age 45 instead of 40 may mean that some aggressive prostate cancers may be missed, and ending screening at age 61 instead of 69 may result in a larger portion of aggressive prostate cancers being missed. While we recognise the need to balance the risk for harm in older age groups, **we encourage the UK NSC to consider the evidence from**

the IMPACT trial, including more recent unpublished findings, to determine the best age-range to maximise benefit and minimise harms.

Considerations of trials:

The IMPACT trial is a valuable study and is a key source of evidence for screening those with pathogenic variant in BRCA1 or BRCA2, however this trial has not been cited in the UK NSC's evidence review. **The UK NSC should review the evidence from the IMPACT trial, including most recent findings, to help inform their decision-making.**

It should be noted that there are key limitations regarding the applicability of the IMPACT trial's findings in real-world settings and in particular, for men from non-White ethnic groups given that the cohort participating in the IMPACT trial was 97% White, meaning it does not reflect the diversity of the wider population. The researchers also note the likelihood of selection bias, as individuals already aware of their BRCA status were more likely to participate and adhere to the study protocol compared with non-carriers. These limitations may affect the extent to which the findings can be generalised to wider populations.

It is also important to better understand the natural history of low-risk prostate cancer in men with a pathogenic variant in BRCA1 or BRCA2. BRCA variants are moderately penetrant, meaning some men with these variants will never develop prostate cancer, or may develop a slow-growing cancer that is unlikely to cause harm. Because our understanding of how prostate cancer develops and progresses in BRCA1 or BRCA2 pathogenic variant carriers is still limited, the IMPACT trial could not account for important differences in disease behaviour. As a result, its findings may over- or under-estimate the true balance of benefits and harms of screening in this group, limiting how confidently the results can be applied to real-world screening decisions. Similarly, the IMPACT trial assumes that more aggressive cancers, which are more likely in those with a pathogenic variant in BRCA1 or BRCA2, leads to increased mortality compared to the overall population, meaning that more lives would be saved through screening. While this is a reasonable assumption, longer-term follow-up data to mortality is required to confirm. **CRUK recommends that any targeted programme includes robust long-term evaluation, supported by data linkage between NDRS and the genetic predisposition registry to monitor outcomes and evaluate the balance of harms and benefits.**

[Targeted screening programme implementation considerations](#)

If a targeted prostate screening programme is recommended, it will be essential to ensure it captures the right men at risk, is accessible across all communities, and does not exacerbate existing inequalities. This will require strong data and registry systems to support the accurate identification of BRCA1 and BRCA2 pathogenic variant carriers, and careful planning for capacity, resources and workforce training across primary care, diagnostic and genetic services.

In the sections below, we will cover the following points, including our recommendations for how they can be addressed:

- [Methods for identifying and inviting the target cohort \(men with a *known* BRCA1 or BRCA2 pathogenic variant\) for prostate screening](#)
- [Improving access to genetic testing](#)
- [Accuracy of genetic testing across diverse groups](#)
- [Existing guidance and pathways for managing men with a family history or pathogenic variants in BRCA1 or BRCA2](#)
- [Existing guidance for asymptomatic PSA testing \(i.e., PCRMP\)](#)
- [Considerations for MRI capacity](#)

Methods for identifying and inviting the target cohort (men with a *known* BRCA1 and BRCA2 pathogenic variant) for prostate screening:

There is a practical question of how men with a known pathogenic BRCA variant will be identified and invited into a targeted screening programme. The UK NSC recommendation is specific to those with a *known* pathogenic variant in a BRCA gene. We agree with this recommendation and note that it would not be feasible to have population-wide testing for BRCA1/2 pathogenic variant carriers. However, this still requires mechanisms to support identification and invitation to the target cohort.

At present, carrier status is recorded in different systems in each UK nation, and therefore the ability to identify and invite those eligible varies across the four UK nations. The National Inherited Cancer Predisposition (NICP) register is one mechanism through which eligible men could potentially be identified in England. However, the completeness of the registry is currently uncertain. Equivalent mechanisms exist in Wales, Scotland and Northern Ireland but registries are managed by regional genetics services which then require link up with the national public health service.

Overall, this means the programme could fail to reach its target population, reducing cost-effectiveness. In addition, this could also risk widening health inequalities if access depends on prior engagement with genetic services, which is known to be lower in ethnic minority groups.⁴⁸

NHS England, NHS Scotland, the Public Health Agency in Northern Ireland, and Public Health Wales will each need to work closely with specialist clinical genomics services to ensure a clear and consistent national approach to identifying eligible men. This should be supported by strengthened registry systems, improved data linkage between genetic services and cancer registries, and routine monitoring of access and outcomes across demographic groups. Strengthening these systems is necessary to ensure the programme reaches those it intends to benefit and does not exacerbate existing inequalities.

Improving access to genetic testing:

Existing registries or mechanisms for capturing carrier status are restricted to the subset of individuals who have accessed genetic testing, following assessment by clinical genetic services. Currently, criteria exists to help healthcare professionals determine who to refer to specialist clinical genomics services. However, in practice there is variability across the UK in how people are identified and referred. Furthermore, much of the current guidance for referral to specialist services is focused on family histories of breast, ovarian, colorectal or pancreatic cancer and not prostate cancer, and awareness of guidance varies considerably. As a result, many eligible people are currently not referred to specialist clinical genomics services. This means that there are likely many people with a BRCA1 or BRCA2 pathogenic variant that have not undergone genetic risk assessment. It should also be recognised that the introduction of a BRCA1 and BRCA2 targeted prostate screening programme is likely to result in an increase in requests for BRCA testing, which could increase the burden on GPs and specialist clinical genomics services.

Clearer national guidance that outlines who to refer for genetic assessment, including clearer criteria on family history of prostate cancer, is required. Improved support for GPs and genetic services to manage increased demand will also be needed. By enabling timely and equitable access to BRCA testing, the programme can ensure that eligible men are identified and not inadvertently excluded due to gaps or inconsistencies in current pathways.

Supporting men through the testing process will also be important. Many men will be unfamiliar with genetic risk assessment and may need clear information and reassurance to understand what testing involves and what their results mean. Ensuring accessible communication, opportunities to ask questions, and appropriate emotional support will help promote informed decision-making and equitable uptake.

Accuracy of genetic testing across diverse groups:

	There is uncertainty around how accurately BRCA1 and BRCA2 pathogenic variants can be identified across different ethnic groups, and what this means for the proposed targeted screening programme. There are different variants in the BRCA1 and BRCA2 genes that confer increased risk of cancer. The frequency of these variants will be broadly similar amongst populations (unless due to specific founder effects such as in Ashkenazi Jewish populations and Shetland ancestry populations), however, the evidence base used to identify and classify these variants is not representative. Most of the research used to identify and understand BRCA variants has been carried out in people classified as having genetic similarity to European populations, so we know far less about the frequency of variants across diverse genomic profiles. As a result, current tools for interpreting BRCA variants are less accurate for non-European populations. Variants in these groups are more likely to be misclassified or left as 'variants of uncertain significance' (where there is uncertainty in the relationship to disease), making it harder to reliably identify true high-risk individuals. Inaccurate recognition of BRCA variants in non-European groups could result in high-risk individuals being missed, while others may be incorrectly identified as high-risk. Both scenarios could lead to inequitable access to screening, unnecessary interventions, and reduced overall effectiveness of the programme in certain ethnic groups. CRUK recommends investment in research and data from diverse populations to enable more accurate variant classification across genomically diverse groups. As this takes time, in the interim it is important to identify mechanisms to optimise existing genetic analysis pipelines. Monitoring access and outcomes of genetic testing across demographic groups to understand the extent of the impact of current biases in genetic testing pipelines is also important. Furthermore, existing outreach and engagement initiatives need to be built on to increase awareness and uptake of genetic testing. Existing guidance and pathways for managing men with a family history, or pathogenic variants in BRCA1 or BRCA2: There are already existing pathways, such as specialist familial cancer services, that are used to manage men with a family history and/or confirmed BRCA1 or BRCA 2 pathogenic variant. These services are important as they aim to provide counselling on risk and appropriate management for individuals and family members. However, it is unclear how these pathways would fit in and/or adapt with the introduction of a targeted prostate screening programme. Furthermore, current recommendations by some systems such as the UK Clinical Genetics Group (UKCGG) and NHS England advise offering annual PSA testing from age

	40 for men with pathogenic BRCA2 variants. This forms part of clinical management and though it is unclear whether this is typically overseen by GPs and/or clinical genetics teams. Implementation is variable across the UK, and it is unclear how consistently these recommendations are followed in practice. In contrast to these existing recommendations, the UK NSC's proposed recommendation is PSA testing every two years for men with BRCA1 or BRCA2 pathogenic variants, starting at age 45 and continuing until age 61. This differs from existing clinical guidance which creates a risk of inconsistent advice to clinicians and patients. Given the overlap between men eligible for clinical management and those who would be invited into a screening programme, diverging recommendations could lead to confusion, variation in care, or missed opportunities for early detection. Therefore, it is important that existing recommendations are amended to align with the final UK NSC recommendation. The UK NSC should collaborate with the UKCGG and the NHS to ensure all clinical advice is based on the best evidence and is consistent. Since pathways are already in existence, operational processes need to be carefully considered. It is currently unclear how a screening programme would work with other parts of the health services including urology services, clinical genetics teams, and primary care to ensure that men eligible are offered BRCA testing, appropriately counselled, and accurately captured within the call-recall system. Although out of scope for the UK NSC, it is still important to note that health system stakeholders at national, regional and local level will need to consider, plan, and direct resource downstream of the screening programme, including for additional MRI capacity, biopsy services, and treatment capacity, to manage the increase in demand. As a wider range of services may be involved in providing risk information, based on genetic factors, resources need to be committed to supporting risk communication strategies and enabling appropriate education and supervision of health professionals who will be involved in delivery at different points in the pathway. CRUK recognises that a formal screening programme could also bring important benefits over the current clinical approach. It would enable consistent recording of uptake, outcomes and harms, allow long term linkage with cancer registries to assess mortality impact, and support routine monitoring of inequalities in access and outcomes across demographic groups. These improvements could strengthen the evidence base and support more equitable delivery of prostate cancer early detection.

However, there must be alignment between or integration of the proposed screening programme and existing clinical pathways, and this should be supported by clear national guidance for clinicians and consistent management advice for patients. Strengthened coordination between screening, urology and specialist clinical genomics services, alongside adequate workforce and capacity planning, is also essential.

Existing guidance on asymptomatic PSA testing (i.e., PCRMP):

Currently, all men without symptoms can request a PSA test through primary care, though access varies across the UK and some men still face barriers. The Prostate Cancer Risk Management Programme (PCRMP) provides information for primary care professionals on counselling asymptomatic men who request a PSA test. It includes information about the possible advantages and disadvantages of PSA testing. Although it is framed as a programme, the PCRMP is essentially an information provision document to help support primary care professionals. The positioning of it as a programme can cause confusion regarding its purpose. **The UK NSC should review the PCRMP to clarify its purpose and what actions primary care professionals should take from it. Consultation and collaboration with health care professionals, including primary care, should be considered as part of this.**

The PCRMP document currently lacks more specific guidance for GPs to help navigate conversations and decision-making for higher incidence groups. Some parts of the PCRMP, such as the more detailed evidence document that links to the UK NSC decision, are out of date and have been withdrawn. **Updating PCRMP to align with the most recent evidence and UK NSC decision should be considered an urgent content update.**

Additionally, it is important that information provided as part of PCRMP is considered by primary care professionals alongside other guidance (e.g., guidance on familial cancer risk, NICE clinical knowledge summaries), especially if a targeted screening programme is recommended. Currently, the UK NSC and Department of Health and Social Care (DHSC) host the PCRMP. **We urge the UK NSC and other relevant health organisations such as the NHS and NICE to consider whether it is more appropriate for the content to be embedded in other guidance and support for primary care.**

Considerations for MRI:

	CRUK supports the inclusion of pre-biopsy MRI within the targeted screening pathway. Any future screening programme for prostate cancer would have to prioritise improving MRI capacity, as well as the current variation in image quality and reporting expertise. The implementation of MRI has improved the prostate cancer diagnostic pathway. Research from the PROMIS trial⁴⁹ showed that using mpMRI (the current gold standard) before biopsy reduced unnecessary biopsies by 27% and diagnosed 5% fewer 'clinically insignificant' cancers (defined in the study as Gleason 3+3 or 3+4, or a core length <6mm). However, the proposed targeted screening programme will increase demand on already stretched imaging services. Emerging evidence suggests that biparametric MRI (bpMRI) may provide similar diagnostic accuracy to mpMRI, therefore it's possible that bpMRI may be able to replace mpMRI in most cases.^{50,51} This would be advantageous because bpMRI does not require a contrast agent making the scan quicker, cheaper, and less prone to patient side effects or allergy to the contrast agent. The UK-based PACIFIC trial will provide more definitive evidence on whether bpMRI can be used instead of mpMRI in the diagnostic pathway.⁵² CRUK urges the UK NSC to consider the evidence from the PACIFIC trial once completed, alongside evidence from other trials, to determine whether bpMRI can be used in the proposed screening programme to mitigate some of the concerns around MRI capacity. A further issue is scan quality, which remains highly variable across the NHS and Health and Social Care system in Northern Ireland. MRI scanners must be appropriately configured, and good MRI scan quality is vital for distinguishing high-grade lesions from low-grade lesions.^{53,54} Yet, one study evaluating 14 hospitals in England found that 40% of patients who were referred for a prostate MRI scan had non-diagnostic quality scans, with Direct Contrast Enhancement (DCE) only used in 53% of sites.⁵⁵ Health systems need to ensure that MRI scanners are appropriately configured and are capable of producing optimal image quality to allow a safe and effective delivery of the proposed screening programme. Accurate reading and reporting of mpMRI relies on the skills of radiologists and urologists, and this specialist expertise is not always available.^{56,57} A panel of UK prostate cancer specialists agreed detailed recommendations in 2018 for how mpMRI should be implemented, including that scans should be reported by urologists or radiologists with specific mpMRI expertise, and that training should be available to support accurate reporting.⁵⁸ CRUK recommends that the rollout of a targeted screening programme for prostate cancer strengthens efforts to provide adequate training for health professionals on reading and reporting an mpMRI scan in line with the Prostate Imaging-Reporting and Data System (PI-RADS).

		In order to optimise the adoption and implementation of a targeted prostate screening programme the health system needs the right resources to ensure there is sufficient MRI capacity and that scan quality and reporting expertise are strengthened. This should include consideration of bpMRI when appropriate, investment in workforce training, and system-wide action to improve and monitor scan quality.
	CRUK feedback on limitations within the SCHARR modelling (relevant across scenarios)	CRUK recognise that there are significant evidence limitations within available published research on prostate cancer. While the SCHARR team have tried to mitigate these limitations in producing their model, there are a few evidence limitations and assumptions remaining which are likely to meaningfully impact the model findings and recommendations. These are applicable across the different screening scenarios. We flag these below along with our recommendations. <u>Thresholds for PSA</u> It is well established that PSA levels increase with age.^{59–61} This is why current symptomatic referral guidance like NICE NG12,⁶² the Scottish Referral Guidelines,⁶³ and the Northern Ireland Suspected Cancer Referral Guidelines⁶⁴ all include age-adjusted PSA thresholds. There is also increasing evidence to suggest that PSA levels may be dependent on ethnicity: • A systematic review comprised of mostly evidence from the US showed that asymptomatic Black men without prostate cancer have higher natural PSA levels compared to asymptomatic White men without prostate cancer.²⁰ • A UK-based cohort study that included anyone who had a PSA test in a primary care dataset (i.e., could be symptomatic or asymptomatic) showed that Black men and men of mixed ethnicity have the highest PSA levels.¹⁷ More evidence in the asymptomatic context in the UK is needed to support what optimal PSA thresholds would be for different ethnic groups, especially given substantial diversity in broad ethnic groupings. Despite evidence suggesting PSA levels are dependent on age and ethnicity, the SCHARR modelling uses a fixed PSA threshold of 3ng/mL. A fixed threshold may be too high or too low for some men which can increase the risk of missed diagnoses or increase overdiagnosis, especially amongst older men or Black men who may naturally have higher PSA levels. CRUK urges the

Committee to consider age-adjusted PSA thresholds to be used in the targeted screening programme and closely monitor the evidence base around PSA levels and ethnicity, with the aim of integrating this into the thresholds when appropriate.

Importantly, there is limited evidence on how PSA levels are naturally distributed amongst those with a BRCA1 or BRCA2 pathogenic variant. **If a targeted screening programme for men with a BRCA1 or BRCA2 pathogenic variant is implemented, CRUK recommends detailed data collection on PSA levels and close monitoring on what an appropriate threshold should be to maximise benefit and minimise harm of screening.**

Uptake of PSA testing

For BRCA1 or BRCA2 pathogenic variant carriers, uptake of PSA testing is likely to be higher than what was shown in the CAP trial. This has been shown in trials studying breast cancer surveillance uptake for those with BRCA1 or BRCA2 pathogenic variants. One international study found that uptake of breast MRI for those with a BRCA1 or BRCA2 variant who completed genetic testing in 2009 or later was 81.3%.⁶⁵ A smaller US-based study found similar results where 83% of those with a BRCA1 or BRCA2 variant adhered to NCCN screening guidelines for high-risk individuals.⁶⁶ Notably, there may be gender differences with a prostate cancer screening programme, given that men are less likely to engage with other cancer screening,⁶⁷ in general uptake for a targeted prostate cancer screening programme for BRCA1 or BRCA2 pathogenic variant carriers is likely to be much higher than the 36% used in the model, which may mean a more favourable benefit-harm ratio, and a more cost-effective programme. **The Committee should consider whether the model should be re-run using a higher uptake for the BRCA1 and BRCA2 scenarios.**

Sensitivity and specificity of PSA

The SCHARR report rightly notes that most literature reporting sensitivity and specificity of the PSA test is in symptomatic populations. To overcome this, data from the PCPT trial was used.⁶⁸ However, the PCPT trial does not provide sensitivity and specificity estimates by age nor does it provide information on how PSA levels change with age. To address this, PSA levels from the trial's mean age group were extrapolated to older and younger groups by using a study conducted in Northern Iran.⁶⁹ This study may not be adequately representative of the UK population, and it's lowest age group was 60, whereas the targeted recommendation

		is for men as young as 45. We acknowledge that in the absence of better evidence, this approach may have been necessary. However, research into PSA diagnostic accuracy in asymptomatic populations and age-related PSA changes should be prioritised to better inform future modelling and screening decisions. <u>Consideration of harms such as erectile dysfunction and bladder/bowel leakage</u> The ProtecT trial suggests that a large number of men experience long-term side effects from treatment such as erectile dysfunction and bladder/bowel leakage. The trial also found that after 10 years, 53% of men assigned to active surveillance switched to radical treatment, but the reason for switching remains uncertain. For some men, the switch from active surveillance to active treatment may be warranted due to disease progression, but for others, anxiety and stress of the cancer potentially progressing may result in an unnecessary switch to treatment. This exposes men unnecessarily to the long-term side effects from treatment. The SCHARR model assigned average costs based on several factors, including utilities such as health-related quality of life (HRQoL). It is noted that the HRQoL captures the negative impact of a cancer diagnosis, including treatment harms, however it is unclear how this is considered outside of costs, including in determining the balance of benefits to harms. The UK NSC should further clarify how treatment harms such as erectile dysfunction, bladder/bowel leakage, anxiety, and stress are considered in the model, especially in determining the benefits to harms ratio.
	Reflections on the wider landscape and implications	The draft recommendation on targeted screening for men with a BRCA1 or BRCA2 pathogenic variant represents an important opportunity to advance prostate cancer early detection. As approaches to prostate cancer early detection continue to evolve, it will be important that any new programme aligns with the wider direction of travel towards more personalised, risk stratified models of care. The development of tools such as CanRISK prostate can be used to enable more precise and individualised risk assessment. These tools take into account a variety of factors including rare variants, common variants, and family history. In the context of breast cancer, such tools are used to enable more granular risk assessment that can be used in decision-making by individuals and healthcare professionals. Prostate cancer risk-stratification approaches are currently being evaluated in large-scale studies such as the TRANSFORM trial, which aims to determine how genetic, biological, and demographic risk factors can be combined to refine early detection strategies.

		It is important to ensure that pathways that are implemented for targeted screening are flexible enough to adapt and evolve as evidence emerges in support of a risk-based approach or for other high-risk cohorts.
	Concluding thoughts	Within this consultation response, we highlight the current gaps and limitations in evidence and outline the impact this may have on the SCHARR modelling. These include outlining evidence that challenges the assumptions used in the SCHARR model for defining Black men and men with a relevant family history, as well as assumptions around disease aggressiveness in these groups. We also highlighted evidence from the IMPACT trial which may have impacts on the optimal age range for men included in the recommendation, as well as evidence suggesting men with Lynch syndrome may be at higher risk for more aggressive prostate cancer and therefore, should be considered in the evidence review and modelling. There are also important implementation considerations, including the need for robust data systems, improvements to variant-classification tools, sufficient diagnostic and treatment capacity, and alignment with existing clinical pathways which are outlined above. Based on our assessment of the current evidence, CRUK supports the UK NSC’s recommendation to introduce a targeted prostate cancer screening programme for men with a confirmed pathogenic variant in BRCA1 or BRCA2 genes, though we urge the Committee to review the evidence regarding the most optimal age-range as well as prostate cancer risk associated with Lynch syndrome. The Committee should consider whether a surveillance programme with enhanced data collection and close monitoring of real-world outcomes, test performance, and potential harms may be more appropriate for BRCA1 pathogenic variant carriers given the current limitations in the evidence. We recommend that the UK NSC ensures the targeted programme is built on robust data collection, clear eligibility processes, and routine monitoring of access and outcomes across all demographic groups. This is essential not only to maximise benefits and minimise harms, but to identify and address any inequalities in who is offered screening, who takes part, and who benefits from it. Without this, there is a risk that a targeted screening programme could widen existing disparities rather than reduce them. Alongside this, we recommend continued investment in research on improving early detection tools and risk-stratification, as well as tackling unwarranted variation in access to high-quality diagnostics and treatment in order to improve prostate cancer outcomes for all and inform future screening decisions.

References

1. Prostate cancer statistics [Internet]. Cancer Research UK. [cited 2026 Feb 2]. Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer>
2. How should I assess a person with suspected prostate cancer? [Internet]. NICE. [cited 2025 Feb 17]. Available from: <https://cks.nice.org.uk/topics/prostate-cancer/diagnosis/assessment/>
3. Draisma G, Boer R, Otto SJ, van der Cruijsen IW, Damhuis RAM, Schröder FH, et al. Lead Times and Overdetection Due to Prostate-Specific Antigen Screening: Estimates From the European Randomized Study of Screening for Prostate Cancer. *J Natl Cancer Inst.* 2003 Jun 18;95(12):868–78.
4. Pashayan N, Powles J, Brown C, Duffy SW. Excess cases of prostate cancer and estimated overdiagnosis associated with PSA testing in East Anglia. *Br J Cancer.* 2006 Aug;95(3):401–5.
5. Gulati R, Inoue LYT, Gore JL, Katcher J, Etzioni R. Individualized Estimates of Overdiagnosis in Screen-Detected Prostate Cancer. *J Natl Cancer Inst.* 2014 Jan 6;106(2):djt367.
6. Pathirana T, Hayen A, Doust J, Glasziou P, Bell K. Lifetime risk of prostate cancer overdiagnosis in Australia: quantifying the risk of overdiagnosis associated with prostate cancer screening in Australia using a novel lifetime risk approach. 2019 Mar 1 [cited 2026 Feb 16]; Available from: <https://bmjopen.bmj.com/content/9/3/e022457>
7. Martin RM, Turner EL, Young GJ, Metcalfe C, Walsh EI, Lane JA, et al. 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):1460–70.
8. Roobol MJ, Vos II de, Månsson M, Godtman RA, Talala KM, Hond E den, et al. European Study of Prostate Cancer Screening — 23-Year Follow-up. *New England Journal of Medicine.* 2025 Oct 29;393(17):1669–80.
9. Cancer Stats Data Hub [Internet]. Cancer Research UK. [cited 2026 Feb 16]. Available from: <https://crukcanerintelligence.shinyapps.io/CancerStatsDataHub/>
10. Donovan JL, Hamdy FC, Lane JA, Young GJ, Metcalfe C, Walsh EI, et al. Patient-Reported Outcomes 12 Years after Localized Prostate Cancer Treatment. *NEJM Evid.* 2023 Apr;2(4):EVIDoa2300018.
11. Andriole GL, Crawford ED, Grubb RL, Buys SS, Chia D, Church TR, et al. Mortality Results from a Randomized Prostate-Cancer Screening Trial. *New England Journal of Medicine.* 2009 Mar 26;360(13):1310–9.
12. Heijnsdijk EAM, Adolfsson J, Auvinen A, Roobol MJ, Hugosson J, Koning HJ de. The Impact of Design and Performance in Prostate-Specific Antigen Screening: Differences Between ERSPC Centers. *European Urology.* 2019 Sep 1;76(3):276–9.
13. Re: PSA screening cuts cancer mortality by 13%, study shows, amid debate about national programme. 2026 Feb 2 [cited 2026 Feb 2]; Available from: <https://www.bmj.com/content/391/bmj.r2288/rr>
14. Shoag JE, Mittal S, Hu JC. Reevaluating PSA Testing Rates in the PLCO Trial. *New England Journal of Medicine.* 2016 May 5;374(18):1795–6.
15. Navarro S, Hu X, Mejia A, Ochoa CY, Pickering TA, Ballas L, et al. Racial/ethnic disparities in patient experiences with care and Gleason score at diagnosis of prostate cancer: a SEER-CAHPS study. *Cancer Causes Control.* 2022 Apr;33(4):601–12.
16. Fry A, White B, Nagarwalla D, Shelton J, Jack RH. Relationship between ethnicity and stage at diagnosis in England: a national analysis of six cancer sites. *BMJ Open.* 2023 Jan 3;13(1):e062079.
17. Down L, Barlow M, Bailey SER, Mounce LTA, Merriel SWD, Watson J, et al. Association between patient ethnicity and prostate cancer diagnosis following a prostate-specific antigen test: a cohort study of 730,000 men in primary care in the UK. *BMC Med.* 2024 Mar 1;22(1):82.
18. Batura D, Patel A, Gandhi A, Pradhan A, Bachoo S, Tetea AA, et al. Ethnic differences in prostate cancer presentation: a time for testing advocacy. *World J Urol.* 2023 Dec;41(12):3543–9.
19. NPCA State of the Nation Report 2024 [Internet]. National Cancer Audit Collaborating Centre. [cited 2026 Feb 2]. Available from:

<https://www.natcan.org.uk/reports/npca-state-of-the-nation-report-2024/>

20. Barlow M, Down L, Mounce LTA, Merriel SWD, Watson J, Martins T, et al. Ethnic differences in prostate-specific antigen levels in men without prostate cancer: a systematic review. *Prostate Cancer Prostatic Dis.* 2023 Jun;26(2):249–56.
21. Littlejohns TJ, Travis RC, Key TJ, Allen NE. Lifestyle factors and prostate-specific antigen (PSA) testing in UK Biobank: Implications for epidemiological research. *Cancer Epidemiol.* 2016 Dec;45:40–6.
22. Nderitu P, Van Hemelrijck M, Ashworth M, Mathur R, Hull S, Dudek A, et al. Prostate-specific antigen testing in inner London general practices: are those at higher risk most likely to get tested? *BMJ Open.* 2016 Jul 12;6(7):e011356.
23. Carlsson SV, Carroll PR, Hamdy FC. Reevaluating the definition of “Clinically significant” prostate cancer as Grade Groups 2-5: An imperative for improved risk stratification. *J Urol.* 2025 Feb;213(2):238–41.
24. Bruner DW, Moore D, Parlanti A, Dorgan J, Engstrom P. Relative risk of prostate cancer for men with affected relatives: systematic review and meta-analysis. *Int J Cancer.* 2003 Dec 10;107(5):797–803.
25. Johns LE, Houlston RS. A systematic review and meta-analysis of familial prostate cancer risk. *BJU Int.* 2003 Jun;91(9):789–94.
26. Clements MB, Vertosick EA, Guerrios-Rivera L, De Hoedt AM, Hernandez J, Liss MA, et al. Defining the Impact of Family History on Detection of High-grade Prostate Cancer in a Large Multi-institutional Cohort. *Eur Urol.* 2022 Aug;82(2):163–9.
27. Chen YC, Page JH, Chen R, Giovannucci E. Family History of Prostate and Breast Cancer and the Risk of Prostate Cancer in the PSA era. *Prostate.* 2008 Oct 1;68(14):1582–91.
28. Brook MN, Ni Raghallaigh H, Govindasami K, Dadaev T, Rageevakumar R, Keating D, et al. Family History of Prostate Cancer and Survival Outcomes in the UK Genetic Prostate Cancer Study. *European Urology.* 2023 Mar 1;83(3):257–66.
29. Barber L, Gerke T, Markt SC, Peisch SF, Wilson KM, Ahearn T, et al. Family history of breast or prostate cancer and prostate cancer risk. *Clin Cancer Res.* 2018 Dec 1;24(23):5910–7.
30. de la Calle CM, Jing Y, Fountain J, Fletcher SA, Mamawala MM, Landis P, et al. Family History of Prostate, Breast, Ovarian, and/or Pancreatic Cancer and Associations with Grade Reclassification in a Large Prostate Cancer Active Surveillance Cohort. *Eur Urol Oncol.* 2025 Sep 5;S2588-9311(25)00200-7.
31. Karsh L, Symanowski J, Shore N, Lin D, Russell D, Kral P, et al. CHARACTERISTICS, TREATMENTS, AND OUTCOMES OF PATIENTS WITH A FAMILY HISTORY OF PROSTATE CANCER AFTER PROGRESSION TO MCRPC: A POST HOC ANALYSIS OF THE TRUMPET REGISTRY. *Urologic Oncology: Seminars and Original Investigations.* 2024 Mar 1;42:S16–7.
32. Kote-Jarai Z, Leongamornlert D, Saunders E, Tymrakiewicz M, Castro E, Mahmud N, et al. BRCA2 is a moderate penetrance gene contributing to young-onset prostate cancer: implications for genetic testing in prostate cancer patients. *Br J Cancer.* 2011 Oct;105(8):1230–4.
33. Page EC, Bancroft EK, Brook MN, Assel M, Hassan Al Battat M, Thomas S, et al. Interim Results from the IMPACT Study: Evidence for Prostate-specific Antigen Screening in *BRCA2* Mutation Carriers. *European Urology.* 2019 Dec 1;76(6):831–42.
34. Nyberg T, Tischkowitz M, Antoniou AC. BRCA1 and BRCA2 pathogenic variants and prostate cancer risk: systematic review and meta-analysis. *Br J Cancer.* 2022 Apr;126(7):1067–81.
35. Oh M, Alkhushaym N, Fallatah S, Althagafi A, Aljadeed R, Alsowaida Y, et al. The association of BRCA1 and BRCA2 mutations with prostate cancer risk, frequency, and mortality: A meta-analysis. *The Prostate.* 2019;79(8):880–95.
36. Nyberg T, Frost D, Barrowdale D, Evans DG, Bancroft E, Adlard J, et al. Prostate Cancer Risks for Male BRCA1 and BRCA2 Mutation Carriers: A Prospective Cohort Study. *Eur Urol.* 2020 Jan;77(1):24–35.
37. Li S, Silvestri V, Leslie G, Rebbeck TR, Neuhausen SL, Hopper JL, et al. Cancer Risks Associated With BRCA1 and BRCA2 Pathogenic Variants. *J Clin Oncol.* 2022 May 10;40(14):1529–41.
38. ecancer. ESMO 2025: Men with BRCA1 and BRCA2 gene mutations should get annual prostate cancer screening - ICR - ecancer [Internet]. [cited 2026

Feb 2]. Available from: <http://ecancer.org/en/news/27145-esmo-2025-men-withbrca1andbrca2gene-mutations-should-get-annual-prostate-cancer-screening-icr>

39. Evans DG, Burghel G, Schlecht H, Sachdeva A, Hudson A, Parikh O, et al. UK-based clinical testing programme for somatic and germline BRCA1/2, ATM and CDK12 mutations in prostate cancer: first results. *BMJ Oncol*. 2025 Feb 24;4(1):e000592.
40. Dominguez-Valentin M, Joost P, Therkildsen C, Jonsson M, Rambech E, Nilbert M. Frequent mismatch-repair defects link prostate cancer to Lynch syndrome. *BMC Urol*. 2016 Mar 24;16:15.
41. Grindedal EM, Zucknick M, Stormorken A, Rønne E, Tandstad NM, Isaacs WB, et al. Outcomes of 10 years of PSA screening for prostate cancer in Norwegian men with Lynch syndrome. *Prostate*. 2024 Jul;84(10):945–53.
42. Rosty C, Walsh MD, Lindor NM, Thibodeau SN, Mundt E, Gallinger S, et al. High prevalence of mismatch repair deficiency in prostate cancers diagnosed in mismatch repair gene mutation carriers from the colon cancer family registry. *Fam Cancer*. 2014 Dec;13(4):573–82.
43. Raymond VM, Mukherjee B, Wang F, Huang SC, Stoffel EM, Kastrinos F, et al. Elevated Risk of Prostate Cancer Among Men With Lynch Syndrome. *J Clin Oncol*. 2013 May 10;31(14):1713–8.
44. Haraldsdottir S, Hampel H, Wei L, Wu C, Frankel W, Bekaii-Saab T, et al. Prostate cancer incidence in males with Lynch syndrome. *Genet Med*. 2014 Jul;16(7):553–7.
45. Ryan S, Jenkins MA, Win AK. Risk of Prostate Cancer in Lynch Syndrome: A Systematic Review and Meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2014 Mar 6;23(3):437–49.
46. Leongamornlert DA, Saunders EJ, Wakerell S, Whitmore I, Dadaev T, Cieza-Borrella C, et al. Germline DNA Repair Gene Mutations in Young-onset Prostate Cancer Cases in the UK: Evidence for a More Extensive Genetic Panel. *Eur Urol*. 2019 Sep;76(3):329–37.
47. Bancroft EK, Page EC, Brook MN, Thomas S, Taylor N, Pope J, et al. A prospective prostate cancer screening programme for men with pathogenic variants in mismatch repair genes (IMPACT): initial results from an international prospective study. *The Lancet Oncology*. 2021 Nov 1;22(11):1618–31.
48. Bains M, Qureshi N, Bajwa R, Leonardi-Bee J, Hassanein Z, Hassan S, et al. Ethnic inequities in genomics and precision medicine [Internet]. NHS – Race and Health Observatory. 2024 [cited 2026 Feb 2]. Available from: <http://>
49. Ahmed HU, Bosaily AES, Brown LC, Gabe R, Kaplan R, Parmar MK, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *The Lancet*. 2017 Feb 25;389(10071):815–22.
50. Ng ABCD, Asif A, Agarwal R, Panebianco V, Girometti R, Ghai S, et al. Biparametric vs Multiparametric MRI for Prostate Cancer Diagnosis: The PRIME Diagnostic Clinical Trial. *JAMA*. 2025 Oct 7;334(13):1170–9.
51. Ahn H, Park MY, Shin JI, Lim B, Kyung YS, Ahn B, et al. Fast Biparametric Versus Multiparametric Magnetic Resonance Imaging for Triage of Men with Elevated Prostate-specific Antigen: The PRO-TRIAGE Prospective Comparative Trial. *European Urology Oncology* [Internet]. 2025 Jul 25 [cited 2026 Feb 2]; Available from: <https://www.sciencedirect.com/science/article/pii/S2588931125001932>
52. Mayor N, Light A, Rawlins F, Cullen E, Klimowska-Nassar N, Sasikaran T, et al. Prostate Assessment using Comparative Interventions - Fast MRI and Image-fusion for Cancer (IP7-PACIFIC): A prospective, multi-centre, dual sequential randomised controlled trial. *Contemp Clin Trials*. 2025 Aug;155:107983.
53. Brizmohun Appayya M, Adshead J, Ahmed HU, Allen C, Bainbridge A, Barrett T, et al. National implementation of multi-parametric magnetic resonance imaging for prostate cancer detection – recommendations from a UK consensus meeting. *BJU Int*. 2018 Jul;122(1):13–25.
54. Fütterer JJ, Tempany C. Prostate MRI and image quality: The radiologist's perspective. *Eur J Radiol*. 2023 Aug;165:110930.
55. Burn PR, Freeman SJ, Andreou A, Burns-Cox N, Persad R, Barrett T. A multicentre assessment of prostate MRI quality and compliance with UK and international standards. *Clinical Radiology*. 2019 Nov 1;74(11):894.e19-894.e25.
56. Khan A, Moore CM, Minhaj Siddiqui M. Prostate MRI and image quality: The urologist's perspective. *Eur J Radiol*. 2024 Jan;170:111255.
57. Kang HC, Jo N, Bamashmos AS, Ahmed M, Sun J, Ward JF, et al. Accuracy of Prostate Magnetic Resonance Imaging: Reader Experience Matters. *Eur*

Urol Open Sci. 2021 May;27:53–60.

58. Brizmohun Appayya M, Adshead J, Ahmed HU, Allen C, Bainbridge A, Barrett T, et al. National implementation of multi-parametric magnetic resonance imaging for prostate cancer detection – recommendations from a UK consensus meeting. *BJU Int.* 2018 Jul;122(1):13–25.
59. Matti B, Xia W, van der Werf B, Zargar-Shoshtari K. Age-Adjusted Reference Values for Prostate Specific Antigen - A Systematic Review and Meta-Analysis. *Clin Genitourin Cancer.* 2022 Apr;20(2):e114–25.
60. Winkler MH, Mayer EK, Carter A, Kulinskaya E, Green JSA. Age-specific PSA reference values based on a screening population of British men. *British Journal of Medical and Surgical Urology.* 2008 Jul 1;1(1):25–30.
61. Matti B, Zargar-Shoshtari K. Age-adjusted reference values for prostate-specific antigen in a multi-ethnic population. *Int J Urol.* 2021 May;28(5):578–83.
62. Suspected cancer: recognition and referral [Internet]. NICE. NICE; 2015 [cited 2026 Feb 2]. Available from: <https://www.nice.org.uk/guidance/ng12/chapter/Recommendations-organised-by-site-of-cancer#urological-cancers>
63. Scottish referral guidelines for suspected cancer [Internet]. NHS Scotland. [cited 2026 Feb 2]. Available from: <https://www.rightdecisions.scot.nhs.uk/scottish-referral-guidelines-for-suspected-cancer/>
64. Primary Care Guidance [Internet]. Northern Ireland Cancer Network. [cited 2026 Feb 2]. Available from: <https://nican.hscni.net/info-for-professionals/primary-care/primary-care-guidance/>
65. Metcalfe K, Eisen A, Senter L, Armel S, Bordeleau L, Meschino WS, et al. International trends in the uptake of cancer risk reduction strategies in women with a BRCA1 or BRCA2 mutation. *Br J Cancer.* 2019 Jul;121(1):15–21.
66. Assad H, Levitin M, Petrucelli N, Manning M, Thompson HS, Chen W, et al. Uptake of screening and risk-reducing recommendations among women with hereditary breast and ovarian cancer syndrome due to pathogenic BRCA1/2 variants evaluated at a large urban comprehensive cancer center. *Breast Cancer Res Treat.* 2024 Jul 1;206(2):261–72.
67. Patnick J. Why do we see gender differences in bowel cancer screening? – UK Health Security Agency [Internet]. 2014 [cited 2026 Feb 2]. Available from: <https://ukhsa.blog.gov.uk/2014/12/05/why-do-we-see-gender-differences-in-bowel-cancer-screening/>
68. Ankerst DP, Hoefler J, Bock S, Goodman PJ, Vickers A, Hernandez J, et al. PROSTATE CANCER PREVENTION TRIAL RISK CALCULATOR 2.0 FOR THE PREDICTION OF LOW- VERSUS HIGH-GRADE PROSTATE CANCER. *Urology.* 2014 Jun;83(6):1362–8.
69. Reza HS, Ali Z, Tara H, Ali B. Age-specific reference ranges of prostate-specific antigen in the elderly of Amirkola: A population-based study. *Asian J Urol.* 2021 Apr;8(2):183–8.

S58			The NSC has done it's job and carefully appraised all of the currently available evidence on a range of potential screening scenarios. It is clear the committee have come to the recommendation based on the best available evidence, in keeping with the aim of balancing benefit and harm. The judgement is that the propositions to screen, with the exception of the BRCA group, will still lead to more harm than good. ***** would like to make 4 observations in support of the draft recommendation. 1. It is common for lay and even expert interpretations of evidence on screening to over estimate benefit, underplay harm and risk. This is very much in play by those arguing against the NSC draft recommendation. As ever there are nuances. "Screening saves lives" vs "all screening does harm, some does good, very little does more good than harm and is cost effective and affordable". Harms are exceptionally hard to communicate and make real. There will be fierce lobbying from those with personal lived experience or their relatives, and from stakeholders with a commercial interest. There is also pressure from those persuaded by campaigns that do not properly explain the harms and opportunity costs incurred by false-positive screens, and the complex nature of things like lead-time biases and the wider ethics of screening. There is certainly more to do in order to explain the ethics of screening more clearly 2. As it stands were the draft recommendation be reversed, too much work would be left to shared decision making. It would need massive resources to do that. Is it worth it? It's still screening but badly resourced and executed will be one way to tip the harm benefit balance further in the wrong way. It feels like this would also be a recipe for postcode lottery situations and would likely worsen inequalities. 3. It is clear that those arguing for screening are doing so from concern for mens health. Given what we know about the benefit harm balance, and the appraisal of the evidence by the secretariat, it is hard to see how advancing with prostate cancer screening (beyond the case being put to the committee) would advance mens health. There are far more impactful targets for improving men's health. To recommend screening is to knowingly harm a cohort of men, the Committee judged this wasn't an acceptable balance of benefit and harm. 4. Proceeding may hugely undermine the point of the Transform trial. This trial will provide the critical evidence on which to truly understand the risk / benefit balance of the contemporary screening question (PSA + MRI + genomic risk). If the trial result ends up being clouded and difficult to interpret as there is also routine screening happening, we may never find out what is the right mix of diagnostics the men in these groups and we may be dooming men to more harm than good. To proceed with population or high risk cohort screening now would obviate to point. And we

		simply will not know if we are harming more men than who benefit. We agree it is critically important black men are well represented in the TRANSFORM study. It's also worth highlighting that spending money where there is insufficient evidence of benefit (or even equipoise) is unethical. Not only will this be “dooming men to more harm than good” it will be displacing resource away from areas where the evidence of benefit is clearer by comparison. That is both irrational and not in keeping with the utilitarian ethic by which allocative efficiency decisions are taken with regard to healthcare in this country. This would therefore not only undermine the NSC, but would also undermine the principles of cost-effectiveness and value for money upheld by other organisations such as NICE. Finally, many will call for alternative expertise to consider the NSC recommendation who may come to an alternative conclusion. This would be to obviate the point of the NSC. There may be a case to be made that the UK NSC should go further and say that PSA should not be done outwith cancer monitoring and trials. Just like we don't do extra cervical screening on request, or prescribe coproxamol, or given extra MMR. More detailed information supporting our points is set out below. 1 It is common for lay and even expert interpretations of evidence on screening to over estimate benefit, underplay harm and risk. This is very much in play by those arguing against the NSC draft recommendation. Very few of the public commentators actually understand the principles of screening. There are many who see “screening” is the “test” bit not the “programme” bit. To recommend screening is to knowingly harm a cohort of men, the Committee judged this wasn't an acceptable balance of benefit and harm. As ever there are nuances. “Screening saves lives” vs “all screening does harm, some does good, very little does more good than harm and is cost effective and affordable”. Harms are exceptionally hard to communicate and make real. 1.1 We may over estimate benefit of screening See for example Roobol et al – European Study of Prostate Cancer Screening – 23-Year Follow-up. There were many very optimistic headlines about lives saved following this study. These will have influenced and shaped public opinion, often will have shaped clinical and policy maker opinion. The nuances are less compelling:

		• showed a 13% reduction in mortality from prostate cancer, not a 13% all cause mortality reduction. However, over the period 50% of the men in the trial died – Thus the report of 13% is misleading. • 1.6% of men in control group died from prostate cancer and that was reduced by 0.22% by PSA testing (1.4% in the screening group). A difference of 2/1000. Again, during this period, close on 50% of all participants died of other causes • NB – this was in men aged 55 to 69 years of age at the time of entry (to spell it out, thus hard to draw conclusions about benefits and risks in younger men!) 1. 2 And under estimate harm. This can be expressed in many ways Limits of PSA. Of course with PSA testing, prostate cancer may be detected before symptoms develop and may extend life or facilitate a complete cure. The Committee is live to the risks. False-negative PSA tests (about 15% of asymptomatic people with a normal PSA level may have prostate cancer) & false-positive PSA tests – about 75% of people with a raised PSA level have a negative prostate biopsy (false-positive PSA test may lead to invasive investigations, such as prostate biopsy, and there may be adverse effects) Invasive biopsy. Significantly reduced, but a long way away from being eliminated, by the use of MRI pre biopsy. Many men still may undergo unnecessary biopsy. This comes with consequences. Ignore or downplay overdiagnosis and unnecessary treatment. Slow growing tumours are common and may not cause any symptoms or shorten life A third of men above the age of 50 have little areas of prostate cancer, which do not grow and do not spread. Men may have unnecessary treatment such as prostatectomy or radiotherapy carry complications. Urine leakage requiring pads can occur in 30% of men who have surgery. Erectile dysfunction can affect 50% long term. Radiotherapy can cause rectal problems in 5% to 20%. Harms at individual level vs harm multiplied when recommending policy and recommendations that affect millions of men. Even if the harm profile is trivial at individual level (which it isn't in this case), once amplified across millions of men it becomes

			substantial. There are a lot of very senior clinicians who seem to not understand this. Again, Roobol et al acknowledge this clearly: • “The associated risks of overdiagnosis and unnecessary interventions remain considerable. Future screening strategies should focus on risk-based approaches to minimize these harms while maintaining the benefits.” • “With only 16% of PSA tests yielding elevated results and merely 24% of the subsequent biopsies confirming prostate cancer, a considerable number of these tests and procedures may have been unnecessary. More important, considerable harm arises from the overdiagnosis and subsequent overtreatment of tumors that are unlikely to cause prostate cancer illness or death, as indicated by the excess incidence of prostate cancer of 27 cases per 1000 men and, in particular, the doubling in detection of low-risk cancers in the screening group” A lot of this is well captured in the evidence review from NSC secretariat. 1. 3 However there are non captured opportunity costs. These are underplayed in the evidence review and draft recommendation. For example: 2. MRI – Affordability, opportunity cost. Money and clinician time 3. GP time in addressing the many issues that will come out of a screening programme. These are obviously on the edge of the scientific case for screening, but are very real world considerations in practice. 1. 4 there is more to do in order to explain the ethics of screening more clearly Offering screening to populations are well (or think they are), the result of which may benefit some but actively harm others is a fundamentally different concept to diagnosis. The ethics of screening (populations who think they are well) to diagnosis (people who approach health care with signs or symptoms and a diagnostic process follows). Ethically these are fundamentally different. Screening programmes are good at turning well people into patients. This might be better explained going forward. Obviously a policy point beyond just prostate cancer screening.

		2 As it stands were the draft recommendation be reversed, too much work would be left to shared decision making We overestimate real world reliability of shared decision making and ability to communicate and understand statistical probabilities. This is of obvious and critical importance to true informed consent, and is even more important when the harm / benefit balance is as it is in this screening question. The NSC infographic is excellent and telling. EVEN when MRI is in the mix the net harm / benefit ratio doesn't seem to make an overwhelming case. For the men who are diagnosed following MRI, many of them (up to half) will have slow indolent disease (and more likely to die with than of + harms of RT / risks of surgery etc). This is set out in the detailed papers esp the one from SSHaRR. The episode of inside health in the immediate wake of the Hoy diagnosis set out the difficulties exceptionally well. Olympian Sir Chris Hoy wants more tests for prostate cancer – should it happen? This gives an excellent explanation of a difficult and emotive issue with no clean answer. From about 14 mins a very good specific section on age threshold and black men. This covers – the nature of the disease, incidence at different ages (and thus predictive value of the test), test sensitivity and specificity (and the implications of this), harms that can come from diagnostic pathway, and treatment. All of this needs to be in in the mix in ensuring shared decision making and informed consent. Whether this will be well executed in exceptionally resource constrained and time limited primary care is debatable. 3 this recommendation in the context of improving men's health It is clear that those arguing for screening are doing so from concern for mens health. We need to see the level of concern for this issue as an opportunity to improve men's health. however, given what we know about the benefit harm balance, and the appraisal of the evidence by the secretariat, it is hard to see how advancing with prostate cancer screening (beyond the case being put to the committee) would advance mens health. There are far more impactful targets for improving men's health. To recommend screening is to knowingly harm a cohort of men, the Committee judged this wasn't an acceptable balance of benefit and harm.

		4 proceeding may hugely undermine the point of the Transform trial. The £42m Prostate Cancer UK and UK government Transform trial will bring these elements together to fill the evidence gaps identified by the National Screening Committee. The study offers immense potential through using short MRI scans (Prostagram), plus PSA, plus genomics to reduce biopsy rates even further. One of the critical POINTS of the TRANSFORM study to test the evidence for best diagnostic pathway in a screening context. Esp the negative predictive value of MRI, but also with PSA and genetic risk stratification in the mix. It is being run by PRUK, who are simultaneously lobbying against where NSC have got to. This seems illogical. If the lobbyists force a screening programme for high risk groups then TRANSFORM will never find out what to do for the men in these groups and they will for ever (or 20 years to the next trial) be doomed to more harm than good. To proceed with population or high risk cohort screening now would obviate to point. And we simply will not know if we are harming more men than who benefit NB really important black men are well represented in the TRANSFORM study. further improvements in evidence base to enable more targeted treatment may further change the harm / benefit balance. There is also the potential for improving protocols for active surveillance, so men are reassured it is safe to stick on monitoring. This may reduce the impact of radical treatment in a similar way to how lumpectomy for breast cancer rather than mastectomy transformed harms of breast cancer treatment. Focal therapy leads to a 5- to 10-fold lower risk of side effects, with similar survival at 10 years compared with radical surgery or radiotherapy.
S59	Peter Corbishley	Over the past four years we have been engaged in offering PSA testing events to men in Worcestershire. In 2026 we will be arranging for 2,000 men in total to be tested free of charge at 8 venues across the county at a cost of £52,000. Talking to these men (mainly aged 45-65) we hear time and time again how many of them aged 50+ have been turned away by their GPs, even if they are Black and have a family history of PC or potential symptoms. The poorer the area we test in, the greater the number of men unable to get GP appointments or having been refused access to a PSA test. Despite this, I am not yet convinced a national screening programme is the answer. I am, however, more than persuaded that targeted screening for Black men and men with family history of PC is now overdue.

			In Worcestershire we are privileged to have a county PC support group of 574 members, awareness events averaging two per month and a PSA programme second to none. If every county was as well served as ours, my campaigning for targeted screening would possibly be not so strong, but I am driven on by the need to reduce the shocking health inequalities across the U.K. By offering tests free of charge and by working closely with PCNs to ensure they invite men from lower socioeconomic backgrounds to the tests, we are doing all we can to disprove the idea that our community PSA testing can do more harm than good. But how much more effective this would be if testing became screening and was systematic and within the NHS.
S60	Chris Byrne	Healthwatch Worcestershire	In summary: Too many men are being diagnosed at stages 3 and 4 with PCa, typically around 50%. Asymptomatic men with earlier more readily treatable PCa are being missed. Current GP guidance is unclear, evidenced by the wide interpretation of this guidance resulting in men who have close family history of PCa or breast cancer being turned away by GP surgeries if they are asymptomatic. Healthwatch Worcestershire has carried out a number of surveys showing wide spread inconsistent GP responses to such asymptomatic men. HWW recommend this guidance needs to be clearer and delivered more consistently so more men can be diagnosed at stages 1 and 2. HWW recommend that higher risk men are targeted by active campaigns to discover these men at stages 1 and 2 with the benefits to the men and the financial benefits of the local health economies. HWW also recommends increased support for GPs to deliver targeted focus on higher risk men through financial incentives like LES, and increased diagnostic availability and secondary care support. We have recorded an interview with a prostate cancer patient – stage 4 which is available for you to view on You Tube – https://www.youtube.com/watch?v=HqaVcdZHSrU Here is a real world example of why your prostate cancer recommendations needs to focus on identifying high risk asymptomatic men. Currently advice for men is unclear and depends often on how a GP views PSA testing. GP guidance is variable – Healthwatch Worcestershire surveys with men attending PSA testing clinics has evidence of black men with family histories of PCa being refused a

		GP appointment and told to come back when they have symptoms. Listen to Phil's story: 00:02:55 – Phil's Story: Missed Opportunities & Late Diagnosis 🌱 Mixed advice, rising PSA to 18, and a stage 4 diagnosis – Phil reflects on what happened. 00:04:57 – The Variation Problem: GP Inconsistency Across Worcestershire 🇬🇧 Men report very different experiences – even within the same practice. The current guidance is not producing early diagnosis of PCa: 00:07:09 – Understanding the NHS PSA Testing Guidelines 🇬🇧 Breaking down what the PCRMP guidance says – and how it's applied. The current system relies on men who are at high risk coming forward and hopefully get through the receptionist barrier to have a discussion with their GP. The NHS is aware that black men with a family history of PCa and mothers with breast cancer – BRCA genes are at very high risk. Where is the awareness campaign so these men at very high risk are encouraged to talk to their GPs? Current guidance is not working, men are voting with their feet by attending private PSA testing sessions – like those run by the Worcestershire Prostate Cancer Support Group who typically find between 8% to 12% of men tested need to be referred to their GPs for further investigation resulting in watchful waiting or active treatment. Local public health data shared with HWW shows just under 50% of men diagnosed with PCa are at stages 3 or 4 in Worcestershire. This is not good enough and we are concerned that just targeting BRAC gene patients, while welcomed, is not enough to turn the tide. Never mind how you go about identifying who has these genes your draft recommendations seem to ignore the high risk men. There needs to be active case finding recommendations, funding GPs to actively seek out these high risk men rather than just wait for them to attend surgery, especially those men from lower socio-economic groups and those in high deprivation areas where proactive health care is furthest from their minds. 00:12:20 – Identifying High Risk Men Today 🎯 The role of better records, early GP conversations, and risk awareness. 00:13:32 – Should Screening Target BRCA1 & BRCA2 Carriers? 🧬 The UK screening committee's draft recommendation and what it could mean.

		We have a gap that needs attention today. While we await the outcomes of the Transformation trial and other such trials to read out useful evidence based information, in likely 2/3 years, around 12,000 men a year will continue to die from PCa. Changing nothing or identifying only a tiny percentage of high risk men with BRCA genes condemns these numbers to remain high. 24,000/36,000 men will likely die as you wait for data to come in over 2/3 years when we know today that asymptomatic men with risk factors are being missed due to poor current guidance – evidence by the number of high profile men who have bravely shared their stories with the public. The current system is not working. When I asked for a PSA test (brother is on watchful waiting) I had to fill in a form on my GP website giving a reason why I wanted a test. No other cancer type asks patients to justify why they should be given an appointment to see their GP. You are clearly told if you have any concerns go see your GP. For prostate cancer you have to fill in a form first. Those 8% to 12% of men that are identified for follow up at private PSA testing sessions, when they get seen by their GP most, if not all have their PSA test run again by their doctor. There is a danger here of widening health inequalities so that those men that can afford private testing get seen while those who because of their socio-economic status are ignored until it's too late. Whether you add additional screening groups to your recommendations or not, we would like you to recommend that the current GP guidance is overhauled in line with the consensus messages that the major charities like Prostate Cancer UK have carefully put together. Fund GP case finding e.g. through the use of LES and ensure there is sufficient diagnostic availability to focus on high risk men with additional secondary care support. The unintended consequence of all the private PSA testing is taking place is that many men are trying to talk to their GPs who are not at high risk. Better, clearer GP guidance and public education to identify high risk men is surely the best way to improve earlier PCa diagnosis and make better use of GP time. 00:12:20 – Identifying High Risk Men Today  The role of better records, early GP conversations, and risk awareness. 00:13:32 – Should Screening Target BRCA1 & BRCA2 Carriers?  The UK screening committee's draft recommendation and what it could mean. This interview with Phil shows the impact on him of GPs not asking about his family history with the consequence of late diagnosis. 00:22:48 – What Men Should Do When GPs Refuse PSA Tests 

			Practical steps: try another GP, attend support group testing, contact Healthwatch. The last two chapters in the interview have a closing message about consistency awareness and access. 00:26:12 – Why PSA Testing Should Be NHS Funded 📺 Community testing often relies on donations – why access matters. 00:27:06 – The Call to Action: Ending Inequality in Prostate Cancer Testing 🔔 A closing message about consistent practice, awareness and fair access. And the link for the You Tube video: https://www.youtube.com/watch?v=HqaVcdZHSrU A comment on gene testing. Is there capacity in the system to carry out the expected rise in testing for BRCA1 & BRCA2 genes? HWW evidence from local surveys shows inconsistencies of approach by the NHS to identifying high risk men result in too many men being diagnosed at stages 3 and 4. Many more men could be caught earlier and treated more cost effectively if high risk screening, clearer health messages for men and their families and better GP guidance were delivered more consistently. The NHS Cancer Plan has improved prevention as a cornerstone of future care. Here is an opportunity to do just that.
S61	Brent William DALE	Cotswolds Prostate Cancer Support Group	The PSA Blood Test is regarded as an inaccurate test by many GP's and professionals bodies. This quite simply is not true. The test is extremely accurate down to several decimal places. The PSA level and PSA Free to Total ratio do not by themselves determine PCa but they do give a very definite indication that there is may or may not be a problem with a gentleman's Prostate. An unusually high PSA level for a man of a certain age whilst not showing PCa would warrant further blood tests, examinations and possible referral to a Urologist who might then determine that an MRi scan is needed and the results of this could lead to a Biopsy of the prostate to determine if a man has PCa or not. The PSA blood test does not lead to over diagnosis or over treatment of PCa. It is purely an indicator of what is happening with the prostate and it is currently the only available indicator that we as men have for a disease that is affecting 1:8 of us men.

		There are screening tests available for many female cancers and these have been developed to save lives and to this end they are very successful. There are no screening tests available for male concerns and PCa is the largest single sex cancer responsible for the death of one man every 45 minutes. Despite the lack of screening, charities like us are striving to give awareness to men of PCa. Unfortunately many men find out that they have PCa when it is at too late a stage for successful treatment. If we hold a public testing event it is very likely that around 10% of those men tested will have raised PSa levels and be signposted towards further examination or referral. Again none of the men tested at any of our public awareness events have gone on to be over diagnosed or over treated based on a single PSA blood test. Many years of effort has gone into preparing the background work in support of a national screening program for PCa. The figures obtained do not lie they show that many lives could be saved through a national screening program. The private cost of a PsA blood test is £26. This small figure could easily save someone's life or enable them to make lifestyle changes that will go on to extend their life. If PCa is detected at an early stage then the treatment outcome is nearly always excellent. If PCa is detected at a later stage the the treatment is very limited and the outcome is generally poor. If you are a man aged over 50 then you are currently entitled to a PSA blood test from your GP but without NICE guidelines many GPs push back on this simple blood test, many tell a patient that if they have no symptoms then they should not worry about PCa and to come back for a PSA blood test when symptoms are noticed. In this case it is likely too late for an excellent outcome. If a man has a family history of PCa in his father, brother, uncle then there is a 25% chance that he will have PCa. If a man is of Afro Caribbean background then again there is a 25% chance that he too will develop PCa. A national screening program will help all men to understand their risks better. It will save large amounts of money on treatments as PCa can be spotted sooner leading to less invasive treatment and it could save thousands of lives in the UK each year. To not offer such a program will lead to expensive late treatments and palliative care for many families who would otherwise not lose their loved ones.

			Our group will continue to provide PCa awareness and public testing events. But, our work would be so much more effective with the backing of a National PCa Screening Program. Thank You
S62	Donald Schloss	Black Prostate Cancer Network	Dear UK National Screening Committee, Please find attached the Black Prostate Cancer Network's formal response to the consultation on prostate cancer screening. We are submitting: • Completed Consultation Comments Pro-forma • Full report: "Community Voices in Prostate Cancer – Volume Two" (20 February 2026) Together these documents set out our evidence-based case for a governed, MRI-first, risk-stratified early detection pathway for high-risk men in England, specifically Black men and men with a first-degree family history, alongside BRCA1/2 carriers. We would welcome further engagement on modelling refinement, pilot design and implementation within NHS infrastructure. Kind regards, Donald

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name: Donald Schloss

Email address: *****

Organisation: Black Prostate Cancer Network (BPCN)

Role: Founder

Consent to publish name alongside response: Yes

Comments:

Section / Page	Text or Issue	Comment
Whole document	Overall conclusions of modelling study and draft recommendation	Please see attached full submission: 'Community Voices in Prostate Cancer – Volume Two (BPCN), 20 February 2026', which sets out detailed clinical, epidemiological, economic and equality analysis supporting a governed, MRI-first, risk-stratified pilot for high-risk groups.
Modelling assumptions	Ethnicity-specific risk parameters	Current modelling does not fully parameterise ethnicity-specific incidence and progression risks despite documented differences in NPCA data and natural history modelling (Tsodikov 2017; Down 2024). Updated modelling incorporating ethnicity-stratified data is

		requested before final policy determination.
Harms and diagnostic pathways	Use of legacy PSA-only paradigms	Harms appear partially derived from historic transrectal, PSA-only pathways. Contemporary NHS practice uses MRI-first triage and transperineal biopsy, which materially reduce unnecessary biopsy and serious infection risk. Modelling inputs should be recalibrated accordingly.
High-risk populations	Scope limited to BRCA carriers	Limiting structured screening to BRCA1/2 carriers excludes higher-incidence groups such as Black men and men with first-degree family history. These groups should remain within scope for modelling and evaluation-ready pilot design.
Equity and data quality	Missing ethnicity data in NPCA (21%)	With 21% missing ethnicity data in NPCA records, modelling uncertainty partly reflects remediable data gaps. Mandatory ethnicity capture and stratified reporting should be embedded in any pilot and considered in equality impact assessment.
Programme development	Feasibility of high-risk pilot	Evidence from NHS Cancer Alliance targeted case-finding initiatives demonstrates operational readiness for evaluation-ready high-risk pilots delivered through NHS

infrastructure and
embedded within NPCA
reporting.



BLACK PROSTATE
CANCER NETWORK

**COMMUNITY VOICES IN
PROSTATE CANCER:**
RESEARCH, TRUTH AND SUPPORT

VOLUME TWO



Thursday, 19 February 2026

© Black Prostate Cancer Network (BPCN) 2026

Purpose of this Report

This report is written to support a clear and urgent policy decision by the UK National Screening Committee (UK NSC) in March 2026 on the introduction of a risk-based, targeted prostate cancer screening programme for high-risk groups in the United Kingdom.

It brings together:

- The latest clinical evidence on Prostate-Specific Antigen (PSA) testing, MRI-first pathways, transperineal biopsy and active surveillance from UK and international trials.
- National Audit data: definitive findings from the National Prostate Cancer Audit (NPCA) 2024 and 2025 reports, highlighting systemic failures in early diagnosis, data reporting and persistent inequalities by ethnicity and deprivation.
- A detailed equity and lived experience analysis with a focus on Black men, men with a strong family history and men in deprived communities, including direct patient testimony.
- The economic case for targeted early detection in the NHS, including cost comparisons of late-stage versus early-stage treatment, litigation risk and potential savings.
- Evidence of health system readiness, including modern diagnostic pathways (MRI-first, transperineal biopsy), active surveillance protocols, community delivery models and existing Cancer Alliance infrastructure.
- International comparison evidence demonstrating that the UK is falling behind comparable health systems in implementing risk-stratified approaches.
- A set of clear, evidence-based recommendations that can be implemented now within a governed, evaluation-ready pilot framework.

This report is designed for:

- UK NSC members (hosted by the Department of Health and Social Care)
- Ministers and officials in the Department of Health, NHS England and HM Treasury
- Parliamentarians in the House of Commons and House of Lords
- Cancer Alliances, Integrated Care System leaders and public health bodies
- Charities, clinicians and community organisations

This version has been reviewed for accuracy as of Friday, 20th February 2026 and includes additional NHS Cancer Alliance pilot evidence.

Contents

1. Executive Summary
2. Who BPCN Is and Why We Are Responding
3. Summary of the UK NSC Draft Recommendation and Scope
4. Direct Responses to the Consultation Questions
5. National Prostate Cancer Audit Evidence – Where the Gaps Are Today
6. Epidemiology and High-Risk Groups – Why Targeted Strategies Are Justified
7. Advances in Diagnostic Pathways and Reduction of Harms
8. Modelling and the Case for Recalibration
9. Proposed Risk-Stratified Targeted Screening Model
10. Monitoring, Governance and Safeguards
11. Policy Alignment and Government Ambition

Sector alignment with BPCN's position

BPCN's position is that the next step for England should be a governed, risk-stratified targeted early-detection pathway for men at highest risk—particularly Black men, men with a first-degree family history and BRCA1 or BRCA2 carriers—using contemporary MRI-first, transperineal and active-surveillance pathways, with equity and real-world evaluation at its core. During this consultation, other national organisations have published commentary that converges with elements of this approach, including calls for risk-stratified strategies that go beyond a BRCA-only offer, updated modelling that reflects modern diagnostic practice and explicit consideration of inequality impacts. These converging views reinforce that the policy question is now how to evaluate targeted pathways safely and fairly, not whether higher-risk men exist.

12. Ethical and Equality Considerations
13. Specific Questions to the UK National Screening Committee
14. Formal Recommendations
15. Conclusion
16. Appendices

17. References

1. Executive Summary

This submission responds to the UK National Screening Committee (UK NSC) consultation on its draft recommendation on prostate cancer screening, the 2025 evidence review and the Phase 3 modelling work. The draft recommendation proposes a targeted screening offer for men with confirmed BRCA1 or BRCA2 pathogenic variants and does not recommend population screening or a targeted offer for Black men or for men with a first-degree family history at this stage.

We argue that a modern, MRI-first, risk-stratified targeted screening pathway should be commissioned and evaluated for clearly defined high-risk groups, specifically Black men, men with a first-degree family history of prostate cancer and men with BRCA1 or BRCA2 variants.

National Audit Evidence: The National Prostate Cancer Audit (NPCA) shows Black men are diagnosed younger (median age 67 vs 71 years for White men), with higher PSA at diagnosis (9.2 vs 7.8 ng/ml) and at more advanced stages than White men (18% metastatic vs 15%; 40% high-risk or locally advanced vs 35%). After case-mix adjustment, Black men are 15% less likely to receive radical treatment for localised disease (OR 0.85, 95% CI 0.78–0.93). The NPCA State of the Nation Report 2025 documents that approximately 21% of men have missing ethnicity recording, limiting equality monitoring.

Natural History and Epidemiology: Tsodikov et al. (Cancer 2017) estimated 44–75% higher metastatic progression risk in Black men. Down et al. (BMC Medicine 2024) analysed 730,000 men in UK primary care, confirming ethnicity-associated diagnostic differences. Barlow et al. (Prostate Cancer and Prostatic Diseases 2022) reviewed 654,197 men, showing ethnic differences in PSA distribution.

Modern Diagnostics: The PRECISION trial (NEJM 2018; n=500) demonstrated MRI-targeted biopsy reduces unnecessary biopsies by 28% while improving detection of clinically significant cancer. Systematic reviews (BJU International 2019) report serious infection rates falling from 1–4% with transrectal biopsy to near-zero with contemporary transperineal approaches.

Cost-Effectiveness: The Active Together evaluation (Sheffield Hallam University 2024) reported delivery cost £712.86 per participant, NHS acute service benefit £1,079.22 per participant and net saving £366.36 per participant in a rehabilitation context, demonstrating that structured community approaches can be cost-saving when designed appropriately.

International Context: Risk-stratified early detection approaches that explicitly recognise higher risk in men of African and Caribbean ancestry are being piloted

or recommended through the PRAISE-U programme in Europe, guidance from the Prostate Cancer Foundation (USA) and Canadian expert consensus.

Policy Alignment: The Men's Health Strategy for England acknowledges that three-quarters of all suicides are men, with suicide a leading cause of death for men under 50 and includes £3.6 million investment in suicide prevention targeting middle-aged men. The National Cancer Plan and Core20PLUS5 prioritise earlier diagnosis and reducing inequalities. Yet prostate cancer remains without a structured, evaluated risk-stratified pathway for the highest-risk groups.

TRANSFORM Integration: The TRANSFORM trial (£42 million, up to 300,000 men, at least 1 in 10 invitations to Black men) will provide important data but final results are not expected until 2028. We propose interim data be used prospectively to refine targeted parameters rather than waiting years while maintaining an evidence gap.

Our Proposal: We are not proposing universal population screening. We propose that the NSC keeps targeted strategies for Black men and men with first-degree family history in scope, commissions updated modelling with ethnicity-specific parameters and contemporary MRI-first harm profiles and supports evaluated pilots of a risk-stratified pathway for high-risk men, with robust monitoring, equality safeguards and patient-reported outcomes embedded from the outset. This is how we close the gap together.

2. Who BPCN Is and Why We Are Responding

The Black Prostate Cancer Network (BPCN) aims to improve the quality of life for those affected by prostate cancer in the Black community in the UK and worldwide. It brings together support groups, researchers, clinicians and innovators to find solutions for service discrepancies affecting Black communities and provides support, education and awareness on prostate and other urological conditions, mental health and physical inactivity. BPCN's work is grounded in the lived experience of Black men, their families, partners and communities, while supporting better outcomes for all men at risk of or living with prostate cancer.

BPCN is responding to this consultation because Black men in the UK face a substantially higher lifetime risk of prostate cancer (1 in 4 compared with 1 in 8 for White men), are more likely to be diagnosed at a later stage and experience inequalities in treatment and outcomes, yet there is currently no structured, targeted early-detection pathway for this group. Our members and partner groups see the consequences of late diagnosis and fragmented opportunistic testing in everyday practice, including emergency presentations and avoidable advanced disease.

Patient voice is central to our submission. Guy Griffiths, a 76-year-old Black man from Coventry, told the BBC following the draft recommendation: “Me and my type as black, who are vulnerable, are overlooked. I honestly believe there is a compromised view of black people in the health service.” (BBC, 3 February 2026).

His experience illustrates how structural and perceptual barriers intersect for Black men at risk of prostate cancer. Organised screening is not just about detection—it is about legitimacy, trust and equity of access. Closing the gap means listening to these voices and building pathways that work for the communities most at risk.

3. Summary of the UK NSC Draft Recommendation and Scope

The current UK NSC consultation concerns its draft recommendation on whether to introduce a prostate cancer screening programme and if so for which groups and using which tests. The draft recommendation proposes a targeted screening offer for men with confirmed BRCA1 or BRCA2 pathogenic variants, using prostate-specific antigen testing with defined age ranges and intervals and does not recommend population screening for all men at this stage. It also does not currently recommend a targeted screening offer for Black men or for men with a first-degree family history of prostate cancer, despite recognising that these groups have elevated risk.

The stated rationale for not recommending screening for Black men is “uncertainties in the data,” with the NSC committing to work closely with the TRANSFORM trial to resolve these uncertainties as soon as possible. The accompanying evidence review and modelling work identify ongoing concerns about the balance of mortality benefit and harms at a population level, concerns about overdiagnosis and overtreatment and the need to ensure cost-effective use of NHS resources. For annual screening of Black men aged 55–60, the SCHARR model estimated that approximately 44% of detected prostate cancers would be overdiagnosed and the committee judged this balance of benefit to harm as insufficiently certain to recommend implementation at this stage.

However, we submit that the “uncertainties in the data” framing implies that uncertainty is a fixed property of the evidence base when it is in fact a function of remediable data quality gaps (21% missing ethnicity in NPCA records), modelling assumptions built on prostate-specific antigen only and outdated biopsy-harm pathways and trial design timelines that defer action for three years. Each of these sources of uncertainty can be addressed now through updated modelling, improved data collection standards and prospective use of TRANSFORM interim data rather than waiting until 2028.

The NSC explicitly invites evidence on new studies, on the natural history and risk in high-risk groups, on the performance and harms of modern MRI-first pathways and on the feasibility and equity of any proposed targeted programme. This submission addresses those questions in turn, with a focus on high-risk men and on how targeted screening can be evaluated safely and fairly in contemporary practice. We aim to show how the gap can be closed together through evidence-based collaboration.

4. Direct Responses to the Consultation Questions

The NSC consultation asks, in substance, whether stakeholders agree with the draft recommendation not to introduce a population screening programme and to offer targeted screening to men with BRCA1 or BRCA2 variants, whether there is sufficient evidence to consider targeted screening offers for other high-risk groups including Black men and men with family history, whether the modelling and evidence review appropriately reflect current diagnostic pathways and harms and what additional evidence or programme features would be needed to ensure that any screening offer is effective, proportionate and equitable.

On these points, BPCN's position is as follows.

We do not advocate for immediate universal population screening for prostate cancer and we recognise the historical concerns about prostate-specific antigen only screening, overdiagnosis, overtreatment and treatment-related harms. We agree that targeting screening to groups at demonstrably higher risk is more appropriate than a universal offer provided that the pathway reflects modern MRI-first, transperineal and active surveillance practice and is evaluated rigorously.

We support the recognition of BRCA1 or BRCA2 carriers as a high-risk group but consider a BRCA-only targeted offer too narrow from the perspectives of equity and public-health impact. The NPCA Ethnicity Briefing and Annual Reports demonstrate that Black men are diagnosed at a younger median age (67 vs 71 years), with higher PSA at diagnosis (9.2 vs 7.8 ng/ml) and a higher proportion of high-risk or metastatic disease (40% high-risk or locally advanced vs 35%; 18% metastatic vs 15%) than White men. After adjustment for case mix, Black men are 15% less likely to receive radical treatment for localised disease (OR 0.85, 95% CI 0.78–0.93). Men in more deprived areas are also more likely to present late and less likely to receive radical treatment. Men with a first-degree family history have a substantially elevated lifetime risk, yet current practice largely relies on ad hoc PSA testing rather than a structured, audited pathway.

The NPCA State of the Nation Report 2025 also documents persistent data quality challenges that limit our ability to monitor and address inequalities. Ethnicity recording is missing for 21% of men with prostate cancer, with variation across hospitals. This limits the ability to monitor inequalities and evaluate whether new pathways improve outcomes for groups at higher risk. When ethnicity data are incomplete, any model that stratifies by ethnicity, including SCHARR's, inherits uncertainty that is partly a function of data quality rather than intrinsic scientific ambiguity. Mandatory ethnicity recording with validated collection frameworks, as recommended by the NHS Race and Health

Observatory, should be implemented as a precondition for credible equity monitoring.

We therefore ask the NSC to keep targeted strategies for Black men aged 45–70 and men of any ethnicity with a first-degree family history, alongside BRCA1 or BRCA2 carriers, within scope for modelling and programme design. We further ask that the SCHARR modelling be updated to incorporate ethnicity-specific incidence and progression parameters informed by Down et al. (2024, n=730,000 UK primary care patients), contemporary MRI-first and transperineal harm rates from PRECISION and UK practice audits and realistic uptake and cost patterns informed by Active Together and similar community delivery models, so that the benefit-harm balance for these high-risk groups can be assessed under today's diagnostic practice rather than yesterday's.

Finally, we agree that any screening programme must be implementable, monitored and equitable. We propose that any targeted high-risk pilots are delivered through National Health Service infrastructure with clear eligibility criteria, standardised MRI-first pathways and mandatory ethnicity-stratified data collection aligned with NPCA indicators, so that stage at diagnosis, treatment patterns, harms and patient-reported outcomes can be tracked and addressed across regions. This collaborative approach is how we close the gap together.

5. National Prostate Cancer Audit Evidence – Where the Gaps Are Today

The National Prostate Cancer Audit (NPCA), delivered through the National Cancer Audit Collaborating Centre (NATCAN), provides robust, registry-based data on prostate cancer care in England and is the most authoritative UK source on real-world patterns of diagnosis and treatment by ethnicity and deprivation. Closing the gap requires starting from a clear understanding of where inequalities are already documented.

Key NPCA Ethnicity Briefing Findings:

- Black men diagnosed at median age 67 years vs White men 71 years
- Median PSA at diagnosis: Black men 9.2 ng/ml vs White men 7.8 ng/ml
- High-risk or locally advanced disease: Black men 40% vs White men 35%
- Metastatic at presentation: Black men 18% vs White men 15%
- After case-mix adjustment, Black men 15% less likely to receive radical treatment for localised disease (OR 0.85, 95% CI 0.78–0.93)

Provider Variation: The NPCA State of the Nation Report 2025 documents wide variation between hospitals in the proportion of men diagnosed with advanced disease (range 12% to 31% across hospitals) and in the proportion of men with high-risk or locally advanced cancer receiving radical treatment (range 46% to 87% across hospitals).

Deprivation Gradients: Men living in the most deprived areas are more likely to be diagnosed with metastatic disease (18% most deprived vs 13% least deprived) and less likely to receive radical treatment (58% most deprived vs 67% least deprived).

Data Quality: The NPCA reports that 21% of men with prostate cancer have missing ethnicity data, with variation across providers. This limits the ability to monitor inequalities and evaluate whether new pathways improve outcomes for groups at higher risk.

Taken together, NPCA data demonstrate that ethnicity and deprivation currently influence how early prostate cancer is detected and what treatment is received and that there is substantial variation between hospitals and areas. Any decision on screening and early detection for high-risk men should be read against this backdrop of documented inequality. A targeted, evaluated screening pathway for high-risk groups offers an opportunity to reduce the proportion of Black men and

deprived men presenting with advanced disease and to support more equitable access to appropriate treatment.

6. Epidemiology and High-Risk Groups – Why Targeted Strategies Are Justified

Black men in the UK have a substantially higher lifetime risk of prostate cancer than White men and are more likely to be diagnosed at a later stage, with higher PSA and more aggressive disease. Cancer Research UK and Prostate Cancer UK estimate that about 1 in 4 Black men will be diagnosed with prostate cancer in their lifetime, compared with about 1 in 8 White men.

Down et al. (BMC Medicine 2024) analysed 730,000 men in UK primary care and found that ethnicity is associated with the probability of prostate cancer diagnosis following a raised PSA, with Black men having higher risks at comparable PSA levels than White men.

Martins et al. showed that ethnic minority groups, including Black men, are more likely to be diagnosed via emergency presentation or other non-elective routes, which are associated with more advanced disease and worse outcomes.

Tsodikov et al. (Cancer 2017) used natural history modelling to estimate that Black men have 44–75% higher risk of metastatic progression than White men, suggesting that, for the same age and PSA, Black men are more likely to harbour clinically significant disease.

Barlow et al. (Prostate Cancer and Prostatic Diseases 2022) conducted a systematic review of 654,197 men, reporting ethnic differences in PSA levels, which is directly relevant to the design of risk calculators and thresholds in a targeted programme.

Weiner et al. (Nature Communications 2021) identified differences in immune cell infiltration and plasma-cell signatures in localised prostate cancer in Black men compared with White men, indicating that biological as well as structural factors may contribute to observed disparities.

Family History: Men with a first-degree relative who has had prostate cancer have a markedly elevated lifetime risk. International guidance increasingly proposes earlier and or more frequent testing for this group, particularly when combined with Black ethnicity or multiple affected relatives.

International Evidence: Guidance from the Prostate Cancer Foundation (USA) recommends earlier baseline PSA assessment and more frequent testing over a longer age range for Black men, based on higher risk of lethal disease and modelling of potential mortality reductions with tailored screening. Canadian expert groups have proposed risk-stratified screening approaches that include

Black men and men with strong family history as priority groups for trialling early detection.

For the NSC, the key epidemiological points are that Black men and men with first-degree family history are at demonstrably higher risk of clinically significant and advanced prostate cancer, that UK data confirm these differences in real-world practice and that current opportunistic approaches do not systematically account for that risk. A risk-stratified targeted screening pathway for these groups is about addressing documented differences in baseline risk and stage at diagnosis in a proportionate, evidence-based way.

7. Advances in Diagnostic Pathways and Reduction of Harms

Historic concerns about prostate cancer screening were shaped by experience with prostate-specific antigen only strategies, transrectal ultrasound-guided biopsy and early eras of radical treatment, where overdiagnosis, overtreatment and treatment-related morbidity were common. Those concerns remain relevant but must be reassessed in light of contemporary diagnostic and treatment pathways, which have changed substantially in the last decade.

MRI-First Pathways: The PRECISION trial (NEJM 2018; n=500) demonstrated that MRI-targeted biopsy reduces unnecessary biopsies by 28% while improving detection of clinically significant cancer compared with systematic biopsy alone. By allowing men with non-suspicious MRI to avoid biopsy and focusing sampling on suspicious lesions, MRI-first pathways reduce overdiagnosis of indolent disease and the associated risks of biopsy.

Transperineal Biopsy: The shift from transrectal to transperineal biopsy has reduced rates of serious infection and sepsis. Systematic reviews (BJU International 2019) report serious infection rates falling from 1–4% with transrectal biopsy to near-zero with contemporary transperineal approaches. These procedural improvements mean that harm estimates derived from older transrectal, non-MRI-triaged practice likely overstate risks in current NHS pathways.

Active Surveillance: Contemporary active surveillance protocols, with structured PSA, MRI and repeat assessment schedules, are widely used to monitor low-risk and selected intermediate-risk prostate cancers, reducing overtreatment and its urinary, bowel and sexual side-effects. NICE guidance (NG131) recommends active surveillance as the preferred option for men with low-risk localised prostate cancer.

For high-risk groups such as Black men and men with first-degree family history, the potential benefits of earlier detection of clinically significant and potentially lethal disease must be assessed under these modern pathways. Their higher baseline risk of aggressive and metastatic disease, evidenced by NPCA and natural history modelling, means that the number of clinically meaningful cancers detected per unit of diagnostic activity is expected to be higher, improving the benefit-harm ratio. Updated modelling should reflect contemporary diagnostic practice and the risk profile of the target group rather than extrapolating from outdated pathways.

8. Modelling and the Case for Recalibration

We recognise the scope and complexity of the Phase 3 modelling work undertaken by the School of Health and Related Research (SCHARR) to inform the NSC's draft recommendation. The model provides a structured framework for comparing different screening strategies under specified assumptions about uptake, test performance, disease progression and treatment effects. However, recalibration of key inputs and scenarios is necessary before drawing firm conclusions about targeted screening for high-risk men.

First, ethnicity-specific baseline risks for Black men were not fully parameterised using the latest UK data. High risk is often treated as a generic multiplier rather than being grounded in ethnicity-stratified incidence and progression estimates. Tsodikov et al. (2017) estimate 44–75% higher metastatic progression risk in Black men and NPCA data confirm differences in age at diagnosis, PSA and stage. Without explicit incorporation of these parameters, the model may underestimate potential benefits and overestimate harms for Black men.

Second, much of the harm structure in earlier modelling was informed by prostate-specific antigen first, transrectal-biopsy pathways, whereas current NHS practice increasingly involves MRI-first assessment and transperineal biopsy. MRI-first pathways reduce unnecessary biopsies by 28% and the detection of indolent disease, while transperineal biopsy reduces serious infection risk from 1–4% to near-zero. Economic analyses of MRI-based strategies suggest risk-stratified approaches can improve cost-effectiveness, especially when focused on higher-risk groups.

Third, uptake assumptions for high-risk strategies may not fully reflect recent UK experience with prostate-specific antigen testing and targeted outreach. Down et al.'s analysis of prostate-specific antigen testing in UK primary care (n=730,000) and recent programmes aimed at engaging Black men suggest uptake patterns could differ significantly from older assumptions, particularly if pathways are co-designed with communities and supported by trusted intermediaries.

We are not asking the NSC to disregard modelling. We are asking that the model be updated to incorporate ethnicity-specific incidence and progression parameters for Black men and men with family history, contemporary MRI-first and transperineal harm profiles and realistic uptake scenarios for co-designed high-risk pathways.

We also ask that sensitivity analyses comparing BRCA-only targeting with broader high-risk targeting, including Black men and men with first-degree family history, be published, so that stakeholders can see how different assumptions

affect outcomes for groups at markedly different baseline risk. This is a recalibration request aimed at increasing the relevance and equity of the modelling, using SCHARR's work to help close the gap together.

9. Proposed Risk-Stratified Targeted Screening Model

We propose that the NSC keeps within scope and supports piloting of a risk-stratified targeted screening pathway for three clearly defined high-risk groups: Black men, men with a first-degree family history of prostate cancer and men with confirmed BRCA1 or BRCA2 pathogenic variants.

Eligibility:

- Black men aged 45–70
- Men of any ethnicity with a first-degree family history of prostate cancer aged 45–70
- Men with confirmed BRCA1 or BRCA2 variants aged 40–70

Identification Routes:

- Primary care electronic record searches for coded ethnicity and family history
- Genetics clinic registers for BRCA carriers
- Self-identification via the NHS App and community outreach, with verification in primary care

Diagnostic Pathway:

- Baseline PSA combined with a risk calculator that includes age, ethnicity and family history
- MRI before biopsy for men whose PSA and risk profile cross a pre-specified threshold
- Transperineal biopsy targeted to MRI-visible lesions where indicated
- Active surveillance as the default management for low-risk disease (NICE NG131)
- Radical treatment according to national guidelines for clinically significant cancer

Screening Intervals: Determined by baseline PSA and risk profile, with shorter intervals (2 years) for men with higher baseline PSA or combined risk and longer intervals (4 years) for those at lower risk within the high-risk cohort.

Delivery: Through NHS Cancer Alliances and primary care, integrating with existing MRI and biopsy capacity. Invitations via general practitioner practices

and the NHS App, with additional engagement through trusted community partners such as Black men's health groups, faith organisations, sports clubs and workplaces.

TRANSFORM Integration: As a £42 million trial recruiting up to 300,000 men and ensuring that at least 1 in 10 invitations go to Black men, TRANSFORM is well placed to provide early information on uptake, test performance and acceptability in high-risk groups. We recommend that the proposed high-risk pathway be designed so that participation and outcomes can be linked with TRANSFORM sub-studies, allowing interim data at 18–24 months to inform NSC deliberations.

10. Monitoring, Governance and Safeguards

Any targeted screening offer for high-risk men must be accompanied by strong monitoring and governance arrangements to ensure safety, equity and accountability. The current position, in which most prostate-specific antigen testing takes place outside a formal programme, creates unmeasured variation and risks widening inequalities.

Operational readiness: NHS Cancer Alliance targeted case-finding (2021–2026)

Evidence submitted to BPCN during this consultation shows that Cancer Alliances are already delivering targeted, risk-stratified prostate case-finding for high-risk men using routine National Health Service primary care systems and established urology referral pathways.

Kent and Medway Cancer Alliance: Gravesend Alliance Primary Care Network targeted prostate-specific antigen case-finding initiative (July 2025–June 2026). Phase one targets Black men aged 45–75 identified via EMIS searches and population health tools. Early results: 492 eligible men identified and contacted, 122 attended for prostate-specific antigen testing, 12 raised results referred to secondary care, 3 under ongoing monitoring. Programme leads: ***** and *****. Clinical oversight: ***** and *****.

Wessex Cancer Alliance: sustained, community-led work with Black men since 2021 in Southampton and Bournemouth to raise awareness of higher risk and address barriers to accessing primary care. Inclusion and Involvement Lead: *****. Outputs include a locally co-produced information page and a consensus statement on prostate-specific antigen testing (2025) that will be reviewed in light of the UK National Screening Committee decision.

North East London Cancer Alliance: Targeted Prostate Health Check clinic model (preliminary findings shared with BPCN via the Alliance's Managing Director's office). Contact: *****, Executive Assistant and Project Coordinator, *****.

North Central London Cancer Alliance: engagement linked to TRANSFORM via University College London plus a call for opportunistic prostate-specific antigen testing for at-risk groups in primary care. Project and Communications Officer: *****.

These real-world programmes support the case that an evaluation-ready, governed national pilot for high-risk men is operationally feasible now, and that national modelling and governance should align with emerging practice rather than leaving England reliant on fragmented local initiatives.

Community delivery infrastructure: leisure-sector cancer pathways that can support pilots

Alongside primary care identification and referral, structured community delivery infrastructure already exists to support prehabilitation and rehabilitation, data flows and measurable outcomes. For example, Places Leisure operates an established cancer pathway with standard operating procedures, inclusion and exclusion criteria, Level 4 cancer-qualified instructors and outcomes capture (including EQ-5D-5L and activity measures) supported by referral and follow-up systems. This type of infrastructure can strengthen pilot delivery, adherence and evaluation when aligned with National Prostate Cancer Audit indicators and mandatory ethnicity and deprivation fields.

NPCA Integration: We recommend that any high-risk pilot be embedded within the NPCA and NATCAN framework, with mandatory ethnicity- and deprivation-stratified reporting of uptake of invitations, PSA levels at testing, stage and grade at diagnosis, use of MRI and biopsy, treatment modality, complications and patient-reported outcomes.

Provider Variation: Cancer Alliances and participating providers should submit data in a standardised format, enabling NPCA to report on variation between hospitals and regions in stage distribution and treatment patterns for high-risk men enrolled in the pathway.

Independent Oversight: Governance should include an independent oversight group with representation from the NSC, clinicians, modellers, public health experts and men with lived experience, including Black men and men with family history. This group would review interim data on harms, benefits and equity and advise on modifications or suspension criteria. Clear safety thresholds and stopping rules should be defined in advance.

Cost-Effectiveness Reassessment: Resource use (imaging, biopsies, treatments) and quality-of-life outcomes should be fed back into updated SCHARR modelling to refine estimates of cost per quality-adjusted life year. The Active Together cancer rehabilitation programme reported a net saving of £366.36 per participant for a structured, community-based intervention, illustrating that well-designed programmes for people affected by cancer can be cost-saving, although specific economic modelling would be required in a screening context.

11. Policy Alignment and Government Ambition

The proposed risk-stratified targeted screening pathway for high-risk men is aligned with existing national policy frameworks on men's health, cancer and inequalities.

Men's Health Strategy for England:

- Emphasises prevention, earlier diagnosis and tackling male health disparities
- Acknowledges that three-quarters of all suicides are men, with suicide a leading cause of death for men under 50
- Includes £3.6 million investment in suicide prevention projects targeting middle-aged men
- Highlights reaching men in community and sporting settings
- Addresses structural barriers that prevent men from accessing timely care

National Cancer Plan:

- Sets ambitions for world-class cancer care, improved survival and faster diagnosis
- Commits to increase proportion of cancers diagnosed at earlier stages
- Prioritises reducing inequalities in cancer outcomes

Core20PLUS5 and NHS Long Term Plan:

- Prioritise earlier diagnosis
- Focus on reducing the gap between most and least deprived communities and between ethnic groups

Political and Professional Support:

Secretary of State Wes Streeting MP: "Ensuring that black men, who face twice the risk of dying from prostate cancer, are at the heart of our research efforts." (BBC, 3 February 2026).

Habib Naqvi, Chief Executive, NHS Race and Health Observatory: "Although it's disappointing that this recommendation will not tackle well established ethnic inequalities in prostate cancer outcomes, it is encouraging that targeted screening for black men has been actively considered." (BMJ 2026;392:s260).

Our proposal aligns implementation architecture with these policy ambitions by introducing a governed, risk-stratified pilot that reflects contemporary diagnostics, modelling and equality duties, rather than leaving high-risk men reliant on opportunistic practice.

12. Ethical and Equality Considerations

Ethically, decisions about screening and early detection for high-risk men must balance potential benefits and harms while recognising existing inequities. The Public Sector Equality Duty requires public bodies to have due regard to the need to eliminate discrimination, advance equality of opportunity and foster good relations between different groups.

In the context of prostate cancer, where Black men and men from more deprived areas experience higher risk, later diagnosis and differential access to treatment, failing to evaluate targeted screening for these groups risks perpetuating and compounding existing inequalities. Equity does not mean treating all men identically irrespective of risk. It means designing pathways that respond proportionately to different levels of risk and barriers to care.

Patient Experience: Qualitative research on Black men's experiences of prostate cancer highlights feelings of being overlooked, mistrust of services and the burden of navigating complex pathways without culturally sensitive support. Guy Griffiths' testimony that Black men are overlooked reflects a wider pattern of disengagement driven by structural and perceptual barriers.

The Ethical Question: The key question is not whether prostate cancer screening is risk-free, but whether the current balance of benefits and harms for high-risk groups is acceptable when weighed against the status quo of opportunistic, unguided testing. Under contemporary MRI-first, transperineal and active surveillance pathways and focusing on groups with substantially higher baseline risk, the potential for net benefit is considerably higher than in historical prostate-specific antigen only, general-population scenarios.

Uncertainty Cuts Both Ways: There is uncertainty about the exact magnitude of mortality benefit and overdiagnosis in different targeted strategies, but there is also uncertainty and current disadvantage in leaving high-risk men without any structured early detection offer. It is more consistent with equality duties and with the aims of the Men's Health Strategy to act in a measured, evidence-generating way than to maintain the current absence of targeted options.

13. Specific Questions to the UK National Screening Committee

1. Will the Committee commit to publishing ethnicity-stratified outputs from the SCHARR model before the March 2026 decision?
2. What specific evidence, beyond TRANSFORM, would be required to reconsider targeted screening for Black men?
3. How will the Committee ensure that its equality impact assessment fully reflects the documented 21% missing ethnicity data in national audit?
4. Will the Committee support a risk-stratified pilot for Black men and men with family history to run alongside TRANSFORM, generating UK implementation data?
5. How does the Committee interpret the Men's Health Strategy commitment to at-home PSA testing from 2027 alongside the draft recommendation excluding Black men?
6. What weight has been given to the Secretary of State's statement that Black men should be at the heart of research efforts in the Committee's deliberations?
7. Will the Committee commission updated modelling incorporating MRI-first pathways, transperineal biopsy complication rates and ethnicity-specific progression parameters (Tsodikov 2017) before final decision?

14. Formal Recommendations

1. Keep targeted strategies for Black men and men with first-degree family history in scope for modelling and programme design, alongside BRCA carriers.
2. Commission updated SCHARR modelling incorporating ethnicity-specific incidence and progression parameters, contemporary MRI-first and transperineal harm profiles and realistic uptake scenarios for co-designed high-risk pathways.
3. Support evaluation-ready pilots of a risk-stratified targeted screening pathway for Black men aged 45–70 and men with first-degree family history, delivered through NHS Cancer Alliances and integrated with TRANSFORM.
4. Mandate complete ethnicity data capture across all prostate cancer pathways, addressing the current 21% missing ethnicity rate, as a precondition for credible equity monitoring.
5. Embed pilots within NPCA and NATCAN reporting frameworks with mandatory ethnicity- and deprivation-stratified indicators and independent oversight.
6. Publish sensitivity analyses comparing BRCA-only targeting with broader high-risk targeting, allowing stakeholders to assess outcomes for groups at different baseline risk.
7. Use interim TRANSFORM data prospectively to refine targeted parameters rather than waiting until final trial reporting in 2028.

15. Conclusion

The UK is currently behind international best practice in risk-stratified early detection for prostate cancer, particularly for Black men and men with family history, despite having world-leading diagnostic tools, modelling expertise and community partners. The NSC's draft recommendation to introduce a targeted offer for BRCA carriers is an important step, but it does not yet address the full spectrum of high-risk men documented in UK and international evidence.

NPCA data, large primary-care cohorts, international guidelines and modern MRI-first pathways together make a compelling case that a carefully designed, evaluated targeted screening pathway for high-risk men is both justified and feasible. We are not asking the NSC to rush into a national programme without evidence. We are asking it to keep targeted strategies for Black men and men with family history formally in scope, commission updated modelling that reflects ethnicity-specific risk, modern diagnostic harms and realistic uptake, support a time-limited, evaluation-ready pilot delivered through NHS infrastructure and co-designed with affected communities and use interim data from this pilot and from TRANSFORM to refine decisions before the next review.

BPCN and our partners stand ready to work with the NSC, NHS England, Cancer Alliances, researchers and community organisations to design and deliver such a pathway. Closing the gap together means recognising high-risk men not just as subjects of evidence but as co-producers of solutions and ensuring that the next generation of prostate cancer screening policy in the UK reflects both the best available science and the lived reality of those most affected.

16. Appendices

Appendix A – Core NSC and Modelling Documents

- UK National Screening Committee. Prostate Cancer Screening Evidence Review 2025 – Narrative report.
- UK National Screening Committee. Prostate Cancer Screening Evidence Review 2025 – Coversheet.
- UK National Screening Committee. Screening for Prostate Cancer – Coversheet 2021 (redacted).
- School of Health and Related Research (SCHARR). Phase 3 Prostate Cancer Modelling Report.
- UK National Screening Committee. Prostate cancer – draft recommendation and consultation page. <https://view-health-screening-recommendations.service.gov.uk/prostate-cancer/>

Appendix B – Audit, Registry and Epidemiology Sources

- National Prostate Cancer Audit (NPCA). State of the Nation Report 2025. <https://www.natcan.org.uk/reports/npca-state-of-the-nation-report-2025/>
- National Prostate Cancer Audit (NPCA). State of the Nation Report 2024 – Appendix (staging and ethnicity). <https://www.natcan.org.uk/wp-content/uploads/2025/07/NPCA-State-of-the-Nation-Appendix-2024-2.pdf>
- Down L et al. (2024). Ethnicity and prostate cancer diagnosis following PSA testing in UK primary care. <https://pmc.ncbi.nlm.nih.gov/articles/PMC10905783/>
- Tsodikov A et al. (2017). Prostate cancer natural history modelling by race and ethnicity. *Cancer* 2017;123:2312-9.
- Barlow et al. (2022). Ethnic differences in PSA distribution. *Prostate Cancer and Prostatic Diseases* 2022.
- Cancer Research UK. Screening for prostate cancer. <https://www.cancerresearchuk.org/about-cancer/prostate-cancer/getting-diagnosed/screening>

Appendix C – Diagnostic Pathway and Treatment Evidence

- Kasivisvanathan V et al. (2018). MRI-targeted or standard biopsy for prostate-cancer diagnosis (PRECISION). New England Journal of Medicine 2018;379:589-95.
- Eklund M et al. (2021). MRI-targeted or standard biopsy in prostate cancer screening (STHLM3-MRI). New England Journal of Medicine 2021;385:908-20.
- BJU International (2019). Systematic review of transperineal vs transrectal biopsy infection rates. BJU International 2019;124:715-23.
- NICE (2019). Prostate cancer: diagnosis and management (NG131). <https://www.nice.org.uk/guidance/ng131>

Appendix D – International Guidance and Comparative Policy

- PRAISE-U (Prostate Cancer Awareness and Initiative for Screening in the EU). https://cancer.ec.europa.eu/eu-cancer-mission/praise-u_en
- Prostate Cancer Foundation (2024). Screening guidelines for Black men. <https://pubmed.ncbi.nlm.nih.gov/38815168/>
- Otiono K et al. (2022). Prostate cancer screening in Black men in Canada: a case for risk-stratified care. CMAJ 2022;194:E1411-5.
- Nyame YA et al. (2022). Eliminating racial and ethnic inequities in prostate cancer care. European Urology 2022;82:341-51.

Appendix E – Community Programmes, Economics and Men's Health Policy

- Sheffield Hallam University (2024). Active Together service evaluation. <https://www.shu.ac.uk/-/media/home/research/awrc/projects/active-together/active-together-service-evaluation-2024.pdf>
- Government of the United Kingdom (2025). Men's health: a strategic vision for England. <https://www.gov.uk/government/publications/mens-health-strategy-for-england/mens-health-a-strategic-vision-for-england-accessible-version>
- Government of the United Kingdom (2025). Government unveils England's first ever Men's Health Strategy. <https://www.gov.uk/government/news/government-unveils-englands-first-ever-mens-health-strategy>

- NHS England (2026). Thousands at risk of inherited cancers to receive regular NHS checks. <https://www.england.nhs.uk/2026/01/thousands-at-risk-inherited-cancers-receive-regular-nhs-checks-genetics-programme/>

17. References

1. UK National Screening Committee (2025). Prostate Cancer Screening Evidence Review – Narrative.
2. UK National Screening Committee (2025). Prostate Cancer Screening Evidence Review – Coversheet.
3. UK National Screening Committee (2021). Screening for Prostate Cancer – Coversheet (redacted).
4. School of Health and Related Research (SCHARR) (2025). Phase 3 Prostate Cancer Modelling Report.
5. UK National Screening Committee (2025). Prostate cancer – draft recommendation and consultation page. <https://view-health-screening-recommendations.service.gov.uk/prostate-cancer/>
6. National Prostate Cancer Audit (NPCA) (2025). State of the Nation Report 2025. <https://www.natcan.org.uk/reports/npca-state-of-the-nation-report-2025/>
7. National Prostate Cancer Audit (NPCA) (2024). State of the Nation Appendix – Staging and Ethnicity. <https://www.natcan.org.uk/wp-content/uploads/2025/07/NPCA-State-of-the-Nation-Appendix-2024-2.pdf>
8. Down L et al. (2024). Ethnicity and prostate cancer diagnosis following PSA testing in UK primary care. BMC Medicine 2024;22:83. <https://pmc.ncbi.nlm.nih.gov/articles/PMC10905783/>
9. Tsodikov A et al. (2017). Is prostate cancer different in Black men? Answers from 3 natural history models. Cancer 2017;123:2312-9.
10. Barlow M et al. (2022). Ethnic differences in PSA levels in men without prostate cancer: a systematic review. Prostate Cancer and Prostatic Diseases 2022.
11. Kasivisvanathan V et al. (2018). MRI-targeted or standard biopsy for prostate-cancer diagnosis (PRECISION). New England Journal of Medicine 2018;379:589-95.
12. Eklund M et al. (2021). MRI-targeted or standard biopsy in prostate cancer screening (STHLM3-MRI). New England Journal of Medicine 2021;385:908-20.
13. BJU International (2019). Systematic review of transperineal vs transrectal biopsy infection rates. BJU International 2019;124:715-23.

14. NICE (2019). Prostate cancer: diagnosis and management (NG131). <https://www.nice.org.uk/guidance/ng131>
15. Cancer Research UK (2023). Screening for prostate cancer. <https://www.cancerresearchuk.org/about-cancer/prostate-cancer/getting-diagnosed/screening>
16. PRAISE-U consortium (2024). EU initiative on risk-stratified prostate cancer screening. https://cancer.ec.europa.eu/eu-cancer-mission/praise-u_en
17. Prostate Cancer Foundation (2024). Screening guidelines for Black men. <https://pubmed.ncbi.nlm.nih.gov/38815168/>
18. Otiono K et al. (2022). Prostate cancer screening in Black men in Canada: a case for risk-stratified care. CMAJ 2022;194:E1411-5.
19. Nyame YA et al. (2022). Eliminating racial and ethnic inequities in prostate cancer care. European Urology 2022;82:341-51.
20. Sheffield Hallam University (2024). Active Together service evaluation. <https://www.shu.ac.uk/-/media/home/research/awrc/projects/active-together/active-together-service-evaluation-2024.pdf>
21. Government of the United Kingdom (2025). Men's health: a strategic vision for England. <https://www.gov.uk/government/publications/mens-health-strategy-for-england/mens-health-a-strategic-vision-for-england-accessible-version>
22. Government of the United Kingdom (2025). Government unveils England's first ever Men's Health Strategy. <https://www.gov.uk/government/news/government-unveils-englands-first-ever-mens-health-strategy>
23. NHS England (2026). Thousands at risk of inherited cancers to receive regular NHS checks. <https://www.england.nhs.uk/2026/01/thousands-at-risk-inherited-cancers-receive-regular-nhs-checks-genetics-programme/>

S63		British Association of Black Surgeons	Black men in the UK face double the risk of prostate cancer compared with other groups, yet have historically been underrepresented in clinical research. We welcome the TRANSFORM trial, which has committed to recruiting at least 10% Black men. While awaiting the results, we would like to recommend an NHS-embedded pilot to target this high-risk population. Targeting this group may lead to greater reductions in mortality, and the small population size would mean the resource impact is limited. Such an approach would generate implementation data specific to this group and support evidence-based policy development without pre-empting the findings of ongoing trials.
S64	Joseph Clift	Prostate Cancer Research	Dear UK National Screening Committee Secretariat, Please find attached Prostate Cancer Research's consultation response to the UK NSC's draft recommendations on prostate cancer screening. Our submission is informed by an independent technical critique of the economic model, carried out by the York Health Economics Consortium, which we reference in PCR's response and which is attached as a separate document for consideration. Best wishes, Joe

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

UK NSC's draft recommendations on prostate cancer screening: Response from Prostate Cancer Research

Introduction

Prostate cancer represents a major and growing public health challenge in the UK. It is now the most commonly diagnosed cancer overall, and remains the second leading cause of cancer death among men. Demographic change alone means that the burden of prostate cancer is expected to rise substantially over the coming decades, driven by population ageing and increased prevalence of risk factors. Globally, by 2040 the number of annual cases of prostate cancer is set to rise to 2.9 million.¹

Risk of prostate cancer has also been well established as not evenly distributed across society. Men of Black ethnicity face a substantially higher lifetime risk of prostate cancer, with 1 in 4 diagnosed in their lifetimes, and are more likely to be diagnosed at a younger age. Men with a strong family history or known pathogenic genetic variants are also at significantly elevated risk. Outcomes are also often dependent on where in the UK you live, with around 31% of men diagnosed with prostate cancer in Scotland presenting with metastatic disease compared to 21% of men diagnosed living in England.² The most recent report from the National Prostate Cancer Audit (NPCA) also highlights that those living in more deprived areas are significantly more likely to present with metastatic prostate cancer.³ Despite this context, prostate cancer remains the largest common cancer in the UK without any national screening programme.

The current consultation is of critical importance. The UK National Screening Committee's (UK NSC) review is the first consideration of prostate cancer screening in five years, and the first to consider screening scenarios targeted at high-risk groups. During this time, there have been significant changes to the diagnostic pathway in the UK that have substantially improved the safety and accuracy of diagnosing prostate cancer.⁴ At the same time, the treatment pathway has evolved. Active surveillance is now firmly established as the standard management strategy for men with low-risk disease. Reports from the NPCA demonstrate sustained high uptake of active surveillance and consistently low rates of radical treatments for these men with slow-growing cancers, with rates for the latter falling from 16% in 2018-19 to 7% in the most recent release.^{5,6} Together, these developments provide real-world evidence that the historical risks of overdiagnosis and overtreatment – central to earlier screening debates – have been materially reduced in contemporary UK practice.

This submission by Prostate Cancer Research (PCR) and supported by several other organisations has been informed by an independent technical critique of the Sheffield Centre for Health and Related Research (SCHARR) economic model which underpins the UK NSC's draft recommendations. This critique was commissioned by PCR and carried out by the York Health Economics Consortium (YHEC), in addition to clinical expertise from a national and international advisory board assembled following the publication of the draft recommendations. While

recognising the complexity of modelling in this area, the critique identifies several structural limitations that materially affect the conclusions drawn.

The reflections and recommendations below represent the views of PCR in light of the findings in the YHEC report, which is submitted alongside (and attached to) our emailed response. We will continue to engage constructively with the UK NSC in addressing the specific technical concerns identified within the YHEC report.

Executive summary

Prostate Cancer Research (PCR) welcomes the UK National Screening Committee's (UK NSC) review of prostate cancer screening, including its first consideration of targeted screening scenarios for high-risk groups. However, based on PCR's commissioned independent critique by the York Health Economics Consortium (YHEC) and clinical expert input, we are concerned that the current draft recommendations are underpinned by a modelling framework with structural features that materially influence its conclusions. The issues identified in this response are not isolated technical disagreements; they relate to core assumptions that shape the direction and magnitude of estimated harms, benefits and cost-effectiveness.

Several critical limitations remain unaddressed in the current assessment, including the:

- Absence of comparator scenarios that reflect some degree of substitution for, rather than addition to, existing opportunistic PSA testing
- Reliance on diagnostic and treatment data from legacy trials that do not reflect contemporary MRI-led pathways or current UK management patterns
- Omission of risk-stratified screening approaches that could reduce harms and system costs compared with uniform, interval-based strategies
- Insufficient modelling of high-risk populations, including failure to model family-history screening scenarios using granular definitions of inherited risk
- Absence of explicit equity analysis reflecting the substantially higher lifetime risk and earlier presentation of prostate cancer in Black men, and the implications of these disparities for proportionate and targeted screening strategies
- Limited use of contemporary UK audit and service data, particularly regarding MRI triage and active surveillance uptake
- Lack of scenario testing for alternative diagnostic thresholds and reflex testing strategies (including modelling the Stockholm3 intermediate triage test)
- A narrow economic perspective that does not adequately reflect wider healthcare utilisation and the burden associated with late-stage and metastatic presentation

In several of these areas, more contemporary UK data are available, and clinically accepted alternative approaches could reasonably have been modelled as scenario analyses. Their omission means the model does not simply reflect imperfect evidence, but modelling choices that materially influence the conclusions reached. Collectively, these limitations mean that the SCHARR model evaluates a version of screening that is unlikely to reflect how organised screening would be delivered in contemporary NHS practice.

Subsequent scenario testing conducted within the existing modelling framework demonstrates that modest, clinically plausible adjustments can materially alter cost-effectiveness estimates, in some cases moving screening strategies below the Committee's benchmark. This underlines the sensitivity of the current model to key structural assumptions.

PCR does not argue that screening is without risk. Rather, we argue that a fair and policy-relevant assessment must evaluate screening as it would realistically operate today and not as if it was functioning in earlier eras.

Given that the economic model will materially shape prostate cancer early detection policy for years to come, the threshold for confidence in its structural validity must be correspondingly high. In addition to the issues highlighted above, the SCHARR report also falls short of best practice in economic modelling reporting, further undermining the transparency and intelligibility of its findings. In its current form, the modelling does not provide sufficient assurance that the conclusions drawn fully reflect contemporary clinical practice, evolving diagnostic strategies, or the NHS's equity commitments.

The recommendations made by Prostate Cancer Research in this submission are intended to strengthen the evidentiary robustness, transparency and equity relevance of the UK NSC's final conclusions.

Our recommendations

The UK NSC's final recommendations will impact early detection policy on prostate cancer across the four UK nations for the next decade and beyond, and so the importance of getting this right within this review period cannot be overstated. In their current form, the draft recommendations risk overlooking a material opportunity to improve early detection of clinically significant prostate cancer in men, to reduce late-stage and metastatic presentation, particularly in higher-risk groups, and to address the inefficiencies and inequities inherent in the current opportunistic PSA testing of asymptomatic men.

Prostate Cancer Research (PCR) is deeply concerned by the narrowness of the draft recommendations, which fail to tackle the harms inherent in the current system and, in particular, leave men of Black ethnicity and those with relevant family history continuing to rely on current routes for testing, and which will in their current form fail to effectively cover all those with BRCA1/2 variants at high risk.

In light of our concerns and rapidly evolving diagnostic pathways and emerging evidence, it would be reasonable and proportionate for the UK NSC to continue work on this review across 2026 rather than draw definitive conclusions at this stage from the current model. Allowing additional time would help ensure that the final recommendation commands public confidence and reflects contemporary clinical practice as accurately as possible. Extending the current review period to allow for amendments to the SCHARR model to be made, fully tested, and as far as practicable, made publicly available would also enable meaningful external scrutiny of the model.

Ahead of the UK NSC completing its review, we recommend:

A. Structural revision and transparency of the economic model

- Extending the current review period to enable structural revisions to the model to be implemented, tested, and (as far as practicable) made available for external scrutiny.
- Structurally rebuilding and recalibrating the economic model provided by SCHARR based on the recommendations within the independent YHEC critique, incorporating parameters that more accurately reflect modern diagnostic and treatment pathways and the likely impacts that organised screening will have on the opportunistic PSA testing currently in place
- Explicit modelling of risk-stratified screening strategies within the core model structure rather than limiting analysis to uniform interval-based models.
- Committing to maintaining the economic model as a living framework, with annual parameter updates as new evidence emerges, and formal review cycles every two years rather than the current five-year interval, with public version control and transparent documentation of changes.
- Ensuring that cost-effectiveness conclusions are aligned with updated NICE cost-effectiveness thresholds and methodological guidance, with transparent justification where assumptions materially influence incremental cost-effectiveness ratios.

B. Explicit evaluation of high-risk and equity-focused scenarios

- Undertaking a rapid and focused review of the contemporary literature relating to screening in men with a family history of prostate cancer, followed by explicit modelling of screening scenarios using a more granular definition of familial risk. This should include differentiation by the number of affected relatives, degree of relatedness, age at diagnosis of affected relatives, and other clinically relevant markers of inherited risk, rather than applying broad or uniform risk multipliers across all men with a family history.
- Undertaking and publishing a formal Equality Impact Assessment, including analysis of differential effects by ethnicity, deprivation and family history, and setting out how equity considerations have been incorporated into economic decision-making. This should include modelling different hazard ratios when assessing the higher risk that individuals with multiple risk factors may have, compared to individuals with fewer risk factors.
- Conducting explicit comparative modelling of family history-based PSA screening versus BRCA testing-triggered screening strategies, including the full costs of genetic identification, counselling infrastructure, and equity implications of differential access to BRCA testing.

C. Evaluation of contemporary diagnostic pathways and real-world impacts

- Providing an additional evaluation of a modelled screening pathway that includes the Stockholm3 test, taking into account the published literature and any additional data made available through formal submission processes, and modelling hypothetical reflex testing strategies following PSA to assist referral decisions for MRI, to assess the potential impact of improved risk stratification on cost, harm and benefit.
- Recommending the commissioning of a number of time-limited, prospective real-world evaluation pilots of innovative diagnostic or risk-stratification strategies within selected NHS settings, particularly in areas of higher deprivation, with data incorporated into the proposed living economic model to inform future review cycles.

Our concerns in detail

1. Limited transparency and reporting that weakens the model's robustness

Given the central role of the Sheffield Centre for Health and Related Research (SCHARR) model in shaping national screening policy, the standards of transparency and reporting must be correspondingly high. Key modelling choices, including the definition of the intervention and comparator, structural assumptions and parameter choices, and the handling of uncertainty, are not always clearly articulated or justified.

Established economic evaluation frameworks, including CHEERS and Drummond's criteria, emphasise the need for explicit specification of comparators, transparent reporting of structural assumptions, comprehensive uncertainty analysis and clear discussion of model limitations. In a decision of this magnitude, it is not sufficient for assumptions to be implicit or inferred. They must be clearly set out, tested and defended.

During this consultation period, PCR engaged with the UK NSC to clarify a number of points raised on the economic model used to inform their recommendations, and we thank them for helping to facilitate engagement with SCHARR to raise technical questions, discuss modelling assumptions and the offer to run a small number of scenarios based on clinical feedback we received through our commissioned work with YHEC. SCHARR reported back on the results of running these new scenarios on 18/02/2026, which are presented in full in the accompanying YHEC report. YHEC highlighted that applying modest, clinically credible adjustments to some of the underlying assumptions within the model materially altered incremental cost-effectiveness ratios across several screening strategies. In particular, for Black men and men with a family history, some strategies moved below the Committee's cost-effectiveness benchmark. These findings demonstrate that the model's conclusions are highly sensitive to key structural assumptions and parameter choices.

PCR and YHEC did not, however, have access to the full economic model itself. As a result, it has not been possible to independently interrogate the full range of structural assumptions or test alternative configurations. For a model that will materially shape national prostate cancer policy for the coming decade, full technical transparency would be expected to enable meaningful external scrutiny. The lack of access to the complete model limits replicability and constrains independent validation of the conclusions drawn.

We also note that the modelling process appears to have involved a relatively small number of external clinical advisors. Given the scale and long-term implications of this decision, broader multidisciplinary input, including transparent reporting of advisory roles and any relevant interests, would strengthen confidence in the robustness and independence of the conclusions.

The concerns outlined in this response do not relate merely to minor parameter choices or technical disagreements. They relate to structural assumptions that materially shape the direction and magnitude of cost-effectiveness results. This is especially important for at-risk subgroups, given that the cost-effectiveness estimates in the model are relatively close to the threshold.

2. An unrealistic baseline that inflates harms and costs

At the heart of our concern is that the SCHARR economic model evaluates a policy scenario that would not be implemented in practice. It assumes that organised screening would be layered on top of existing opportunistic PSA testing, rather than reducing or rationalising it. The relevant policy question for the UK NSC is not whether adding further testing to an already unstructured system increases harms and costs,

but whether a well-designed population-based screening programme could improve early detection while reducing the inefficiencies and inequities of the current approach. The model in its current form does not fully address that question and in assuming an unrealistic comparator, departs from basic principles of economic evaluation.

The model compares organised screening against a single “usual care” scenario that conflates symptomatic testing with widespread opportunistic PSA testing, while assuming that a screening programme would add to existing testing rather than partially or wholly replace it. The narrative review acknowledges significant uncertainty about the extent of PSA testing in asymptomatic men and how GP behaviour might change under a screening programme, yet this uncertainty is not explored through alternative comparator scenarios.

The SCHARR model development team has assumed that the introduction of population-based screening would make no difference to this background testing behaviour and that no wider changes to NHS policy or guidance would occur. In practical terms, this implies that men would continue to seek and receive opportunistic PSA tests even after being invited for screening, an assumption that is difficult to reconcile with how screening programmes are typically implemented or how clinical guidance would be expected to evolve.

Consistent with conventional screening trial design and established health economic evaluation methodology, screening strategies are typically modelled as mutually exclusive policy options – such as no screening, opportunistic testing, or organised population-based screening – rather than as additive combinations of organised screening layered on top of existing practice.^{7,8}

In practice, the introduction of a national screening programme would reasonably be expected to be accompanied by changes in clinical guidance and commissioning policy, including clarification of how asymptomatic PSA testing is delivered within primary care alongside a national programme. It would be reasonable to expect that testing outside the organised programme would be restricted or rationalised, with PSA primarily offered either through the screening pathway or for men presenting with relevant symptoms or ongoing follow-up care.

By modelling an approach that has not been advocated in practice or policy, the model effectively evaluates the consequences of adding further PSA testing to an already disorganised system, contributing to the high estimates of overdiagnosis and biopsy volume. However, this does not meaningfully inform the question facing policymakers, which is whether a population-based screening programme, accompanied by rationalisation and restriction of opportunistic PSA testing, could reduce harm while improving early detection.

International experience and recent modelling work suggest that organised screening programmes would be expected to substantially reduce PSA testing in older men, where harms are most concentrated, and lower rates of overdiagnosis by concentrating testing in age groups most likely to benefit.⁹ For example, in Lithuania data show that for men over 70 there was a reduction in PSA testing of around 80% following the introduction of screening.¹⁰ By failing to model substitution effects or scenarios in which opportunistic PSA testing is reduced or ended, the SCHARR model compares screening to a baseline that is unlikely to persist under an organised national screening programme and systematically overestimates incremental harms and costs.

3. Reliance on outdated comparators that no longer reflect modern diagnostic and treatment pathways

A central limitation of the economic model is that it relies on comparators drawn from a diagnostic and treatment era that no longer reflects contemporary NHS practice, thereby anchoring estimates of benefit and harm to outdated pathways.

3.1 Diagnostic pathway evolution: MRI and targeted biopsy

The UK NSC's narrative report chooses to highlight two research articles published since their 2020 review providing follow-up data for two trials: the UK Cluster Randomised Trial of PSA Testing for Prostate Cancer (CAP Trial), and the European Randomised Study of Screening for Prostate Cancer (ERSPC).

Long-term follow-up studies from CAP and ERSPC remain valuable in demonstrating the natural history of prostate cancer and the potential for mortality benefit from population-level early detection via PSA and biopsy over extended time periods. However, both trials were conducted in a very different diagnostic and management context, before routine MRI, modern risk stratification and widespread use of active surveillance became embedded in clinical practice – developments that fundamentally shape how a future screening programme would operate. As a result, while informative, their findings should not be relied on to model the balance of harms and benefits of a contemporary MRI-led screening pathway. A systematic review published in 2025 included analysis of the benefit-harm balance from four studies where MRI was used as a second-stage test after PSA, and concluded that utilising targeted biopsies in second-stage MRI screening optimises clinically significant prostate cancer detection, while reducing the number of biopsies.¹¹

Emerging international consensus work, including the forthcoming Prostate Imaging Standards for Screening Magnetic Resonance Imaging (PRISM) initiative developed using the RAND/UCLA Appropriateness Method and informed by systematic review, reflects the extent to which screening MRI protocols are being standardised and streamlined specifically for population-level use.

PRISM recommends non-contrast-enhanced MRI (biparametric MRI using T2-weighted and diffusion-weighted imaging only), streamlined acquisition protocols of no more than 15 minutes, risk-stratified screening intervals, and stage-gated reporting approaches designed specifically for screening rather than routine diagnostic practice. It also supports earlier screening initiation from age 45 in Black men, reflecting established differences in lifetime risk. Recent pooled head-to-head evidence also supports this approach: an updated 2026 meta-analysis incorporating the PRIME trial found biparametric MRI to be non-inferior to multiparametric MRI for clinically significant cancer detection at the patient level.¹²

These recommendations demonstrate that screening MRI represents a simplified, lower-intensity, and standardised diagnostic architecture distinct from historic multiparametric diagnostic pathways. The current modelling does not incorporate this contemporary screening framework and instead relies on assumptions derived from earlier studies. As a result, the balance of harms and benefits may be evaluated against a version of screening that does not reflect emerging international standards.

3.2 Uptake assumptions and organised screening behaviour

Additionally, in the case of CAP, unlike ERSPC, there is also a serious limitation from it using a single invitation for a PSA test – which is acknowledged as “not typical of organised screening programs” within the CAP paper.¹³ However, as the narrative report makes clear, this was used as the benchmark for uptake of prostate cancer screening being set at 36% within the model, and for uptake of invitations to receive any MRI test being matched to CAP's biopsy uptake rate being set at 85%. For PSA uptake, this is far lower than other trials that more closely resemble a national screening programme with multiple invitations for testing – for example, in the ERSPC trial 23-year follow-

up, 60,259 of the 72,888 men in the screening arm received at least one PSA test (83% of the total).¹⁴ Data from the Schoots et al systematic review also highlighted the very high rate of uptake of biopsies, with no-biopsy rates in MRI-positive screened men of 6%, 8%, and 9% in the OPT, Göteborg-2, and STHLM3-MRI studies respectively.¹⁵

In Lithuania, analysis of their population-based national screening programme for prostate cancer showed that 70% of the target population were screened at least once in the first 10 years of screening.¹⁶ Performance data from other screening programmes also show much higher uptake rates in a real-world setting, such as the NHS Bowel Cancer Screening Programme in England for 2023-24 where uptake of invitations was around 65% for men.¹⁷ A nationally representative Healthwatch England poll of 3,575 men found 79% said they would be likely to attend an appointment when invited, if the NHS introduced prostate screening routinely, which was even higher for Black men at 81%.¹⁸

These data suggest that uptake assumptions based on CAP may significantly underestimate achievable participation within a structured national programme, with implications for projected stage shift and cost-effectiveness estimates.

3.3 Absence of risk-stratified screening strategies

The current modelling evaluates screening as uniform population-wide strategies defined primarily by interval (e.g. annual or biennial PSA testing). However, contemporary screening proposals increasingly emphasise risk-adapted approaches, in which screening intensity is tailored using baseline PSA (and other risk factors), thereby concentrating testing on men most likely to benefit while reducing unnecessary testing and downstream harms in low-risk men.

There is substantial evidence from ERSPC and related cohort analyses that risk stratification can reduce overdiagnosis, biopsy burden and unnecessary testing among low-risk men, while concentrating resources on those most likely to benefit. In ERSPC follow-up, the actuarial probability of clinically significant prostate cancer at 16 years was approximately 1.2–1.5% in men with baseline PSA <1.0 ng/ml, compared with 13.3–13.8% in men with PSA ≥3.0 ng/ml, a more than 10-fold difference.¹⁹ Evidence from population-based cohorts also supports extending re-testing intervals in men with low baseline PSA levels. For example, in men aged 50–55 with an initial PSA <1.0 ng/ml, the short-term incidence of prostate cancer over three years was extremely low, supporting consideration of longer screening intervals for this substantial subgroup.²⁰ Recent European data suggest that approximately two-thirds of men aged 50 have a baseline PSA <1.0 ng/ml. Under a risk-adapted framework, this substantial subgroup could be offered extended screening intervals, materially reducing testing intensity, downstream investigations and system costs without compromising safety.²¹

By modelling only blunt, interval-based strategies applied uniformly across the population, the current analysis does not assess whether risk-adapted screening could improve the balance of benefit, harm and cost-effectiveness. This omission is important because risk-stratified approaches are specifically designed to reduce overdiagnosis, biopsy burden and system costs relative to uniform screening strategies.

3.4 Treatment and surveillance harms: ProtecT and contemporary practice

In addition, contemporary management of localised prostate cancer differs materially from the era in which major treatment trials were conducted. The ProtecT trial, frequently cited in discussions of treatment harms, was undertaken in a pre-MRI diagnostic context. Biopsy strategies were largely systematic and unguided, resulting in imperfect correlation between biopsy findings and true tumour burden. As a

result, at randomisation men often had more aggressive disease at surgery than was suggested by initial biopsy, and risk stratification was substantially less precise than is now possible with MRI-targeted biopsy.

In contemporary MRI-led pathways, improved imaging and targeted biopsy enable more accurate risk stratification and more selective treatment allocation including increased use of active surveillance in men with favourable intermediate disease.

Historically, active surveillance was also based on PSA monitoring with repeat systematic biopsy, without routine MRI integration. Modern active surveillance protocols in the UK now incorporate MRI at baseline and during follow-up, reducing the frequency of biopsy and improving identification of clinically significant progression. The 2019 update to NICE guidance (NG131) formalised active surveillance as the recommended primary management strategy for men with low-risk (CPG1) localised disease.²²

NPCA data demonstrate a marked reduction in the proportion of men with low-risk disease receiving radical treatment within 12 months of diagnosis – falling from approximately 16% in 2018–19 to around 7% in 2022–23.^{23,24} This represents a greater than 50% relative reduction within five years and reflects a sustained shift towards surveillance rather than immediate intervention. Surveillance today is less invasive and more accurately risk-stratified than the approach reflected in historic trial data, although continued efforts to standardise surveillance practice nationally remain important.

Modelling harms using parameters derived from the pre-MRI ProtecT era risks overstating the downstream harms associated with diagnosis under contemporary practice, as fewer men are now exposed to radical treatment and surveillance pathways are less invasive.

Similarly, both radical prostatectomy and radiotherapy techniques have evolved significantly. Robotic-assisted surgery, image-guided radiotherapy and intensity-modulated radiotherapy are now widely adopted, with improved functional outcomes compared with earlier techniques.²⁵ In parallel, current NHS cancer policy, including the recently published National Cancer Plan for England, emphasises reducing unwarranted variation in treatment quality and centralising complex surgical and radiotherapy services into higher-volume specialist centres. While variation remains and continued improvement is needed, the direction of travel is towards greater standardisation and quality assurance across cancer care.

Taken together, these changes mean that the downstream harms associated with diagnosis and treatment in contemporary UK practice are not directly comparable to those observed in historic trials. Economic modelling that relies heavily on legacy treatment and monitoring harm estimates therefore risks overstating the disutility associated with modern MRI-led detection and management pathways.

4. Inflated and incomplete costing assumptions

The economic model appears to overstate diagnostic and underestimate treatment and non-treatment costs in several areas while failing to reflect efficiencies that already exist within the NHS.

Diagnostic costs are based on assumptions that do not reflect current service delivery. MRI is modelled primarily as a cost driver rather than as a triage tool that substantially reduces downstream biopsies and unnecessary interventions. As outlined above, emerging international consensus supports streamlined, non-contrast MRI protocols designed specifically for screening. Failure to incorporate this approach may

overstate MRI acquisition time, contrast-related costs, and downstream biopsy volume within the model.

The use of simplified biparametric MRI protocols, combined with stricter PI-RADS 4/5 thresholds for biopsy referral, would be expected to reduce both unnecessary biopsies and overdiagnosis. Recent data from the PRIME study (supported by a recent systematic review that incorporates these data) demonstrate that biparametric MRI is as effective as multiparametric MRI for detecting clinically significant cancer, supporting its use as a lower-cost screening tool.^{26,27} This contemporary screening pathway has not been meaningfully incorporated into the SCHARR modelling and may therefore result in inflated cost and harm estimates relative to current and emerging NHS practice.

Systemic anti-cancer therapies (SACTs) significantly impact the overall costs within the model and the potential benefits in costs saved from earlier diagnosis. Within the model, the numbers SCHARR states as the proportion of patients receiving SACTs at stage 3 and 4 are significantly less than recent data have shown. For example, in the most recent NPCA data, 47% of men newly diagnosed with metastatic prostate cancer received systemic treatment intensification therapy within 12 months of diagnosis.²⁸ Clinical guidance supports systemic treatment intensification for almost all men with metastatic hormone-sensitive prostate cancer, with limited exceptions (such as very poor performance status or life expectancy under 12 months). Efforts to improve compliance with national standards will therefore increase the proportion of men receiving these high-cost therapies, amplifying the economic consequences of late-stage diagnosis within screening models.

In addition, SCHARR has only modelled stage 4 costs up to 3 years, when the most recent survival data indicates that 53% of men diagnosed at stage 4 in England are alive 5 years after diagnosis.²⁹ PCR shared with the UK NSC its work with Deloitte to estimate the average treatment costs for men diagnosed with stage 4 prostate cancer, with this being estimated at £127,000 (compared to estimates of £21,000 for men diagnosed at stage 3).³⁰ This is reflective of costs such as novel hormonal therapies costing over £4,000 per month. All clinical experts consulted by YHEC also confirmed that SACTs would be administered for the rest of a patient's lifetime, unless the treatment stopped responding.

Also, the economic framework is too narrowly confined to direct NHS costs. Preventing late-stage presentation represents substantial value not fully captured in the model. Metastatic disease requires lifelong systemic therapy, generates significant emergency admissions, and imposes severe psychological burden on patients and families. The model's narrow NHS cost perspective excludes many of these downstream impacts, while the quality-of-life burden of advanced disease on patients and caregivers is not equivalently weighted against the modelled psychological harms of earlier detection. Sensitivity analyses incorporating these would strengthen confidence in the robustness of the conclusions.

The independent critique by YHEC further identifies that several key cost inputs in the SCHARR model – including the extrapolation of treatment costs from the ProtecT trial and the omission of biparametric MRI – are either outdated or applied in a way that does not reflect how services are currently delivered in the NHS.

5. A modelling approach that overemphasises harms

The independent critique by YHEC highlights that the model's structure may systematically increase estimated harms relative to benefits. In

particular, assumptions regarding the mapping of Grade Groups to disease stage, and the modelling of screening as additional to existing opportunistic PSA testing rather than as a reduction or rationalisation, materially influence estimates of overdiagnosis and overtreatment.

Overdiagnosis is assumed to be high by default, while contemporary evidence on MRI triage and risk stratification is not incorporated to mitigate this effect. For example, the GÖTEBORG-2 trial showed that using MRI-directed targeted biopsy for screening and early detection in men with elevated PSA levels reduced the risk of overdiagnosis by half compared to systematic biopsy use.³¹

Active surveillance is modelled predominantly as a source of cost and disutility, rather than as a risk-management strategy that actively reduces overtreatment and preserves quality of life for men with low-risk, and increasingly for men with favourable intermediate-risk, disease – despite strong UK evidence that modern surveillance pathways have significantly reduced treatment-related harms.³²

While psychological harms of false-positive diagnosis are explicitly modelled, the psychological and quality-of-life burden associated with late-stage diagnosis, advanced disease and metastatic progression on patients and their families is not equivalently explored. This imbalance risks overstating the harms of earlier detection relative to the harms of later-stage presentation.

Contemporary UK practice also demonstrates that detection of low-risk disease does not automatically lead to radical treatment. NPCA data show that rates of radical treatment for men diagnosed with low-risk disease under the Cambridge Prognostic Group classification system (CPG 1) have remained low and stable, at approximately 7%, reflecting widespread adoption of active surveillance.³³ In modern MRI-led pathways, improved risk stratification reduces both misclassification and unnecessary intervention.³⁴ Active surveillance is now MRI-led and substantially less invasive than in historic trials. The narrative report cites a paper from the ProtecT trial to support the statement that “more than half of men who initially start on an active surveillance pathway will move onto having radical treatments (surgery or radiotherapy) over 15 years”, but this trial recruited men between 1999 and 2009 – at a time before MRI was used in the diagnostic pathway, and before more modern criteria for active surveillance came into practice.

Modelling approaches that rely on data from legacy trial data, without adjusting for contemporary treatment allocation patterns, risk overstating the harms associated with detection under current practice. Most recent NPCA data suggest that overtreatment rates are materially lower than those reflected in these trials.

Taken together, these modelling choices mean that harm estimates do not fully reflect how prostate cancer is currently diagnosed and managed in the NHS. This increases the likelihood that screening appears less cost-effective and more harmful than it would under contemporary practice.

We acknowledge that screening is not without risk. However, the current model evaluates an outdated version of screening that does not reflect contemporary practice or policy reality. A fair assessment must evaluate screening as it would be delivered today, not as it was delivered two decades ago.

6. Understatement of potential benefits in modern practice

In contrast to the detailed modelling of harms, the potential benefits of earlier detection appear underrepresented. The YHEC report notes the

consistently conservative approach taken in the SCHARR modelling, both in the parameters used and the ensuing discussion. While YHEC acknowledges that a degree of conservatism in public health modelling is appropriate, they also recognise how the cumulative impact of repeated conservative assumptions could potentially lead to a systematic underestimation of the benefit of prostate cancer screening.

Evidence from contemporary MRI-led pathways demonstrates that clinically significant cancers can be detected more selectively, with far lower rates of unnecessary biopsy and treatment than those observed in earlier PSA-only trials.³⁵ These advances are particularly relevant when assessing the balance of harms and benefits in screening scenarios.

The infographic that the UK NSC released as part of its consultation materials (Figure 1) appears to anchor diagnostic assumptions primarily to a single age-restricted study (GÖTEBORG-2, ages 50–60), rather than drawing on the broader evidence base now available across multiple age groups and contemporary pathways. While GÖTEBORG-2 represents an important advance, reliance on a single study risks over-anchoring modelling assumptions to a specific trial population and implementation context.

PCR's analysis incorporates GÖTEBORG-2 alongside five additional modern studies (STHLM3-MRI, OPT, PROSA, IP1-PROSTAGRAM, Targeted Prostate Health Check), comprising 62,078 men in total (see Appendix A). When aggregated across these six studies, the downstream patient flow through the diagnostic pathway differs materially from single study or earlier PSA-era assumptions. This substantially impacts the proportion of men that receive an MRI or a biopsy. In particular, MRI-based triage substantially reduces unnecessary biopsies: for every one man who underwent a benign biopsy, approximately eight men avoided biopsy entirely due to MRI-based risk stratification.

PCR's alternative infographic (Figure 2), based on this aggregated contemporary evidence, therefore reflects a broader and more generalisable estimate of diagnostic performance in modern practice.

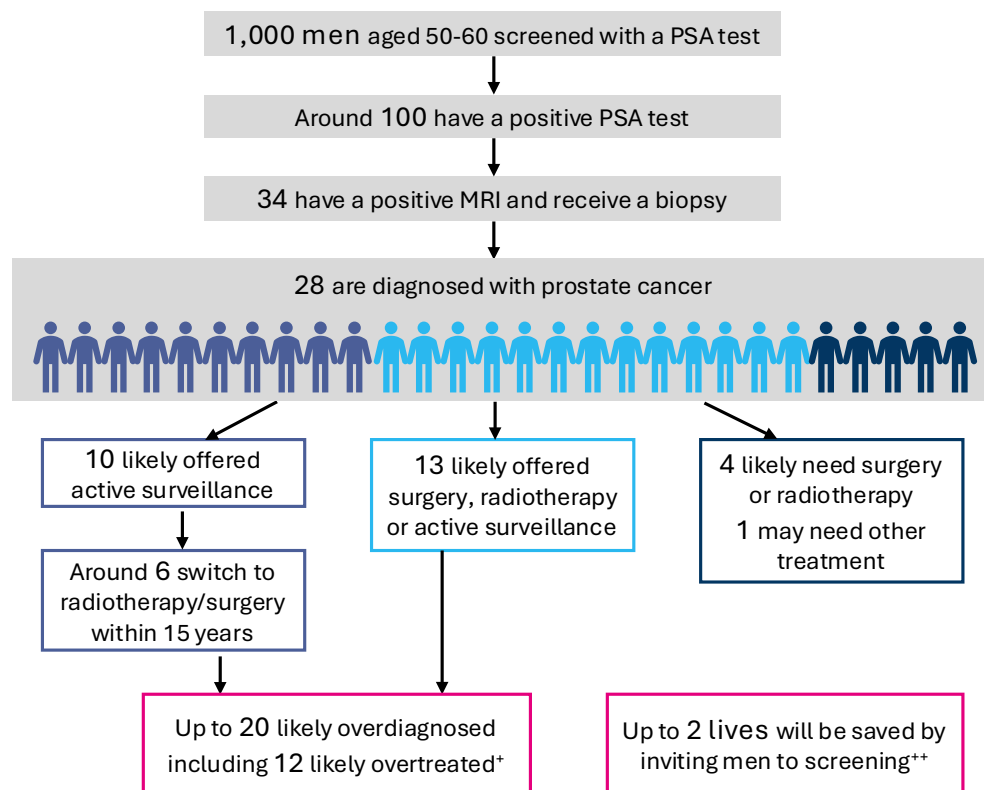
In addition, the UK NSC infographic appears to treat a substantial proportion of Grade Group 2 (GG2) cancers as overdiagnosed or overtreated, drawing in part on clinical opinion and the ProtectT trial. PCR does not accept that GG2 disease should predominantly be considered overdiagnosed, particularly in the context of MRI-led pathways.

GG2 and above is widely used as the definition for clinically significant cancer in many contemporary studies, including the PRECISION trial, although some studies apply stricter thresholds. Unlike GG1 disease, GG2 carries a meaningful risk of progression. Significant numbers of men with GG2 disease may therefore benefit from timely detection and appropriate risk-stratified management.

Overdiagnosis is defined as the detection of a cancer that would not have caused harm within a patient's lifetime. Treating a substantial proportion of GG2 cancers as effectively equivalent to overdiagnosed disease represents a modelling judgement rather than an outcome-based classification. There is insufficient evidence to assume that the majority of GG2 cancers represent overdiagnosis, and such an assumption should not be embedded in the base-case model without explicit justification and sensitivity analysis. When combined with reliance on a single trial population for patient flow assumptions, this inflates estimates of overdiagnosis and overtreatment and therefore materially influences the harm–benefit balance presented in the UK NSC infographic.

MODELLING THE OUTCOMES OF PROSTATE CANCER SCREENING

Figure 1
UK NSC infographic

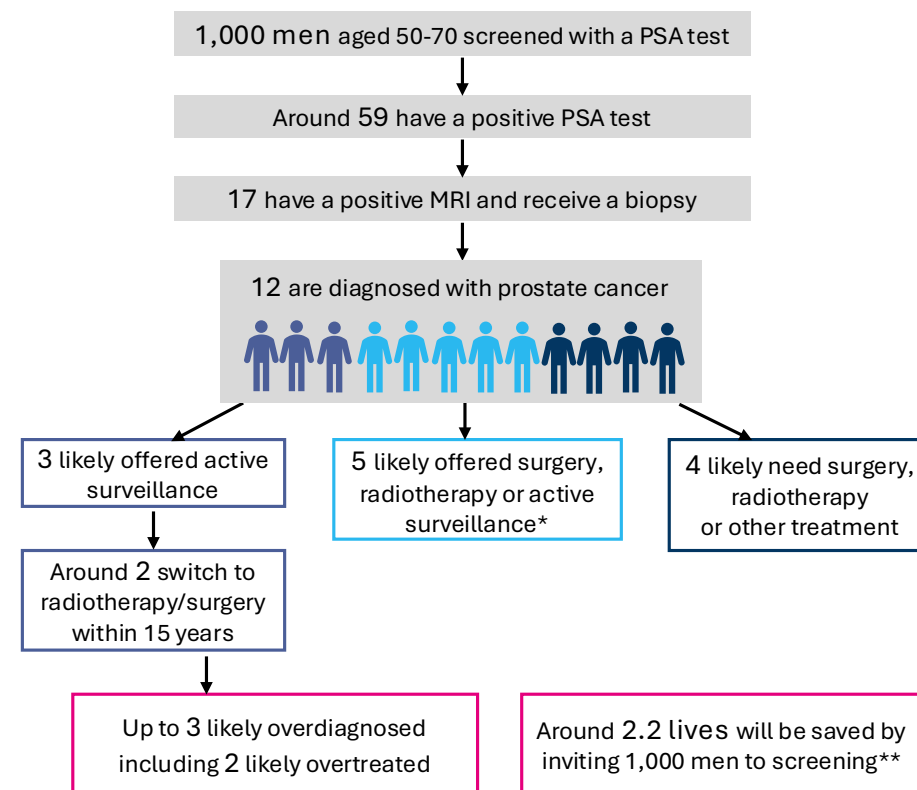


The information in this infographic is based on the Göteborg II screening study using PSA and MRI over 4 years in men aged 50-60 (Hugosson et al, NEJM 2024), deaths prevented in men aged 50-69 from the CAP screening trial (Martin et al, JAMA 2024) and in men aged 55-69 from the ERSPC screening trial (Roobol et al, NEJM 2025), harms in men aged 50-69 from ProtecT (Hamdy et al 2023, Donovan et al 2023).

*This number assumes that some men who switch from active surveillance to radiotherapy/surgery within 15 years did so unnecessarily. And some men who were offered surgery, radiotherapy or active surveillance chose surgery or radiotherapy when active surveillance could have been sufficient.

** Assumes all invited men accept a PSA test.

Figure 2
PCR infographic



The information in this infographic is based on aggregated data of 62,078 men tested in Göteborg-2, STHLM3-MRI, OPT, PROSA, 1P1-PROSTAGRAM, & TPHC (Schoots et al, Eur Urol 2025; Langley et al, Eur Urol 2025; Hugosson et al, NEJM 2024).

* In the absence of outcome-based evidence, in the modern MRI-diagnosis era, demonstrating that GG2 disease represents overdiagnosis - and given that MRI-diagnosed GG2 disease often requires treatment, is widely included in clinical guidelines, and is a valid histologic endpoint in contemporary clinical trials as clinically significant - our base-case model does not classify GG2 cancers as overdiagnosed or overtreated.

**The estimate of 2.2 lives saved per 1,000 men invited is derived from the ERSPC 23-year follow-up (1 death prevented per 456 men invited, Roobol et al, NEJM 2025). NB: ERSPC data suggest 1,000 screened men could save 2.4 lives. Estimates vary depending on screening interval, age range, modelling assumptions and duration of follow-up. For example, lifetime modelling based on ERSPC data has estimated approximately 1 death prevented per 100 men screened under annual screening between ages 55-69.³⁶

As illustrated in the UK NSC infographic (Figure 1) the implied ratio of harms (overdiagnosis and overtreatment) to benefits (lives saved) is:

- 20 overdiagnosed to 2 lives saved
- 12 overtreated to 2 lives saved

Under PCR's updated assumptions (Figure 2) – drawing on aggregated MRI-era patient flow data and widely-used clinical definitions of clinically significant disease – the relationship is:

- 3 overdiagnosed to 2.2 lives saved*
- 2 overtreated to 2.2 lives saved*

*The higher life-saved estimate is consistent with the 23-year follow up data from ERSPC.

Therefore, expressed per life saved, this equates to:

	Overdiagnosed per life saved	Overtreated per life saved
UK NSC's infographic – Figure 1	10	6
PCR's infographic – Figure 2	1.5	1

This represents a substantial reduction in the estimated number of men characterised as harmed per life saved when contemporary diagnostic performance and clinically accepted disease classifications are applied.

While the harms and potentially life-altering impacts of overtreatment must remain central to screening deliberations, modelling must distinguish clearly between low-risk disease that may never progress and clinically significant disease that carries measurable long-term risk.

Where modelling assumptions materially shape the apparent balance of harms and benefits, those assumptions must be transparent, biologically justified, and tested through sensitivity analysis. Anchoring patient flow to a single study population and embedding contestable classification assumptions risks distorting that balance.

Ensuring that contemporary diagnostic performance and clinically meaningful disease classifications are accurately represented is critical to reaching a proportionate, transparent and evidence-based conclusion.

7. Insufficient modelling of high-risk populations

A further limitation of the modelling underpinning the draft recommendation is the incomplete and inconsistent treatment of populations known to be at higher risk of prostate cancer, particularly men with a family history of the disease and men of Black ethnicity. While the narrative review acknowledges elevated risk in these groups, the economic model does not adequately reflect how risk varies, how pathways might differ, or how targeted screening approaches could alter the balance of benefit and harm.

As highlighted in YHEC's independent critique, the model's treatment of family history is highly simplified. The model provides limited exploration of risk in the family history group, despite well-established evidence of earlier age of onset and substantially elevated lifetime risk

among men with affected first-degree relatives.³⁷ Risk is incorporated through broad relative risk multipliers applied to incidence, without sufficient adjustment to reflect earlier age of onset or how screening strategies might be tailored depending on risk factors, including the number of affected relatives, degree of relatedness or age at diagnosis of affected relatives. This limits the model's ability to assess whether targeted or risk-adapted screening could improve outcomes while mitigating harms in this group.

Similarly, the approach to modelling Black ethnicity is limited. While higher incidence and mortality are acknowledged descriptively, reflecting the reality that Black men have double the risk of being diagnosed in their lifetimes, these differences are not meaningfully translated into distinct screening pathways or outcome projections. The model does not adequately explore how earlier invitation, different screening intervals, or risk-stratified thresholds might affect stage at diagnosis, mortality, or overdiagnosis in Black men, despite well-established evidence of higher lifetime risk and poorer outcomes under current practice.^{38,39,40}

The YHEC analysis notes that by modelling screening primarily as a uniform intervention applied to the general population, the model is poorly equipped to assess the value of targeted approaches for high-risk groups. This is particularly problematic in a context where the opportunistic PSA testing we see in practice today already exacerbates inequalities^{41,42}, and where organised screening could plausibly reduce disparities by standardising access and follow-up for those at greatest risk.

8. Equity considerations

Beyond questions of clinical effectiveness and cost, there is a fundamental equity issue that has not been adequately addressed in either the economic modelling or the draft discussion.

As already noted, current opportunistic PSA testing in the UK is not equitably distributed. Uptake is strongly associated with GP engagement, geography and deprivation.⁴³ More affluent regions demonstrate substantially higher incidence of prostate cancer, reflecting higher PSA testing rates, while more deprived areas show higher rates of metastatic presentation. In effect, the current system advantages men who are informed, confident and able to advocate for themselves within primary care.

The NHS Constitution for England makes clear that a core duty of the NHS is to promote equality: “The NHS provides a comprehensive service, available to all. It is available to all irrespective of gender, race, disability, age, sexual orientation, religion, belief, gender reassignment, pregnancy and maternity or marital or civil partnership status. The service is designed to improve, prevent, diagnose and treat both physical and mental health problems with equal regard. It has a duty to each and every individual that it serves and must respect their human rights. At the same time, it has a wider social duty to promote equality through the services it provides and to pay particular attention to groups or sections of society where improvements in health and life expectancy are not keeping pace with the rest of the population.”⁴⁴

Targeted screening for men of Black ethnicity or those with a strong family history is not simply a clinical adjustment; it is inherently an equity-enhancing intervention. It aligns screening intensity with risk. The NHS Constitution for England, the Core20PLUS5 framework (which identifies earlier cancer diagnosis as a key clinical priority for reducing health inequalities in minority ethnic groups), the Cancer action plan in Scotland, and the new National Cancer Plan for England all commit to reducing health inequities, while NICE methods guidance recognises that health inequalities may be relevant to decision-making.⁴⁵ No explicit equity impact assessment or analysis appears to be presented in the modelling documentation. Given the clear and well-evidenced inequalities in prostate cancer risk and outcomes, explicit assessment of the

impact of screening policy options should form part of the decision-making framework. Failing to consider equity explicitly risks embedding and perpetuating the very inequalities that organised screening could plausibly reduce.

9. Absence of considering alternative reflex tests in the diagnostic pathway

The narrative report notes that the modelled screening pathway did not include the Stockholm3 test, citing concerns about data availability and suitability at the time the model was developed. While it is reasonable to exclude specific technologies where evidence is insufficient, the current modelling framework does not appear to incorporate reflex testing as a structural option within the pathway. Having communicated with the developers of the Stockholm3 test concerning this, our understanding is that following a data-sharing agreement between SCHARR and the Karolinska Institute in Sweden being agreed there were concerns over data being used in the model that would remain unpublished on commercial grounds. It is not uncommon within health technology assessments for confidential unpublished data to be made available to NICE by pharmaceutical companies under the condition that these would be fully available to committees but redacted in published documents. We recommend that the UK NSC adopts a similar approach to enable this scenario to be fully modelled should the currently-available published literature on Stockholm3 be insufficient to facilitate this.

Furthermore, a growing range of blood-based and molecular tests are being evaluated and, in some cases, are already accessible in UK clinical settings. Some of these have been proposed as potential reflex tests following an initial PSA, with the aim of improving risk stratification and reducing unnecessary MRI and biopsy. The model does not explore hypothetical or scenario-based use of such tests, nor does it assess the potential impact of reflex testing in principle on patient flow, costs, or harms.

Even in the absence of mature trial data for specific products, it would have been methodologically feasible to model the potential impact of an intermediate triage test. Such analysis would not require endorsement of any particular technology but would allow assessment of how an intermediate triage step with improved specificity could alter projected MRI volume, biopsy rates, overdiagnosis and cost-effectiveness.

The absence of this exploration limits the model's ability to assess how evolving diagnostic strategies could alter projected biopsy volume, overdiagnosis and system costs. In a rapidly evolving diagnostic landscape, this reduces the forward relevance of any conclusions drawn. It further reinforces the need for the economic model to be maintained as a living framework, capable of incorporating emerging evidence as it matures.

10. Limitations and equity concerns in the proposed BRCA screening recommendations

While the draft recommendation to screen men with BRCA1 and BRCA2 variants is a welcome step forward, we have several concerns relating to equity, age eligibility, and screening interval, which warrant further consideration before conclusions are finalised.

The model assumes knowledge of BRCA status without modelling the costs, service implications, or feasibility of identifying carriers within the NHS. In practice, expanding BRCA testing would require substantial investment in genetic testing capacity, counselling infrastructure and cascade testing pathways. By modelling PSA screening in known BRCA carriers without modelling the cost of identifying those carriers, the analysis evaluates an incomplete screening pathway. In economic evaluation, all necessary components required to implement an intervention in practice should be incorporated into the modelled pathway.

There are also material equity concerns. Current BRCA identification in men is not population-based and is typically triggered by family cancer history, female relative testing, private access, or research participation. This creates a structural risk that screening eligibility will correlate with prior healthcare access rather than underlying biological risk, preferentially benefiting wealthier or better-informed individuals, while excluding others at comparable risk.

We also note that the proposed recommendation diverges from established international practice. Based on emerging evidence, European guidance has supported annual PSA screening for BRCA2 carriers from age 40 up to age 69⁴⁶, and research groups involved in the IMPACT study have consistently advocated for a similar age range and screening frequency for both BRCA1 and BRCA2 mutation carriers.

Crucially, the modelling does not directly compare the economic implications of BRCA-based screening with alternative strategies, including family history–based PSA screening. The Diagnostic unit cost for PSA testing listed in the SCHARR report is £23.67, with some sources providing a cost for BRCA testing as £805.⁴⁷ BRCA testing usually requires additional genetic counselling, meaning that this entails substantial upfront costs in genetic identification and counselling. By contrast, PSA testing is inexpensive. Family history is an observable clinical risk factor that can be collected at negligible cost in primary care, whereas BRCA identification requires resource-intensive genetic testing infrastructure. For many men with a significant family history, years of PSA testing may cost less than a single episode of genetic testing. Without explicit comparative modelling of these strategies, it is not possible to conclude that the BRCA-only pathway represents the more economically efficient or equitable approach.

Supporting Organisations

This consultation response has been prepared by PCR and is supported by the organisations listed below. Supporting organisations endorse the overall position and key recommendations outlined in this submission, although responsibility for the detailed analysis rests with PCR.

- Black Equity Organisation
- Black Prostate Cancer Network
- British Association of Urological Nurses
- Cancer Black Care
- Cancer Don't Let It Win CIC
- Can-Survive UK
- Caribbean & African Health Network
- CHAPS
- From Me To You: The Art of Survival CIO
- Help Educate and Raise Awareness Around Cancer CIC
- Orchid
- Prost8 UK
- Prostate Cymru
- Tackle Prostate Cancer

- The Bob Willis Fund
- The Graham Fulford Charitable Trust
- The Prostate Project
- The Rose Thompson Foundation

Name:	Joseph Clift	Email address:	*****
Organisation (if appropriate):	Prostate Cancer Research (and co-signed by the above organisations)		
Role:	Head of Policy, Campaigns and Public Affairs		
Do you consent to your name being published on the UK NSC website alongside your response?			Yes

Please return your completed form to the UK NSC Inbox UKNSC@dhsc.gov.uk by 11.59pm GMT on 20 February 2026.

Appendix A

Aggregated study data used to inform PCR screening infographic

Study name	Year	Inclusion age	Age Median Screened	Undergoing testing	PSA ≥ 3 ng/mL	MRI score 3-5	Biopsy performed (TB +/- SB)	Benign Biopsy	Any PCa detected	GG 1 PCa	GG ≥ 2 PCa
Göteborg-2, 1st round (reference) ^a	2024	50-60	56	6575	444	186	176	68	108	39	69
STHLM3-MRI, 1st round ^b	2021	50-74	66	12750	1532	325	297	79	218	35	183
OPT ^b	2024	50	50	23855	696	236	221	84	137	44	93
PROSA (2026); reference arm ^b	2024	49-69	59	173	61	9	6	4	2	2	0
IP1-PROSTAGRAM ^b	2021	50-69	57	408	41	10	9	3	6	0	6
Targeted Prostate Health Check ^c	2025	50-70	59	18317	865	469	344	81	263	42	221
Totals				62078	3639	1235	1053	319	734	162	572

^a Data taken from Hugosson J, Godtman RA, Wallstrom J, et al. Results after four years of screening for prostate cancer with PSA and MRI. N Engl J Med. 2024;391(12):1083-1095.

^b Data taken from Schoots IG, Ahmed HU, Albers P et al. Magnetic Resonance Imaging-based Biopsy Strategies in Prostate Cancer Screening: A Systematic Review. Eur Urol. 2025 Sep;88(3):247-260. doi: 10.1016/j.eururo.2025.05.038.

^c Data taken from Langley S, Uribe-Lewis S, Uribe J et al. Targeted Prostate Health Checks, a Novel Screening System to Identify Men at Risk of Prostate Cancer: Real-world Evidence from More than 18 000 Prostate-specific Antigen Tests. Eur Urol Oncol. 2025 Nov 3:S2588-9311(25)00280-9. doi: 10.1016/j.euo.2025.10.007. Additional data on PSA and MRI provided on request in Feb 2026.

Sources for UK NSC and PCR screening infographics compared

UK NSC		PCR
10.4% (Göteborg II)	PSA positivity rate	5.9% (Aggregated data of 6 studies inc Göteborg II)
33% (Göteborg II)	Positive PSA to positive MRI	29% (Aggregated data of 6 studies inc Göteborg II)
2.8% (Göteborg II)	% tested diagnosed with cancer	1.2% (Aggregated data of 6 studies inc Göteborg II)
37% (Göteborg II)	% of cancers that are GG1	21.5% (Aggregated data of 6 studies inc Göteborg II)
47% (Göteborg II)	% of cancers that are GG2	58.5% (Aggregated data of 6 studies inc Göteborg II)*
12% (Göteborg II)	% of cancers that are GG3-4	15% (Aggregated data of 6 studies inc Göteborg II)*
4% (Göteborg II)	% of cancers that are GG5	5% (Aggregated data of 6 studies inc Göteborg II)*
Up to 2 (CAP and ERSPC 23-year follow-up)	Number of lives saved per 1,000 invited	2.2 (ERSPC 23-year follow-up)

* Aggregated data of 6 studies provided data for GG≥2, proportions adjusted to match Göteborg II in original infographic. Rates rounded to one decimal place.
Data of 62,078 men tested in Göteborg-2, STHLM3-MRI, OPT, PROSA, 1P1-PROSTAGRAM, & TPHC (Schoots et al, Eur Urol 2025; Langley et al, Eur Urol 2025; Hugosson et al, NEJM 2024)

¹ James ND, Tannock I, N'Dow J et al. The Lancet Commission on prostate cancer: planning for the surge in cases. Lancet. 2024 Apr 27;403(10437):1683-1722. doi: 10.1016/S0140-6736(24)00651-2.

² prostatecanceruk.org/about-us/news-and-views/2026/01/prostate-most-common-cancer [accessed 17/02/2026]

³ National Prostate Cancer Audit. State of the Nation Report October 2025. London: National Cancer Audit Collaborating Centre, Royal College of Surgeons of England; 2025.

⁴ All-Party Parliamentary Group on Prostate Cancer. Reducing the risks: Overdiagnosis and overtreatment in today's prostate cancer pathway; 2025.

⁵ National Prostate Cancer Audit. Annual Report 2020. London: Royal College of Surgeons of England; 2021.

⁶ National Prostate Cancer Audit. State of the Nation Report October 2025. London: National Cancer Audit Collaborating Centre, Royal College of Surgeons of England; 2025.

⁷ Roobol MJ, de Vos II, Månsson M et al; ERSPC Investigators. European Study of Prostate Cancer Screening - 23-Year Follow-up. N Engl J Med. 2025 Oct 30;393(17):1669-1680. doi: 10.1056/NEJMoa2503223.

⁸ National Institute for Health and Care Excellence. Guide to the methods of technology appraisal 2013. NICE process and methods PMG9; 2013

⁹ Vickers A, Brentnall A. Effect of implementing population-based prostate-specific antigen screening on testing rates and prostate cancer overdiagnosis in England: a statistical modelling study. Preprint 26 Jan 2026. doi: 10.64898/2026.01.23.26344710

- ¹⁰ Patasius A, Krilaviciute A, Smailyte G. Prostate Cancer Screening with PSA: Ten Years' Experience of Population Based Early Prostate Cancer Detection Programme in Lithuania. *J Clin Med*. 2020 Nov 26;9(12):3826. doi: 10.3390/jcm9123826.
- ¹¹ Schoots IG, Ahmed HU, Albers P et al. Magnetic Resonance Imaging-based Biopsy Strategies in Prostate Cancer Screening: A Systematic Review. *Eur Urol*. 2025 Sep;88(3):247-260. doi: 10.1016/j.eururo.2025.05.038.
- ¹² Strieder de Oliveira G, Altmayer S, Torri GB et al. Diagnostic Performance of Biparametric versus Multiparametric Magnetic Resonance Imaging for Prostate Cancer Diagnosis: An Updated Systematic Review and Meta-analysis, *Eur Urol* (2026) doi: 10.1016/j.eururo.2026.01.030
- ¹³ 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.
- ¹⁴ Roobol MJ, de Vos II, Månsson M et al; ERSPC Investigators. European Study of Prostate Cancer Screening - 23-Year Follow-up. *N Engl J Med*. 2025 Oct 30;393(17):1669-1680. doi: 10.1056/NEJMoa2503223.
- ¹⁵ Schoots IG, Ahmed HU, Albers P et al. Magnetic Resonance Imaging-based Biopsy Strategies in Prostate Cancer Screening: A Systematic Review. *Eur Urol*. 2025 Sep;88(3):247-260. doi: 10.1016/j.eururo.2025.05.038.
- ¹⁶ Patasius A, Krilaviciute A, Smailyte G. Prostate Cancer Screening with PSA: Ten Years' Experience of Population Based Early Prostate Cancer Detection Programme in Lithuania. *J Clin Med*. 2020 Nov 26;9(12):3826. doi: 10.3390/jcm9123826.
- ¹⁷ NHS England. Bowel cancer screening standards data report 2023-24; 2025
- ¹⁸ healthwatch.co.uk/blog/2025-10-08/men-would-come-forward-prostate-cancer-screening [Accessed 17/02/2026]
- ¹⁹ Remmers S, Bangma CH, Godtman RA et al. Relationship Between Baseline Prostate-specific Antigen on Cancer Detection and Prostate Cancer Death: Long-term Follow-up from the European Randomized Study of Screening for Prostate Cancer. *Eur Urol*. 2023 Nov;84(5):503-509. doi: 10.1016/j.eururo.2023.03.031.
- ²⁰ Aus G, Damber JE, Khatami A et al. Individualized screening interval for prostate cancer based on prostate-specific antigen level: results of a prospective, randomized, population-based study. *Arch Intern Med*. 2005 Sep 12;165(16):1857-61. doi: 10.1001/archinte.165.16.1857.
- ²¹ Bratt O, Godtman RA, Jiborn T et al. Population-based Organised Prostate Cancer Testing: Results from the First Invitation of 50-year-old Men. *Eur Urol*. 2024 Mar;85(3):207-214. doi: 10.1016/j.eururo.2023.11.013. Epub 2023 Dec 1. PMID: 38042646.
- ²² National Institute for Health and Care Excellence. Prostate cancer: diagnosis and management. NICE guideline NG131.
- ²³ National Prostate Cancer Audit. Annual Report 2020. London: Royal College of Surgeons of England; 2021.
- ²⁴ National Prostate Cancer Audit. State of the Nation Report October 2025. London: National Cancer Audit Collaborating Centre, Royal College of Surgeons of England; 2025.
- ²⁵ Lindenberg MMA, Retèl VVP, Kieffer JJM et al. Long-term functional outcomes after robot-assisted prostatectomy compared to laparoscopic prostatectomy: Results from a national retrospective cluster study. *Eur J Surg Oncol*. 2021 Oct;47(10):2658-2666. doi: 10.1016/j.ejso.2021.06.006.
- ²⁶ Ng ABCD, Asif A, Agarwal R et al. Biparametric vs Multiparametric MRI for Prostate Cancer Diagnosis: The PRIME Diagnostic Clinical Trial. *JAMA*. 2025 Oct 7;334(13):1170-1179. doi: 10.1001/jama.2025.13722
- ²⁷ Strieder de Oliveira G, Altmayer S, Torri GB et al. Diagnostic Performance of Biparametric versus Multiparametric Magnetic Resonance Imaging for Prostate Cancer Diagnosis: An Updated Systematic Review and Meta-analysis, *Eur Urol* (2026) doi: 10.1016/j.eururo.2026.01.030
- ²⁸ National Prostate Cancer Audit. State of the Nation Report 2025. London: National Cancer Audit Collaborating Centre, Royal College of Surgeons of England, 2025.
- ²⁹ National Disease Registration Service & NHS England. Cancer Survival in England, cancers diagnosed 2016 to 2020, followed up to 2021; 2023
- ³⁰ Prostate Cancer Research. Socio-economic Impact of Prostate Cancer Screening; 2024
- ³¹ Hugosson J, Månsson M, Wallström J et al; GÖTEBORG-2 Trial Investigators. Prostate Cancer Screening with PSA and MRI Followed by Targeted Biopsy Only. *N Engl J Med*. 2022 Dec 8;387(23):2126-2137. doi: 10.1056/NEJMoa2209454.
- ³² Norori N, Burns-Cox L, Blaney 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, 2024, 100073, ISSN 2949-8201, doi: 10.1016/j.esmorw.2024.100073
- ³³ National Prostate Cancer Audit. State of the Nation Report October 2025. London: National Cancer Audit Collaborating Centre, Royal College of Surgeons of England; 2025.
- ³⁴ Ibid
- ³⁵ Schoots IG, Ahmed HU, Albers P et al. Magnetic Resonance Imaging-based Biopsy Strategies in Prostate Cancer Screening: A Systematic Review. *Eur Urol*. 2025 Sep;88(3):247-260. doi: 10.1016/j.eururo.2025.05.038.
- ³⁶ Heijnsdijk EA, Wever EM, Auvinen A et al. Quality-of-life effects of prostate-specific antigen screening. *N Engl J Med*. 2012 Aug 16;367(7):595-605. doi: 10.1056/NEJMoa1201637.
- ³⁷ Bratt O, Drevin L, Akre O et al. Family History and Probability of Prostate Cancer, Differentiated by Risk Category: A Nationwide Population-Based Study. *J Natl Cancer Inst*. 2016 Jul 10;108(10):djw110. doi: 10.1093/jnci/djw110.
- ³⁸ James ND, Tannock I, N'Dow J et al. The Lancet Commission on prostate cancer: planning for the surge in cases. *Lancet*. 2024 Apr 27;403(10437):1683-1722. doi: 10.1016/S0140-6736(24)00651-2. Epub 2024 Apr 4. Erratum in: *Lancet*. 2024 Apr 27;403(10437):1634. doi: 10.1016/S0140-6736(24)00748-7.
- ³⁹ Vickers A, O'Brien F, Montorsi F et al. Current policies on early detection of prostate cancer create overdiagnosis and inequity with minimal benefit. *BMJ*. 2023 May 17;381:e071082. doi: 10.1136/bmj-2022-071082. PMID: 37197772.
- ⁴⁰ National Prostate Cancer Audit. State of the Nation Report 2025. London: National Cancer Audit Collaborating Centre, Royal College of Surgeons of England, 2025.
- ⁴¹ Ibid

⁴² Vickers A, O'Brien F, Montorsi F et al. Current policies on early detection of prostate cancer create overdiagnosis and inequity with minimal benefit. *BMJ*. 2023 May 17;381:e071082. doi: 10.1136/bmj-2022-071082. PMID: 37197772.

⁴³ Ibid

⁴⁴ Department of Health & Social Care. The NHS Constitution for England; 2023

⁴⁵ National Institute for Health and Care Excellence. Guide to the methods of technology appraisal 2013. NICE process and methods PMG9; 2013

⁴⁶ uroweb.org/guidelines/prostate-cancer [Accessed 17/02/2026]

⁴⁷ ouh.nhs.uk/media/m00maian/price-list.pdf [Accessed 17/02/2026]

PROSTATE CANCER RESEARCH

Review of the Economic Model Used to Inform National Decisions on Prostate Cancer Screening in the UK

Final Report

SAM WOODS, Research Consultant

MADISON MONTGOMERY, Research Consultant

KATIE MURRAY, Research Assistant

ROBERT MALCOLM, Project Director

ANGEL VARGHESE, Project Director

PROFESSOR MATTHEW TAYLOR, Chief Executive Officer

19/02/2026



Table of Contents

Executive Summary	2
Acknowledgements.....	4
Abbreviations	5
About YHEC.....	6
1 Introduction	7
1.1 Objectives	8
2 Methods.....	9
3 Summary of Key Concerns.....	10
3.1 Reporting Quality and the Principles of Robust Analysis	10
3.2 Key Definitions and Opportunistic Screening	12
3.3 Overdiagnosis	15
3.4 Policy Considerations	17
3.5 Parameter Suitability	20
3.6 Model Structure	25
4 Scenario Results	29
4.1 Black Ethnicity	29
4.2 Family History	29
4.3 General Population	30
4.4 Scenario Impact.....	30
5 Discussion	31
5.1 Limitations	33
6 Conclusion.....	34
7 References	35
Appendix A: Other Critique Considerations.....	41
Appendix B: Model Scenario Requests	44
Appendix C: Scenario Results	46
Appendix D: Clinical and Expert Advisors	47

All reasonable precautions have been taken by YHEC to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall YHEC be liable for damages arising from its use. Please note that, unless otherwise agreed, all project documents and models remain the copyright of the Company and may not be published, quoted, or reproduced without the permission of the Company. Material in this report should not be misrepresented by using it whilst omitting key contextual information or any other means. York Health Economics Consortium is a Limited Company. Registered in England and Wales No. 4144762. Registered office as shown.

Executive Summary

1. INTRODUCTION

Prostate cancer is the most common cancer in men in the UK [4, 5]. Recent research has indicated that it has also now become the most common cancer in the UK across men and women, overtaking diagnoses of breast cancer [7]. The most common age for diagnosis in England for prostate cancer is between 70 and 79 years old [6]. There is currently no national screening programme. Instead, prostate-specific antigen (PSA) tests are used for anyone with symptomatic concerns or all males above the age of 50 that request a test. A positive PSA test results in a referral for further diagnostic testing. There is ongoing debate surrounding the utility of PSA testing as a screening tool, with some evidence suggesting it results in overdiagnosis. The UK National Screening Committee (NSC) recently commissioned Sheffield Centre for Health and Related Research (SCHARR) to develop a prostate cancer screening model. The results of this model and recommendations made by SCHARR form a large component of the evidence used by the NSC to inform their decision on whether to implement prostate cancer screening in the UK. It is therefore very important that the modelling choices and evidence used to inform the model are robust, to suitably inform reliable and accurate decision making. Prostate Cancer Research (PCR) commissioned York Health Economics Consortium (YHEC) to provide a critique of the economic model used to inform the NSC recommendations. The points raised within this critique are specific to YHEC, and do not necessarily represent the views of consulted stakeholders.

2. METHODS

The critique of the model had three components.

Component One: We conducted a detailed review of the technical report, including understanding the methods selected, the overarching structure of the model, and the data underpinning the analysis.

Component Two: We facilitated a series of clinical validation workshops that served as a platform for expert elicitation.

Component Three: We approached SCHARR with questions based on our initial review to ensure there was no misinterpretation. We also provided suggestions for scenarios to run in the model, which were provided by SCHARR.

3. RESULTS

The results of the critique highlight concerns relating to the economic model report used for the NSC's prostate cancer screening recommendations. Specifically:

1. The screening policy that was evaluated in the model is to implement additional 'structured' PSA testing for all men in addition to current practice, where men ask their GP for a test (opportunistic testing). It is unlikely that current practice will continue unaffected with the implementation of a structured screening strategy.
2. There are several concerns with how the model deals with clinical parameters, including:

- Calculated overdiagnosis between treatment arms. Currently, it is unclear how overdiagnosis is defined, and only the harms of organised screening on overdiagnosis are considered, not the potential reduction in overdiagnosis as well.
 - Treatment and diagnostic costs. Treatment costs are underestimated for those with late-stage cancers, while there are concerns that some of the diagnostic costs do not match the diagnostic pathway. Both of these factors are likely to bias against screening.
 - The relationship between cancer stage and grade. The mapping between these two aspects means that treatment costs may be overestimated, due to people ending up in higher grades than reality at earlier stages of cancer. This would likely impact the screening arm more, due to the treatment effect of earlier diagnosis.
3. The model and report do not discuss, acknowledge or evaluate the impact on health equity.
 4. Changing some of the underlying data and assumptions within the model, based on the concerns raised, changed the direction of some of the economic results within the scenario analysis we requested. Although these were crude scenarios, it highlights the importance that assumptions made, and data selected have on the modelling outcomes, particularly for Black Men and those with family history of prostate cancer.

4. CONCLUSIONS

Modelling the impact of a national screening programme for prostate cancer is complex and will require various assumptions. However, we recommend that adjustments be made to the economic model to ensure that valid and robust results are used to inform NSC recommendations. It is important for the assumptions and biases of the model to be reflected on and reported appropriately. The concerns highlighted in our critique are all important considerations, particularly for at-risk subgroups, where the cost-effectiveness estimates are relatively close to the threshold.

Acknowledgements

We would like to thank The Sheffield Centre for Health and Related Research (SCHARR) for assisting us in running model scenarios and their time answering clarification questions. We would also like to thank the 15 clinicians and expert advisors, as well as Prostate Cancer Research (PCR) for their time and advice supporting the validation of the model.

The points raised in this critique reflect the opinions of the York Health Economics Consortium (YHEC) project team only. These represent our interpretation of the SCHARR technical report, advice provided by expert advisors, our own knowledge on the topic area, and knowledge identified through targeted literature searches.

Abbreviations

AE	Adverse event
AQuA	Analytical Quality Assurance
ATM	Ataxia telangiectasia mutated
bpMRI	Bi-parametric magnetic resonance imaging
CAP	Cluster randomised trial of PSA testing for prostate cancer
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
ERSPC	European Randomised Study of Screening for Prostate Cancer
FIT	Faecal immunochemical testing
GGG	Gleason Grade Group
GP	General Practitioner
HRG	Healthcare Resource Groups
HRQoL	Health-related quality of life
LATP	Local anaesthetic transperineal
LUTS	Lower urinary tract symptoms
mpMRI	Multi-parametric magnetic resonance imaging
MRI	Magnetic resonance imaging
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NSC	National Screening Committee
PCR	Prostate Cancer Research
PROMIS	Prostate MRI Imaging Study
ProtecT	Prostate testing for cancer and Treatment
PSA	Prostate-specific antigen
PSS	Personal Social Services
QALY	Quality-adjusted life year
SACT	Systemic anti-cancer therapy
SCHARR	Sheffield Centre for Health and Related Research
TRANSFORM	Trial of Randomised Approaches for National Screening FOR Men
UK	United Kingdom
YHEC	York Health Economics Consortium

About YHEC

York Health Economics Consortium (YHEC) is a health economics consulting company owned by the University of York. It provides a range of services, including economic modelling, literature searching, systematic reviews, network meta-analyses, patient-reported outcomes, service review and applied research and training to the National Health Service (NHS) and the pharmaceutical and healthcare industries. YHEC also carries out work for a range of clients outside the health sector, including Local Authorities and the voluntary sector. Current clients include: NHS England, the National Institute for Health and Care Excellence (NICE), a range of local NHS trusts and several large multi-national pharmaceutical, device and nutrition companies.

YHEC is one of a group of Health Economics departments at York, which is the largest and most active group in the United Kingdom. It is the main consultancy provider of Health Economics expertise at York, combining rigorous research standards with efficient project delivery. As well as its own multidisciplinary staff, YHEC often draws on the specific expertise of staff in related academic departments.

1 Introduction

In the United Kingdom (UK), prostate cancer is the most common cancer in men. Recent research has indicated that it is also now the most common cancer in the UK across men and women, overtaking diagnoses of breast cancer [7], with an estimated 64,000 diagnoses in 2022 and approximately 12,000 deaths each year [10]. The most common age for diagnosis of prostate cancer is between the ages of 70 and 79 years in England [6].

There is currently no national screening programme for prostate cancer [11]. Instead, all males above the age of 50 (with or without concerns) can request a prostate-specific antigen (PSA) test from their GP. As part of the national guidelines on recognition of possible prostate cancer, a PSA test is recommended for men with lower urinary tract symptoms (LUTS), erectile dysfunction, or haematuria [12]. A PSA test is a blood test that measures the PSA protein, which is produced in the prostate gland and can assist with the detection of prostate problems, like cancer. Those with elevated PSA levels will then be referred for further diagnostic testing. Consulted clinical experts and the wider academic literature suggest the current opportunistic approach is suboptimal and requires optimising to target those at highest risk [13].

However, there is ongoing global debate surrounding the utility of PSA testing as a screening tool for prostate cancer [14]. PSA is present at some level for all men, and increases with prostate size, and sometimes age, as well as being elevated by active inflammation in the prostate. PSA testing is therefore an imperfect choice for screening due to the high potential for overdiagnosis or false positives, leading to increased harm and unnecessary further testing such as biopsies [15]. It also may lead to the detection of low-risk prostate cancers, which are clinically insignificant and is associated with lead-time bias.

Nonetheless, screening with PSA tests may still provide benefits to the national population. The use of MRI and risk stratification plays a role in the reduction of false positive cases and overdiagnosis. Screening can be beneficial to people by helping to detect the disease early, allowing earlier treatment and potentially improving morbidity and mortality. This is reflected in the European Union's recommendation in 2022, that organised screening programmes should be undertaken for prostate cancer [16]. This should also be balanced with consideration of the costs of implementing the screening programme, and any harms screening may cause.

The UK National Screening Committee (NSC) recently commissioned Sheffield Centre for Health and Related Research (SCHARR) to develop an economic analysis to evaluate the cost-effectiveness of prostate cancer screening [17]. This involved an economic evaluation to determine the cost-effectiveness of introducing a nationwide screening programme. The model captured the impact on the general male population over the age of 50, as well as targeted screening for higher risk subpopulations.

Higher risk populations include those with:

- A familial history of prostate cancer.
- The BRCA gene mutation (BRCA1 and BRCA2).
- Black ethnicity.

The modelling approach adapted the previous MIMIC-Bowel model used to inform the impact of bowel cancer screening. The draft recommendations advise against routine population screening and targeted screening for at-risk populations such as Black men or men with a familial history of prostate cancer. Screening was only recommended for those with a known BRCA gene mutation. The decision by the NSC was informed by the cost-effectiveness model . These recommendations are currently open for public consultation.

1.1 Objectives

Prostate Cancer Research (PCR) approached York Health Economics Consortium (YHEC) to critique the economic model used to inform the NSC's recommendations. This critique involved:

- An assessment of the methodological, structural, and parameter choices made in development of the model, with respect to the current clinical pathway and published literature.
- A review of the model findings, technical report, and the consequent recommendations made to the NSC.
- Engagement with SCHARR, clarifying structural and parameter choices in the model, as well as requesting additional scenarios.
- Engagement with clinical experts and expert advisors for prostate cancer, to support the evaluation of the model's validity.

This report summarises the methods and findings from the critique, including recommendations to improve the robustness of the model.

2 Methods

The first stage of the project included a detailed review of the technical report describing the model used to inform the NSC's decision on prostate cancer screening. YHEC requested the executable model for this critique; however, SCHARR did not provide this. Therefore, this critique is based on the technical report alone and is unable to consider programming errors.

The review of the technical report focused on understanding the methods selected by SCHARR, including the overarching structure of the model, and data underpinning the analysis. Internal validation involved a thorough review of the inputs used to ensure they matched the source materials. This was extended further by conducting targeted literature searches for key inputs, to consider if alternative options were more suitable. The model structure was then compared with national guidelines surrounding prostate cancer diagnosis and treatment, to understand if it appropriately captured diagnostic and treatment pathways. This stage also assessed if the report aligned with established health economic standards for reporting [18-20].

To assess the model's clinical relevance and face validity, we facilitated a series of clinical validation workshops involving 15 clinical experts and advisors from a range of specialities based both in and outside of the UK, including oncologists, urologists, radiologists, and biostatisticians (see Appendix D). These workshops served as a platform for expert elicitation, where clinicians were asked a range of questions on the core assumptions made in the model and supporting data, pathways, and outcomes. The feedback gathered was from a range of experts to construct a comprehensive understanding of the decision problem to support the findings outlined in this report.

Finally, we were able to provide questions to SCHARR based on our initial review of the model, to ensure the approach taken by SCHARR was not misinterpreted. These clarification questions helped shape our understanding of the approach, the rationale for SCHARR's decisions, and the findings of the critique. Further to this, we also provided SCHARR with some suggestions of scenarios which would be useful to run through the model. Given the time available before consultation to the recommendations closed, the scenarios were limited to simpler changes, rather than structural changes or modifications to the scope of the analysis. The scenarios requested are presented in Appendix B. The results of these scenarios are provided in Appendix C and discussed in Section 4.

3 Summary of Key Concerns

This section will address the key concerns identified throughout our review process. Additional, less critical, concerns are provided in Appendix A. Therefore, Sections 3.1 to 3.6 cover the key considerations for any updates to the cost-effectiveness model, or to NSC guidance.

3.1 Reporting Quality and the Principles of Robust Analysis

Transparency, objectivity and a reflection of uncertainty are fundamental concepts of all robust analyses. For example, The Analytical Quality Assurance (AQuA) Book was published in 2015 [21], in response to recommendations from the 2013 Quality Assurance of Government Models Review [22]. Although it is not specific to health, the book outlines principles required for robust economic analysis. The following statement from The AQuA Book outlines the key pillars of any analysis:

“Quality analysis needs to be repeatable, independent, grounded in reality, objective, have understood and managed uncertainty, and the results should address the initial question robustly.”

We recognise that accurately reflecting the patient pathway and complexities of screening is a challenge and that some elements will, by necessity, be subjective or require the use of assumptions. However, it is important to consider whether the analysis meets the standards required to inform policy decisions. Our initial overview of the report identified concerns surrounding the quality and transparency of the reporting. The model was not made available to us for this review when requested, so any insights made in this critique were based solely on the technical report.

In health economics, a common tool used to establish reporting quality is the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist [19]. Another commonly used tool to critically appraise economic evaluation is the Drummond checklist, which focuses on ten key areas for the reporting of economic analysis [23]. As part of our external validation, the model reporting quality was assessed against economic evaluation reporting standards including the Drummond checklist, CHEERS checklist, and The AQuA Book.

We identified several areas where the reporting lacked clarity and transparency to allow for a clear deliberation on the impact of screening.

For example, using the CHEERS checklist, a common tool for assessing health economic analysis reporting, we identified the following concerns, which highlight the wider concerns on reporting quality:

- Lack of clarity on the model decision problem (**Item 5-7**). The report fails to clearly define the comparator or the intervention, making it hard to determine the appropriate allocation of costs and consequences to each model arm. For example, it was only upon further clarification from SCHARR that it was confirmed that there are no differences associated with opportunistic screening modelled between treatment arms. This is not explained or stated with sufficient detail in the report. This lack of context and transparency makes it difficult to critique model outcomes and may produce a misleading interpretation of the results.

- Another key point that is not explicitly mentioned is the model perspective (**Item 8**). It is important to clearly outline the viewpoint from which costs and benefits are being considered to adequately determine the relevant parameters and scope of the model. We understand this to be from a National Health Service (NHS) and Personal Social Services (PSS) perspective.
- The authors also do not state and justify the discount rate used (**Item 10**). The discount rate is only referenced in the scenario analysis, but does not confirm the base case discount rate, and is only shown in the results during scenario analysis.
- There are many assumptions surrounding data, inputs or extrapolated evidence that are not adequately explained (**Item 17**). For example, on page 69 it is stated in the report *“The base case screening uptake was used from the CAP trial: 36% for the PSA test and 85% for the follow up biopsy [28]. It was assumed that mpMRI will have the same uptake as the biopsy.”* However, the rationale for this assumption is not explained any further. Further examples include what year the utility multipliers were calculated from (page 71), what period the palliative care costs cover (page 79), and why cumulative hazards with respect to risk factors were unrealistic (page 36).
- The report does not include any discussion of the distributional effects (**Item 19**), or any equity considerations (**Item 26**). The SCHARR model accounts for certain high-risk populations including those with family history or Black ethnicity. However, this is done with high uncertainty due to the lack of evidence available. Whilst we acknowledge the lack of data, particularly in the Black ethnicity population, there is no discussion of the impact of health inequalities concerning both education and access to current care pathways on this population. The variation in impact, correlated with socioeconomic status within these populations, is not explored qualitatively or quantitatively with respect to an organised screening programme. It is recognised that a complex quantitative equity analysis would not have been possible within the scope and timeframes of this project. However, we recommend that the report be amended to include at least a qualitative discussion of the impact of the model findings with respect to health equity and recommendations for further research surrounding the distributional effects.
- The report does not adequately describe the methods used to identify uncertainty (**Item 20**) or provide an estimate of the impact of various uncertainties on the model outcomes (**Item 24**). Parameter uncertainty is often identified through probabilistic sensitivity analysis. The report includes details of sensitivity analyses run for each subgroup; however, it does not provide sufficient detail to identify the key drivers. For example, on page 98 of the report, it is stated that for the general population *“uncertainty in the natural history parameters, specifically those correlated with age (see Supplementary C) was the most influential factor in determining cost-effectiveness”*. However, there is no further discussion on the cause or impact of this uncertainty, and no other influential factors are identified. Structural uncertainty is validated against the CAP and ERSPC clinical trials to minimise structural flaws. Unfortunately, these trials are outdated and do not reflect modern updates to the diagnostic pathway. The authors fail to sufficiently identify or explore the impact of this uncertainty. Trials such as the PROMIS [24], and GÖTEBORG-2 [25] trials could have been used to validate a more modern diagnostic pathway. We recommend that early results of the TRANSFORM trial [3] also be used to explore this uncertainty with a more modern diagnostic pathway for validation once available. Further sections in this report discuss alternative data that could have been considered.
- The report does not include the breakdown of the costs for the main results (**Item 23**). This makes it very difficult to determine the key drivers of the model outcomes and consequently assess the results appropriately. All health economic evaluations should

break down the core results to show the drivers of change and impact from the model between treatment arms.

- There is limited discussion provided of the study's weaknesses and constraints (**Item 26**). The model limitations are briefly discussed on pages 179-180 of the report. However, there are key limitations such as the model structure not reflecting a modern diagnostic pathway or the use of alternative biomarker tests. Further details on limitations are discussed throughout the rest of this report. All models are expected to have limitations, but these should be clearly identified and the potential impact of these explored and discussed. Some of the limitations discussed in the report were identified only after consultation with SCHARR, rather than directly from the technical report.

Overall, the points raised above with respect to the CHEERS checklist result in concerns around reporting quality. Similar guidance documents referenced suggest similar principles that should be adopted within the analysis. Beyond the reporting quality with respect to economic guidelines, the document is missing sections. For example, in the report it is stated that *"the decrement in utility due to age was detailed in the 'Modelling Changes in Phenotypic Characteristics by Age' on page 70 of the report*. However, this section does not exist in the report, so is difficult to interpret. The list above does not contain an exhaustive list of reporting concerns but highlights that further work should be conducted to make the report more transparent and robust for informing national policy.

Recommendations for updates

We recommend an update of the report to address the concerns outlined above in order to meet key economic reporting standards. The points raised reflect a lack of overall clarity, reducing the credibility and replicability of the work. We recommend that the authors consult key checklists for reporting, including the CHEERS checklist, discussed within this section.

3.2 Key Definitions and Opportunistic Screening

The definitions of the comparator and intervention were not made clear in the report. However, clarification from SCHARR confirmed the following:

- The **comparator** is modelled as 'current care': opportunistic screening for anyone with concerns (i.e. LUTS, erectile dysfunction, haematuria) or any men over the age of 50 who request a PSA test from their GP.
- The **intervention** is modelled as the addition of organised screening to the current care pathway, without the cessation of any opportunistic screening currently occurring.

3.2.1 Definition of comparator

The definition of the comparator is not clearly defined in the report. However, the definition provided by SCHARR is likely not accurately reflected in the model. It is unclear whether the cost of opportunistic PSA testing for those who do not go on to receive a positive diagnosis is included within the model.

Feedback from clinical experts indicated that there are currently a large amount of opportunistic, asymptomatic screening tests happening, which will incur substantial costs to the NHS at a population level. For instance, Vickers and Brentnall (2026) [26] estimate a total incidence of 1.88 million PSA tests under current opportunistic screening practice. Additionally, a paper by Merriel et al (2025) [27] suggested that in 2018, one in five people with prostate cancer in England were diagnosed through asymptomatic screening tests. It is likely that this figure will fluctuate year-on-year due to various factors, such as media campaigns or other events raising awareness. However, considering the sensitivity and specificity of PSA testing, MRI scans, biopsies, and the available evidence on total population screening, approximately 300,000 opportunistic asymptomatic PSA tests were done in 2018 in order to detect this many cancers. Furthermore, previous literature and clinical experts raised how current opportunistic screening is more concentrated among wealthy individuals who are white [28]. This means current practice is likely to exacerbate health inequalities.

As discussed in Section 3.2.2, the intervention arm is likely to overestimate the number of opportunistic asymptomatic PSA tests. Therefore, it does not seem plausible to omit the cost of current opportunistic testing from the economic model.

3.2.2 Definition of intervention

The definition of the intervention provided by SCHARR suggests that the introduction of a screening programme is completely additive to any opportunistic screening occurring. This is unrealistic for several reasons.

Firstly, it does not reflect the process used to introduce other screening programmes such as bowel cancer screening. In this case, when the use of faecal immunochemical testing (FIT) to screen for bowel cancer was introduced, the NSC recommended the permanent discontinuation of bowel scope screening, the current standard of care [29]. Evidence also indicated that FIT testing became more appropriate after introduction of the screening guidelines, with more people tested who were eligible and recommended to be tested [30]. Models exploring the cost-effectiveness of screening for prostate cancer across Europe typically capture the comparator as no screening [31]. They consequently do not account for any opportunistic screening in the intervention arm, only capturing the impact of age- or risk-based screening for the indicated populations. It would, therefore, be feasible to assume that the introduction of prostate cancer screening would be implemented alongside the recommendation to adjust the requirements for opportunistic screening, which will then feed through to clinical practice. This view was supported by the clinicians and expert advisors consulted for this review.

Furthermore, clinical experts highlighted the over-testing currently occurring in older populations. It was agreed that the introduction of a screening programme would likely reduce opportunistic testing for these populations. Anecdotal evidence was provided from clinicians in

the US and Sweden of this being the case. However, there is evidence from Lithuania [32] which has shown that, upon implementation, the opportunistic testing of people not fitting within the criteria for testing reduced year on year by nearly 80%. We acknowledge that the generalisability of this to the UK is uncertain, given differences in health systems and populations. However, we would expect similar results to be achievable with the implementation of suitable changes to policy and standard procedure. There was consensus from experts that we would expect a downwards effect on opportunistic screening in the UK, even if the magnitude of that effect is uncertain [26]. This could be done through the implementation of policy decision for primary care, impacting the ability to order PSA tests for asymptomatic men who do not fit the screening criteria. It is also likely to occur naturally as it is expected that people who test negative through the screening programme are not likely to also attend their GP for additional testing outside of the programme, if asymptomatic.

These expected impacts would likely contribute towards a reduction in opportunistic screening once organised screening is introduced. It is then important to relate the impact of changes to opportunistic screening on the economic model results. Considering the impact on overdiagnosis, the current report highlights the harms of increased overdiagnosis from screening. However, what is not taken into account is the counteractive effect of screening: that a strict screening programme will also likely reduce screening in other lower-risk populations. If opportunistic screening is reduced, overdiagnosis will be reduced in populations that were not suitable for a PSA test, where there is little benefit of testing. Therefore, it is important to consider the overall impact of screening on overdiagnosis, not just focusing on new over diagnosed cases identified in screening.

The second consideration is with respect to cost differences. It is likely that the net number of PSA tests (and subsequent diagnostic tests) is overestimated, given that screening is assumed to be completely additive. It is likely some of the people currently receiving opportunistic tests will fall within categories considered for screening. In this case, the costs from introducing a screening programme are overestimated. Furthermore, if the introduction of a screening programme reduces PSA testing for populations that are not suitable for a PSA test, then this will also overestimate the true cost of rolling out the screening programme. One previous paper has suggested PSA testing would reduce by approximately 25%, of which a proportion would be from opportunistic screening [26].

Thirdly, the screening scenarios modelled for the intervention incorporate minimal risk stratification (See Appendix A for further explanation and supporting literature). Clinician opinion suggested that it would not make sense for those who attended screening with consistently low PSA levels to continue to attend screening every two years. In these scenarios it is more plausible that they would then be advised to reduce attendance. For example, they may then be recommended to only attend screening every 5 years. This contributes to the overestimation of the number of PSA tests occurring in the intervention arm.

Recommendations for updates

We recommend that the comparator be adjusted to reflect the current levels of PSA testing occurring, if it does not already, and the report be amended to clearly define the comparator. This is so the expected impact between the intervention and comparator can be appropriately modelled.

We also recommend that the intervention arm be restructured to reflect organised screening for the indicated populations only, with a range of scenarios covering the cessation of current practice for those outside this population.

This uncertain limitation should then also be explored further in the discussion of the report, so that the uncertainty is fairly reflected in decision making. This discussion should cover the expected impact and bias on the overall results.

3.3 Overdiagnosis

The report initially defines overdiagnosis as *“the proportion of all screen-detected cancers that would not have caused harm during a patient's lifetime”*. However, based on the calculation provided for the overdiagnosis model output (page 17), it is interpreted that *overdiagnosis within the model is estimated as all incremental cases identified through screening that would not have been identified in the comparator arm*. This modelling choice does not reflect the provided definition and suggests that all prostate cancer cases not diagnosed under current care practice would never have caused harm. There is also no clarification provided as to what constitutes ‘harm’ for the purposes of this definition. For example, for the proportion diagnosed who remain on active surveillance, they may never experience cancer progression which needs to be treated in their lifetime. This could be classed as the cancer not causing harm, but a form of management was still provided instead of discharge. Therefore, the lack of clarity on what constitutes harm in the definition results in ambiguity in the estimations of overdiagnosis. Furthermore, if all incremental cases identified through the screening arm are due to overdiagnosis, this assumes that none of these cases would have caused harm in the comparator arm. This would lead to an over-estimation of the consequences of overdiagnosis due to screening. Clinical feedback suggested a more suitable definition to identify diagnosis would be assuming those diagnosed and classified as Gleason Grade Group 1 (GGG1) are likely to be the over-diagnosed cases.

There is a further lack of clarity in the report surrounding the application of the provided definition of overdiagnosis to the comparator arm. The modelled definition of all incremental cases identified through screening implies that any cases detected in the comparator arm that would have caused ‘harm’ in a patient’s lifetime are not defined as over diagnosed. This inconsistency in the application of the definition would overestimate the incremental impact of overdiagnosis by failing to acknowledge the level of overdiagnosis already present in current care. This is an implicit assumption being applied based on how overdiagnosis is currently being captured in the evaluation. Clinical and expert advisors have confirmed that this is unrealistic given that current levels of PSA testing results in high levels of overdiagnosis,

particularly in older men. It is unrealistic to assume that there is no overdiagnosis within standard of care that could be avoided with the implementation of a formal screening pathway [26].

Additionally, the choice to model the intervention as the addition of organised screening to current opportunistic screening also contributes to the overestimation of the impact. This structural choice ignores any benefit of the potential for an organised screening programme to reduce current overdiagnosis occurring as a result of opportunistic screening. We acknowledge that there is uncertainty regarding the impact on opportunistic screening. However, this uncertainty should have been explored through a scenario analysis. The exclusion of this consideration reflects an inherently biased approach to modelling against screening and should be rectified to provide decision makers with a range of potential outcomes from a pessimistic scenario through to an optimistic scenario. The reality of screening impacts is likely to fall somewhere between these two scenarios. This will better capture the possible value, and risks, of a potential national screening strategy. This scenario analysis can be informed by clinical feedback, particularly from those who are involved in exploring screening opportunities in the UK [33], as well as data from European screening studies [32] to estimate the anticipated impact on opportunistic screening with the introduction of an organised screening programme.

It is unclear how the GGG cases were distributed in the over diagnosed cases within the model. If these were spread across the GGGs in the same distribution as diagnosed cases, the treatment costs and health-related quality of life (HRQoL) decrements will be overestimated because it is likely that any cases classified at GGG2 or higher would require treatment to prevent harm and are, therefore, not over diagnosed. Alternatively, if the incremental cases identified as over diagnosed are mostly classified as GGG1, then the method used to allocate treatment costs is flawed. The weighting of treatment costs is based on the current distribution of treatments which is in turn driven by the distribution of GGGs under current practice. Therefore, it would be necessary to reweight the treatment costs for the screening arm to reflect a higher proportion of GGG1 cases. For example, the source used for the weighted treatment costs [34] assumes 37.8% of people with stage 1 cancer still receive treatment compared with between 50.4% and 76.6% for later stages. An increase in the proportion of lower stage cases identified should, therefore, be reflected by an increased proportion of those on active surveillance instead of receiving treatment, and subsequent reduced cost. Further feedback from clinicians also suggested that with the introduction of a screening programme, they would expect behaviour changes, with a larger proportion of GGG1 cases assigned to active surveillance rather than treatment. This would further decrease treatment costs for the intervention arm and treatment-related adverse events (AEs). Lastly, the alternative assumption proposed above, that all GGG1 cases be defined as over diagnosed, would help prevent the overestimation of the negative consequences of screening. This is by avoiding defining any incremental cases identified at a higher GGG, which are likely to cause harm and would benefit from treatment, as over diagnosed.

The definition of overdiagnosis includes both true diagnosed and false positive cases. This definition does not align with clinical feedback and current medical literature stating false positives should not be defined as overdiagnosis [35-37]. Consultation with SCHARR confirmed that false positives were modelled to proceed through diagnostic testing (mpMRI and potential biopsy). Any that continued to have a false positive result were then treated as GGG1 and assigned the costs of active surveillance only. Clinical feedback suggests that this is not a

suitable assumption. We acknowledge that the sensitivity and specificity data may imply that a small number of people will have a false positive diagnosis. However, in clinical practice, following positive results of a PSA test, magnetic resonance imaging (MRI), and biopsy (for those who require it), a multidisciplinary team meeting would be held which would consider this, alongside other clinical factors, to determine a diagnosis. Expert opinion advises that at this stage, a negative diagnosis would likely be decided and no further treatment costs or surveillance would be applied. This population would likely be correctly identified as false positive following a few additional tests and be discharged. Therefore, applying the full active surveillance costs to this population is overestimating the cost impact. A scenario should be run testing this with the alternative approach mentioned above, to explore the total impact on costs.

Recommendations for updates

We recommend that the definition of overdiagnosis is amended to exclude false positives in alignment with accepted modelling practice. We also recommend that overdiagnosis is identified in both the comparator and intervention arm or that this is further clarified within the report if it is already reflected in the model. Similarly, we recommend that false positives are identified separately in both model arms, and that only the diagnostic costs are applied, with no GGG, utility decrement, or active surveillance modelled.

As a point of key importance, we recommend that additional scenario analysis is performed to explore the potential changes to current overdiagnosis levels with the addition of organised screening.

Alongside this, we also recommend that the weighting of the treatment costs for the screening arm be adjusted to reflect the increased proportion of lower grade cases identified and scenario analysis be carried out to explore the impact of an increased proportion of GGG1 cases receiving active surveillance.

If the GGG distribution of the over diagnosed cases reflects the distribution of the known cases, then we would recommend both an optimistic scenario (all incremental cases anticipated to cause harm and require treatment) and a pessimistic scenario (all incremental cases are over diagnosed and do not require any management/treatment) be modelled, to test the impact of this uncertainty surrounding over diagnosed cases.

3.4 Policy Considerations

3.4.1 Health equity concerns

A key subgroup modelled within this analysis is men of Black ethnicity. Black men are known to have a higher risk of prostate cancer compared with the general population [38] and some evidence suggests that Black men are also more likely to experience more aggressive cancer which spreads at a faster rate, and experience worse care outcomes compared with the general population [39]. It is concluded within the report that the data used to model this population was too uncertain to determine whether this would be a cost-effective application of

screening. The recommendations from the report suggest that *“this group would benefit from having better data on how cancer develops, progresses, and what the expected participation rate in screening would be for this population group”* with screening not recommended due to this uncertainty.

However, the report does not include any quantitative analysis surrounding health equity, or a more qualitative discussion surrounding the impact of the recommendations on health equity. The NSC has previously outlined the important principles of health inequalities, and why they are important to be considered, and also aligns with wider government stakeholders [40]. However, the SCHARR report contains no mention of equity, despite this being a core principle of the NHS 10-year plan [41]. Therefore, we expect authors to discuss the implications for health equity and health inequalities, given that these are core values for the NHS. The current report does not make any acknowledgement of wider policy, including the Core20PLUS5 framework [42]. This framework outlines the need to actively target inequalities for minority ethnic groups, with one of the 5 key clinical focus areas being the earlier diagnosis of cancer. If considering wider implications for health inequalities, there is evidence that Black men are less likely to get tested for the BRCA gene, so are likely to be disproportionately affected by current recommendations [43]. Furthermore, there are strategies within the current model, where screening Black men is considered more likely to be cost-effective than not, based on the results presented in Figure 99 of the SCHARR report. It is, therefore, surprising that the balance between uncertainty and health inequalities is not discussed, given the competing factors of ‘value’ to the NHS.

Additionally, the report also does not acknowledge the impact on regional inequities surrounding access to care and current screening. The SCHARR report does not discuss the anticipated effect with respect to income related inequities and their impact on health literacy. Previous studies have shown that areas of higher socioeconomic deprivation in the North of England have lower incidence rates of prostate cancer but higher rates of metastatic cancers [8]. This reflects the lower rates of testing in more deprived areas of the UK resulting in later diagnosis and consequent poorer outcomes. Organised screening could impact this, by increasing testing in areas that are more deprived. However, the true impact on health equity would have to consider by how much testing also increases in less deprived areas.

Variation in health literacy has also been found to disproportionately impact those from lower socioeconomic backgrounds. Previous studies have found people from lower socioeconomic backgrounds are less likely to identify problematic symptoms or know that they are able to request a PSA test from their GP [27].

Finally, deprivation has also been linked to knowledge of BRCA status, with those in more deprived areas found to have lower uptake of BRCA gene testing [44]. The recommendation to continue opportunistic testing and only recommend screening for those with knowledge of BRCA gene mutation may further enhance inequities in more deprived backgrounds.

We acknowledge that limitations on the scope and timeframe of this project would not have allowed for a full quantitative equity analysis. However, this report is intended to inform national decision making and would benefit from a discussion of the impact on health equity from potential recommendations.

3.4.2 Cost-effectiveness threshold

A £20,000 per quality-adjusted life year (QALY) cost-effectiveness threshold was used based on the National Institute for Health and Care Excellence's (NICE's) cost-effectiveness threshold [45]. The justification provided for this was alignment with previous NICE evaluations of screening where the lower bound is used to reflect high uncertainty often found in screening programmes. Screening for the general population is shown to be highly uncertain in the results of the probabilistic sensitivity analysis. However, we can see from the cost-effectiveness planes that for some specific screening scenarios, such as screening men of Black ethnicity starting at age 45 once every 4 years (Figure 94), there is a much tighter cluster of points. This indicates much higher certainty in the results of these scenarios which would provide justification for the use of a higher cost-effectiveness threshold.

Although it is up to the NSC what threshold they choose to use for the economic analysis, we believe that more justification needs to be provided for the use of a lower threshold, other than "screening is uncertain" as stated in the SCHARR report, and a clear rationale should be provided for the selected threshold. We also acknowledge there are trade-offs to using different thresholds, given that opportunity cost estimates (health that will be otherwise forgone) are lower than the NICE threshold [46]. However, it is important to note that if the NSC has previously aligned with the NICE threshold for decision making, it would appear to be inconsistent if they did also not adopt the new NICE threshold. This is particularly the case given the screening committee have expressed an interest in continuing to update the model with more relevant evidence.

Recommendations for updates

We recommend that an additional discussion of the impact of the model results and uncertainty on wider health equity concerns be included in the updated report. This should contextualise the recommendations made based on the model uncertainty and discuss the impact on the NHS focus to reduce health inequities. It is important that factors of value are appropriately discussed, to allow for a transparent, clear and deliberative decision-making process.

We also recommend that the base case cost-effectiveness threshold either be updated from £20,000 to align with the new cost-effectiveness threshold of £25,000 to £35,000, or that the approach is revised to consider aligning with an opportunity cost informed threshold. This would increase the credibility of any recommended decisions made based on the threshold.

3.5 Parameter Suitability

3.5.1 Baseline utilities

The utility reflective of a 70-year-old man was used as a reference value for the general population without cancer, to which multipliers were applied to determine the utility of each stage of cancer. The report does not include a justification as to why this utility was utilised as a baseline value. This assumption is likely an inaccurate reflection of the true utility value for both older and younger ages. The use of this utility value would lead to under valuing utilities for those under 70 years old and over valuing those above 70 years old.

Recommendations for updates

We recommend that the age specific utilities are selected from UK population norms utility data [1]. Further, it is recommended that SCHARR provide justification for their rationale behind parameter choices.

3.5.2 Costs and Resource Use

We have reviewed the costs and resource use inputs within the model as part of this critique. This section of the critique is split into sub-sections where additional considerations are required, to improve the robustness and reliability of the model. Based on our review, there are concerns surrounding the treatment costs, diagnostic costs and palliative care costs.

3.5.2.1 Treatment costs

The key concern with respect to treatment costs is the reliance on extrapolating clinical trial data and applying costs, which does not reflect modern practice. We acknowledge that the nature of research is constantly evolving, and up to date data may not have been available when the SCHARR model was being developed. However, SCHARR has utilised data and structural validation from clinical trials including the CAP [47], ERSPC [48] and ProtecT [49] trials, which may not be representative of current clinical practice. Specifically, SCHARR has used long-term treatment costs that are based on the ProtecT trial and are no longer representative of the costs associated with current practice, given this data was collected up to 2009.

Another key concern around treatment costs is the treatment intensification proportions, and wider costs associated with stage four metastatic prostate cancer. SCHARR has applied a proportion of 1.8% of people receiving treatment intensification to stage 3 prostate cancer, and 28% for stage 4 [34]. However, these proportions are not reflective of the number of people receiving systemic anti-cancer therapies (SACTs) in current practice. Recent National Prostate Cancer Audit data [6] has established that approximately 47% of people with metastatic prostate cancer were receiving SACTs in 2022. Furthermore, a study conducted by Dodkins et al. 2025 [5], identified that out of 45.1% of people with metastatic hormone sensitive prostate cancer, approximately 70% received treatment intensification with either enzalutamide or apalutamide, with approximately 30% receiving other SACTs including docetaxel or abiraterone within 12 months post-diagnosis. We appreciate that SCHARR has adjusted the SACT

treatment costs to reflect current practice. However, the extent of recent advancements and accurate proportions of those receiving high-cost medications are still not adequately reflected in the model. This results in the underestimation of value from detecting earlier stage cancers and preventing their progression to higher cost stage 4 treatments.

Discussions with SCHARR indicated they will try to capture this in future updates, with the NSC indicating that they are open to future iterations of the model. They suggested adjusting down those diagnosed at stage 4, to account for the fact some people will progress to stage 4, and that will make up the whole number of people on SACTs. However, this will weight down the true number of people receiving SACT. 47% of people diagnosed at stage 4 should be allocated to receive SACT based on the available evidence, and this number scaled down for earlier stages, to account for progression. Those diagnosed at stage 4 should not be scaled.

A further concern is that SCHARR has applied SACT costs for a maximum of three years. Realistically, a substantial proportion of people with metastatic prostate cancer will live much longer than three years. Clinicians suggested that life expectancy for metastatic disease has increased from three years to approximately seven years on average. Additionally, published NHS England data identified that people diagnosed with stage four prostate cancer have an overall survival of 60.4% after five years [9]. This increase in life expectancy could potentially double the costs of SACTs for late-stage cancers, which SCHARR has not accounted for in the model; therefore, underestimating the treatment costs. All clinical experts that attended the workshops advised that where possible SACTs would be continued for the duration of a person's lifetime, unless the treatment stopped responding.

Finally, the model does not capture people progressing onto SACT costs from earlier stages. For example, a person diagnosed at stage 4 who dies from other causes after 15 years of follow-up is assigned SACT costs for the period stated. In contrast, a person diagnosed at stage 2 who subsequently progresses to stage 4 is not assigned SACT costs at all, even though it is clear that they experienced advanced disease before death. This is because progression is not explicitly captured. This has two effects in the model. Firstly, because less people are diagnosed at stage 4 in the screening arm, SACTs will be underestimated for those, who are now diagnosed at stage 2 or 3. However, those who are diagnosed earlier due to screening that were not going to be diagnosed at stage 4 in current practice, the value of screening is underestimated, as screening is likely to see less people ever progress to stage 4. Without adjusting the modelling to account for progression, it is not possible to say which bias will have the bigger impact.

Recommendations for updates

We recommend two options to consider for long-term treatment costs. The first is that they should be acknowledged as out of date, and further clarity should be provided on the limitations of using this source, and the potential impact this has on the results (including the direction of the impact). The second option is to review more recent reports of ongoing trials to inform treatment costs. This could include potentially considering alternative trials and observing the resource use, for example, the recently launched TRANSFORM trial [3]. The risk of this is overestimating costs, due to differences in healthcare systems across countries. However, it is worth exploring more recent trials further. At a minimum, a more reflective discussion within the wider report would be helpful to convey transparency about the potential impact of outdated sources such as the ProtecT trial.

We recommend reviewing and adjusting the model parameters and structure to accurately reflect more updated data that is now available such as the National Prostate Cancer Audit 2025 [6] and Dodkins et al. 2025 [8]. This would result in more accurate assessment of late-stage cancer costs. Alongside this, updated survival estimates should be provided for stage 4 [9]. This will further increase treatment costs due to SACTs but may also result in a reduced positive impact on mortality due to screening, if people with advanced stages of cancer are living for longer.

We also recommend that SCHARR applies the SACT costs continuously to those alive with metastatic disease beyond year three.

3.5.2.2 Additional resource use

From the report and additional queries with SCHARR, it is confirmed that the cost of resource use associated with prostate cancer (other than that included in treatment costs) has not been accounted for in the model, potentially introducing bias into the results. We identified previous NICE assessments and published research highlighting that it is likely that people will use more healthcare resource use outside of treatment, and this will likely increase with more advanced stages of the disease [50-55]. This exclusion likely biases the results and disregards the downstream burden imposed on the healthcare system.

Recommendations for updates

We recommend that SCHARR incorporates wider healthcare resource use, beyond just treatment, to reflect real-life healthcare consumption of people with prostate cancer at different stages of disease. Further, SCHARR should account for wider resource use to capture the burden on primary care.

3.5.2.3 Diagnostic costs

The key concern with respect to diagnostic costs is the choice of diagnostic strategy applied in the model. Whilst SCHARR used the NICE guidelines [56] to inform the inclusion of multi-parametric MRI (mpMRI) in the model, a consensus amongst clinicians identified that these guidelines are now outdated as they are not fully reflective of current practice. Additionally, clinician feedback established that bi-parametric MRI (bpMRI) is being routinely used in a substantial number of areas across the country and is typically the preferred imaging technique for asymptomatic people. It also highlighted the substantial difference in costs associated with each of the screening techniques, leading to cost savings when using bpMRI. Further clinician consensus suggested that for any Trusts still using mpMRI, the disruption to practice caused by switching to bpMRI would be minimal and likely to improve capacity.

A second concern identified when cross-checking parameters was the source of the local anaesthetic transperineal (LATP) biopsy cost. SCHARR reported the cost for a transperineal biopsy of £1,138. Initially, this value could not be sourced; however, following additional clarification from SCHARR, it was identified that this cost was correct but not accurately described in the report and instead reflects the overall Healthcare Resource Groups (HRG) cost rather than the outpatient specific cost.

Whilst the cost SCHARR has used is likely reflective of current practice with no organised screening, it is important to acknowledge the recent and ongoing shift in policy and general advice suggesting that LATPs can and should be conducted in an outpatient setting where possible, which may change during screening [57-59]. Therefore, we would recommend running a scenario with LATP costs from outpatient services, to see the impact it has on the results.

Recommendations for updates

We recommend that SCHARR runs a model scenario with bpMRI to capture the potential impact this could have on the model, in addition to reflecting current practice. Other parameters would have to be adjusted for this model scenario; recommendations for these additional parameters can be found in Appendix A.

We recommend that SCHARR update the report with the correct description for the cost used for LATP. It should be stated that this cost reflects that of an overall LATP rather than an outpatient specific cost as is currently reported.

We also recommend that SCHARR runs a model scenario with a cost reflecting an outpatient LATP (£479.04) using the NHS reference cost of a transperineal biopsy (code LB77Z, urology service). It would be interesting to see the potential impact this change in cost would have to align with the shift in policy and general advice.

3.5.2.4 Diagnostic resource use

A further observation of the SCHARR report is that diagnostic resource use has not been adequately accounted for, potentially omitting the pre-diagnosis resources; for example, people

that remain in a 'watchful waiting' period. Additional clarification was sought from SCHARR, and it was confirmed that the number of biopsies was included as a parameter in the model to account for additional resource use. However, including this does not capture the wider diagnostic healthcare use throughout the diagnostic pathway for prostate cancer.

Recommendations for updates

We recommend that SCHARR considers the addition of further resource use associated with the diagnosis of prostate cancer to adequately reflect clinical practice. We also recommend that the inclusion of any resource use within existing parameters is made clearer in the report.

3.5.2.5 Palliative care costs

A concern pertaining to the palliative care costs is the potential double-counting of costs around end-of-life treatments for those with prostate cancer. We were unable to ascertain which treatment costs are applied alongside palliative care costs within the timepoint of 12 months before death due to a lack of reporting clarity. However, in the instance that the palliative care costs are applied alongside treatment costs, the costs associated with active treatment may be accounted for two-fold since the palliative care costs include the cost of some cancer treatments such as opioids for pain-relief. This would subsequently result in the overestimation of costs associated with end-of-life care.

Recommendations for updates

We recommend that SCHARR addresses these concerns by enhancing the transparency in costing methods and reporting quality. Clinical experts have confirmed that the overall difference in costs between a prostate cancer death and non-prostate cancer death are reasonable, so the concern is mainly surrounding double counting.

3.5.2.6 Diagnostic specificity

Following discussions with clinicians, there is a concern with the diagnostic MRI specificity and whether the value used is representative of a screened population, when bpMRI is primarily used, not mpMRI. Please see section 3.6.4 for further details.

Recommendations for updates

We recommend that SCHARR updates the specificity of the MRI as the current value is not representative of a screened population and will therefore not accurately represent the patient flows through the system. We recommend using the specificity of 0.72, which is reported in Bass et al. (2021) [2]. Further, the same value representing a screened population from the STLK3-MRI screening trial (0.72) has been independently quoted by clinical experts.

3.6 Model Structure

The review highlighted some key areas of critique within the chosen model structure for the analysis.

3.6.1 Risk factors

The model included age, ethnicity, family history of breast, ovarian or prostate cancer, and BRCA gene mutation as risk factors for prostate cancer. While the possession of these risk factors is not treated as independent, the individual risk of prostate cancer for a person with multiple risk factors is treated as independent and non-cumulative. The model only applies the highest hazard ratio present when a person possesses multiple risk factors. This is likely to underestimate the risk of prostate cancer for those men who have multiple risk factors. Therefore, this is likely to undervalue the early detection of prostate cancer in certain risk groups. This also leads to overestimation of the harms of over diagnosing low-risk cancers.

It was stated in the report that the risk factors were initially modelled as cumulative. However, the report states that this led to unrealistic results. While it does not state in the report what is meant by 'unrealistic', clarification was provided by SCHARR that this resulted in little to no men within the lower GGGs throughout the model. It is accepted that this result is unrealistic. However, the concern remains, based on feedback from clinical experts, that having multiple risk factors would increase the risk of prostate cancer beyond the highest hazard ratio present. Clinical experts, including geneticists, agreed that the risks are not likely to be completely independent. However, they also stated that they are not perfectly cumulative. Generally, they agreed that having multiple risk factors is greater risk than just having one risk factor.

Published literature, such as Nyberg et al. (2021), highlight that the relative risk of prostate cancer varied by age, ethnicity, and BRCA mutation when multiple risks are present [60]. To explore the impact of the assumption in the model, a scenario could be run where a multiplier is applied to the hazard ratios when multiple risks are present. We recommend eliciting values with geneticists to explore reasonable ranges to consider for this parameter.

We acknowledge that, due to data limitations, assumptions have been applied in the model where these have been conservative estimates. However, lack of appropriate scenario analyses around these assumptions results in producing outcomes that are likely biased against screening. Appropriate testing of the assumption is required, guided by clinical opinion when current assumptions do not reflect the population and real-world practice appropriately, to show the impact of these assumptions on the model results. This allows more transparent and informed decision-making.

Recommendations for updates

We recommend that SCHARR considers conducting scenario analyses to explore the cumulative impact of a person having a multifactorial risk profile and to explore if BRCA1 and BRCA2 variant genes should be treated as independent populations.

3.6.1.1 Familial history subgroup

An additional concern on model subgroups, is that SCHARR has treated familial history as one subgroup and has defined familial history as broad as possible. The definition used is a person having one or more first-degree relatives previously diagnosed with prostate, ovarian or breast cancer. Clinical feedback suggests that this should be defined as a family member presenting with cancer prostate, ovarian or breast cancer before the age of 60. This is because those diagnosed at later ages may not necessarily increase the risk of a family relative also getting prostate, ovarian or breast cancer.

However, previously published evidence has also suggested that risks differ depending on the type of family history. A nationwide study conducted by Bratt et al, 2016 established that those with no family history of prostate cancer were associated with a 13% risk [61]. However, those with family history had an increased absolute risk of 26% for an affected father, 35% for two affected brothers, and for those two combined the risk rose to 48% [61]. Additionally, the study identified that family history cannot be used to determine cancer aggressiveness and that having relatives diagnosed at an earlier age is associated with a higher absolute risk of developing prostate cancer at an earlier age. According to the report, the current definition of family history represents approximately 1/3 of all men. It may not be cost-effective to provide a screening to this whole subpopulation, but it may be cost-effective to provide screening to a narrower subpopulation, based on higher risk.

Recommendations for updates

We recommend that SCHARR further defines the familial history subgroup. Clinician feedback suggests a definition of people presenting before the age of 60 years old.

We recommend that SCHARR further refines the familial history subgroup based on risk, exploring in scenario analysis, to determine the impact of more specific definitions of family history on the cost-effectiveness results.

3.6.2 Mapping to cancer stages and progression

The methods used to map GGG 1 to 5 to cancer stages in the model are ambiguous. The report states that the incidence rates of GGG by stage were taken from the Get Data Out dataset from the National Cancer Registration and Analysis Service 2020. Due to a different staging system being used (localised, locally advanced, and metastatic) compared with the model, they were loosely converted to stages 1 to 4. The report then goes on to state that weighted averages were applied to avoid conflict with NHS Digital data. However, there is a lack of detail regarding how these were calculated. This assumption has a substantial impact on the results of the model, due to the current approach of treatment distribution across the GGGs. A flawed mapping approach could lead to an increase in the number of men within higher GGGs, resulting in inflated treatment costs and health-related quality-of-life (HRQoL) decrements. It was also noted by clinicians that the treatment allocation within the GGGs is not reflective of current practice, which is especially evident for GGG 1. It is believed that almost all patients within this GGG should be receiving active surveillance. In turn, this would result in lower treatment costs.

The approach adopted in the model to mapping GGG to cancer stage appears to suggest the notion that priority was placed on fitting the decision problem into the model, rather than fitting the model to the decision problem. Previous economic models (e.g. NG131) do not use the staging system of 1 to 4 that is used in this current model. It is possible that altering the structure of the model to incorporate alternative cancer staging could have led to improvements in clarity of the modelling methods.

In addition, it is unclear how this differs between the intervention and comparator particularly for over diagnosed cases. As stated in Section 3.3, the distribution of over diagnosed cases across the GGGs is not explored. The mapping of an over diagnosed case should result in a lower cancer stage, due to the assumption that the cancer diagnosed would not cause harm over the person's lifetime. This evident lack of clarity impacts the assumption regarding the progression of GGG, as it is unknown how the link between GGG and cancer stage was made. Additional clarification is required regarding how GGG was mapped to the cancer stages. The difference in mapping between the comparator and intervention arm should be clearly outlined, with particular emphasis on the assignment of GGG scores to those classed as over diagnosed.

Furthermore, the progression time of undiagnosed cancer was sampled from a Weibull distribution, with the assumption of perfect correlation. In turn, meaning that those who progress rapidly through stages 1 and 2, would do the same for remaining cancer stages, and vice versa if initial progression was slow. Clinical opinion was mixed on this. Some experts considered this a fair assumption, and that progression was relatively linear. However, other experts suggested that progression may become faster, particularly as people move into more advanced stages. Further scenario analysis surrounding this is likely to be useful.

Recommendations for updates

We recommend that SCHARR provides clarification regarding how GGG was mapped to the cancer stages. We also recommend that SCHARR provides clarification on the difference in mapping between the comparator and intervention arm, with particular emphasis on the distribution of GGG scores for those classed as over diagnosed.

3.6.3 Application of discounting

There is a lack of clarity within the report regarding the application of discounting in the model. The report states that discounting is applied from (a) *"the cycle of the youngest age across all interventions"*, and (b) *"the cycle in which each intervention began"*. It is unclear whether this means that discounting is applied at two different points in the model at the same time or if a combination of methods has been used. The report also states that discounting was applied *"from the first cycle of the intervention for both the intervention and comparator arms"*, which adds further uncertainty. At present we understand this to mean that discounting occurs at two separate time points in the intervention and comparator arms, which is incorrect. If modelled appropriately, people may be undergoing their first diagnostic tests at different time points in the intervention and comparator arms, for each simulated patient. This reflects the variation in practice that will be introduced from a formal screening strategy. Therefore, it is recommended that further clarity is provided, if the above is misinterpreted. Alternatively, if the above is true,

discounting must be applied from the same cycle equally in the comparator and intervention arms.

Recommendations for updates

We recommend that SCHARR provides clarification on the application of discounting in the model.

3.6.4 Diagnostic pathway

The diagnostic pathway used in the model includes the use of mpMRI prior to biopsy. This was chosen based on the current NICE guidelines for prostate cancer diagnosis [51]. However, it was stated by numerous clinicians that there is an ongoing transition to the use of bpMRI within the healthcare system. Evidence suggests that bpMRI is as equally effective as mpMRI [62], as well as increasing efficiency [63].

This accelerated imaging time will reduce the diagnostic costs associated with prostate cancer screening but has also been shown to potentially have a higher specificity [2, 64]. Additionally, multiple clinicians noted that bpMRI would be easy to implement into the diagnostic pathway for prostate cancer. As a result, it is recommended that a scenario is run where a proportion of patients receive bpMRI prior to biopsy as well as a scenario where all patients receive a bpMRI. This will enable a better understanding of what the impact on the model results will be from switching the cohort to have a bpMRI.

Discussion with clinicians has outlined that the introduction with bpMRI is likely to substantially improve specificity. Previous evidence suggests that the use of strict PI-RADS 4/5 cutoffs with bpMRI enables much higher specificity, thereby preventing the diagnosis of indolent cancers. The specificity value of 0.45 used in the model currently is extrapolated from routine urological outpatient settings (PI-RADS 3-5), where diagnostic priorities differ from those in population screening. Therefore, this underlying specificity does not represent a screened population. As a result, the patient flow through screening is likely to be substantially different, with a much lower number of false negatives than currently estimated. Further, previous studies suggest that bpMRI is likely to have much higher specificity, but with minimal change to sensitivity [65].

Recommendations for updates

We recommend that SCHARR alters the base case so that men receive bpMRI rather than mpMRI.

4 Scenario Results

As part of this critique, we requested that scenarios were run by SCHARR (see Appendix B). The results of these scenarios have been provided (see Appendix C). There were 4 scenarios run for both the Black ethnicity and familial history subgroups in an additive manner (e.g. scenario 1; scenario 1 and 2; scenario 1,2, and 3; and finally, all 4 scenarios together).

One final scenario was run to see the impact of all 4 scenarios together on the general population to make a total of 9 scenarios. Following the discussion with SCHARR (see Appendix B for further details) the scenarios applied were as follows:

- **Scenario 1:** The cost of biopsy for the screening arm has been decreased to model a scenario where all biopsies are performed as outpatient procedures.
- **Scenario 2:** The cost, specificity and sensitivity of MRI in the screening arm have been updated to model the use of bpMRI rather than mpMRI.
- **Scenario 3:** The weighting of the SACT costs was altered across both arms to reflect a greater proportion of people receiving them, reflected in an increased weighted cost.
- **Scenario 4:** The SACT costs in both arms have been assumed to continue, remaining constant until death for those who were not discontinued by the end of the third year.

Before running these scenarios, additional changes were made by SCHARR to the model base case and any interpretation of the scenario results assumes these changes were also applied (see the “Summary of changes” document in Appendix C for an overview of the adaptations to the model base case).

It is important to note that the scenarios conducted were likely to be crude, given the time limitations associated with running scenarios. Therefore, the aim of the scenarios was to understand the sensitivity of the results to underlying assumptions and data points in the model. We acknowledge the uncertainty of these results because of the crude changes, and we do not advocate that these scenarios should represent the new base case. The scenarios also only cover a limited number of concerns raised in this report.

4.1 Black Ethnicity

All screening strategies with multiple screenings become more likely to be cost-effective when all recommended scenarios were applied, when compared with the new base case. Screening every 4 years, 3 years, and yearly between 55 and 60 years of age has an incremental cost-effectiveness ratio (ICER) substantially below the £20,000 per QALY threshold (all less than £9,000 per QALY). Additionally, all single age screening scenarios, except from screening at 45, 65, and 68, may be cost-effective at a £20,000 threshold, with screening at age 58 having an estimated ICER of £951 when all scenarios were applied.

4.2 Family History

All screening strategies with multiple screenings become more likely to be cost-effective when all recommended scenarios are run, when compared with the new base case. All screening strategies with multiple screenings become more likely to be cost-effective at a £20,000 per

QALY threshold. The greatest ICER reduction evident for annual screening between 55 and 62 years of age, with new ICERs ranging between £11,709 per QALY and £15,126 per QALY. Also, single age screening populations for ages 50, 55, 58, 60 and 62 were estimated to be cost effective at a £20,000 per QALY threshold.

4.3 General Population

The incremental results from the new base case with the additional requested scenarios estimated that a single screening scenario for ages 55 or 60 would be cost effective under the £20,000 per QALY cost-effectiveness threshold with an ICER of £12,800 and £19,800 per QALY respectively. In addition, considering a £25,000 per QALY threshold, in line with the updated NICE cost-effectiveness threshold recommendations, the testing every 5 years between 50 and 60, testing every 3 years between 55 and 61, and single screening at age 58 are all cost-effective. The scenarios were not applied incrementally for the general population. However, the results of the combined scenarios indicate that further exploration would be useful to explore the cost-effectiveness of specific screening methods for all men.

4.4 Scenario Impact

Overall, the scenario analysis results suggest that scenario 4 had the greatest impact on the results when compared to the other scenarios. Scenario 4 resulted in the largest ICER reductions, leading to more screening populations being more likely to be cost effective at a £20,000 threshold. It is important to note that this scenario is likely to overestimate SACTs costs, given it may not adequately reflect discontinuation after year 3. However, given that SACT costs were underestimated in the base model, understanding the potential impact, highlights the importance of accurately predicting these long-term treatment costs. This is because a substantial proportion of people with stage 4 disease will still be on SACT, as discussed in Section 3.5.2.1.

When considering the incremental impact of each scenario we see that for both the familial history and Black ethnicity subgroups, the most impactful incremental effect was between the base case and the introduction of scenario 1. The introduction of a screening programme alongside guidance to perform transperineal biopsies as outpatient procedures may change the picture of for both subgroups for specific screening methods, regardless of any other concerns raised with respect to the model.

We acknowledge the limitations of the scenarios discussed. For instance, scenarios 1 and 2 were based on clinical advice surrounding adaptations to the current testing process that could be plausibly implemented with the introduction of a screening programme. These do not necessarily reflect current practice, and it is likely that the adherence to this guidance would not be 100%. Additionally, due to structural constraints, the application of scenarios 3 and 4 is uncertain (see Appendix C). It is also important to note the results from the scenarios do not cover the uncertainty from a probabilistic sensitivity analysis. However, we believe the results suggests that further modelling should be conducted to address the concerns raised within this report, given it could change the direction of the economic results.

5 Discussion

Our review identified a range of concerns regarding both the modelling choices and reporting of the SCHARR model. This discussion focuses on the points raised and the recommended updates that are anticipated to have the greatest impact on the model outcomes and subsequent decision making. Additional concerns are detailed in Appendix A.

A key concern identified throughout the report is that the model does not capture a system where the introduction of organised screening for prostate cancer reduces opportunistic screening or negates the need for it entirely. It is unrealistic that the scale of opportunistic PSA testing would remain constant with the addition of organised testing, which has a knock-on effect on the model results. The current model structure fails to accurately capture the potential variability in changes to the clinical pathway when organised screening is implemented. Therefore, it is difficult to apply the results of the model to the real world. It is necessary to update the intervention and comparator definitions in the model to adequately reflect what would occur in practice to provide valid results.

Another concern is the direction of bias in the assumptions made. It is reported throughout that assumptions are mostly conservative with respect to screening and, as a result, are likely to be biased against the introduction of organised screening. This includes (but is not limited to) assumptions surrounding opportunistic screening, the definition of overdiagnosis, application of treatment costs and definitions of family history. These assumptions are particularly important for subgroup results for populations with family history and Black men, given the estimated results are close to the cost-effectiveness threshold. Adjustments in these assumptions could lead to the results changing direction, and organised screening within these subpopulations becoming cost-effective.

The conservative nature of the modelling approach is also reflected in the phrasing of discussion throughout the report, with a primary focus on the harms of overdiagnosis. We believe it is important to make sure that balance is given to the discussion, so that potential biases are appropriately described, including their direction. We acknowledge that assumptions are unavoidable in a modelling process and best practice, and often the more conservative assumption is taken in the base case. However, due to the large number of assumptions necessary in this model, the cumulative effect is likely to be underestimating the potential value of organised screening, and the impacts of relaxing these assumptions are not appropriately explored. As a result, we recommend further exploration of the impact of these assumptions, utilising clinical feedback to inform plausible parameter values in the absence of appropriate evidence. This will help provide a report which better acknowledges the uncertainties, to support NSC in making a more informed decision.

Furthermore, treatment and diagnostic costs are not reflective of current practice. For instance, recent innovation concerning the use of SACTs for late-stage cancers are anticipated to have a substantial effect on overall treatment costs. SACTs are associated with a high cost and are currently recommended for the remainder of the person's lifespan, which is not reflected in the current model. SACTs are also expected to increase life expectancy, essentially increasing the costs associated with stage 4 disease, but may also reflect lower than expected improvements in survival from screening. SACT costs are also not applied to earlier stages, which will bias the results in two ways. It will bias in favour of screening, for those diagnosed earlier than stage 4

because of organised screening but would otherwise be diagnosed at stage 4, given a stage 2 diagnosis in the model does not capture any future SACTs being used. However, it will also bias against screening, given some people will be diagnosed at stage 1 instead of 2 or 3 because of organised screening, and the earlier diagnosis means they are less likely to ever need SACTs.

Another key concern highlighted within our review is in relation to the way in which GGG was mapped to cancer stages. There is a lack of clarity provided for the calculation, how this differed for over-diagnosed cases, and how it differed between the intervention and comparator arms of the model. The current approach is likely to increase treatment costs due to the distribution across GGG between diagnosed and over diagnosed cases. We recommend that further clarity on the method used to map GGG to cancer stage be added to the report. It would also be beneficial to perform scenario analysis to explore the impact of structural uncertainty introduced here, concerning the treatment costs, by reweighting treatment distribution by GGG for cases identified through screening and the subsequent mapping and impact on cancer stages.

The definition and modelling of the family history high-risk subgroup is an area that will benefit from further exploration. Feedback from clinicians consistently emphasised the importance of additional exploration of this risk factor. The application of an equal hazard regardless of the number of relatives with cancer, type of cancer, age of diagnosis for the relative, and cancer stage for diagnosed relative was deemed to be insufficient and over-generalised. As stated in previous sections, previous published evidence has stratified this risk further, and it is likely that the current definition of family history is not fit for purpose. For example, the relative risk of prostate cancer for someone with multiple close family members diagnosed with aggressive prostate cancer at a young age is much higher than for someone with one family member diagnosed with low-grade ovarian or even prostate cancer at an older age. It is therefore important to consider if family history could be narrowed down, to understand if screening is cost-effective in specific populations with familial history, rather than considering family history as one collective group.

Finally, the methods used to identify and estimate the associated impact of over diagnosed cases are not made clear in the report. The provided definition does not appear to align with the application to the model. Additionally, the omission of a results breakdown increases the difficulty with determining whether this has been consistently applied to both arms and the extent of the impact this has on incremental results. The definition of the intervention including organised screening as completely additive to current practice also contributes to the overestimation of the incremental impact of overdiagnosis. Therefore, we recommend that the definition of overdiagnosis be clearly defined and the method of application be adjusted to reflect this. We also recommend scenario analysis to explore the uncertainty surrounding the distribution of GGG and the associated treatment costs, as well as the impact on the incremental effect if the intervention definition is altered to reflect an adjustment to current opportunistic screening with the introduction of an organised screening programme.

The scenario analysis to explore the potential impact of assumptions made as part of the modelling approach also highlighted the sensitivity of the results to these assumptions, particularly in sub populations where the risk of prostate cancer is higher. Therefore, it is

important to consider the potential concerns raised in this report, to reflect a more robust analysis of prostate cancer screening in the UK.

The concerns raised throughout this report are important to be considered by the NSC, as well as how they may impact the cost-effectiveness results. The concerns raised are also likely to have much more impact on the specific at-risk populations. This is because for those with family history and Black men, the cost-effectiveness results were uncertain, close to the cost-effectiveness threshold, and were sensitive to changing assumptions and data. We believe the recommendations throughout this report should be taken forward into future analysis, to provide the most robust evidence to inform evidence-based policy surrounding prostate cancer screening.

5.1 Limitations

This critique provides a comprehensive overview of the main concerns identified. However, there were also limitations to the critique.

A key limitation of this critique was the lack of access to SCHARR's executable model, on which the report and recommendations were formed. Not having access to the model hindered the validation process of key structural and parameter choices, which would have been easier to understand with access to the model. The lack of reporting clarity led to calculations, such as the mapping of GGGs to cancer stage, being unclear, and therefore difficult to interpret and validate. It was also difficult to determine the key drivers of the model with uncertainty surrounding the resources, costs, and utilities assigned to each model arm. Therefore, all recommendations in this critique are based solely on the technical report and may not be applicable in instances where the SCHARR report incorrectly reflects the methods used in the model. We assumed that there are no programming errors in the model calculations. We were unable to verify the calculations made so any suggested amendments assume that all methods outlined in the report were correctly applied.

Additionally, this critique did not include an exhaustive literature search. Instead, pragmatic literature searches were conducted, targeting areas where the report stated a paucity of available evidence. Therefore, we acknowledge that more suitable data may be available to inform certain parameters that we did not capture within our targeted searches. However, to mitigate this potential omission of evidence, we consulted an extensive range of clinical experts to assist with the process so that the most recent and appropriate known evidence was considered.

As discussed in Section 4.4, we also acknowledge the limitations of the crude scenarios conducted to explore the potential impact of certain assumptions on the model. We believe more comprehensive updates should be made to the model, to more accurately reflect the concerns in this report. As a result, we also believe the results presented in scenario analysis should not present the new base case for the economic analysis.

6 Conclusion

We acknowledge the important work that the NSC conducts on screening recommendations, and the work of SCHAAR in modelling a complex screening intervention. We also recognise the challenges faced by analysts in providing robust analysis to inform evidence-based policy. Initiating screening involves a complex array of factors that must be quantified in the analysis and, as such, assumptions are necessary to estimate the impact. Whilst we do not expect the economic analysis to be able to capture every possible complexity, a transparent description of the analysis, including a thorough discussion of uncertainty and the challenges encountered is required.

We also believe that there are a range of concerns surrounding the economic analysis that can be updated, beyond a more detailed and thorough write up of the analysis. Some of these changes are simple amendments to make, while others are more complex and will be more time consuming. However, the concerns are all important considerations, particularly for at-risk subgroups, where the cost-effectiveness estimates are relatively close to the threshold. We recommend that the updates listed throughout this document are implemented, to provide a more robust economic analysis to inform the NSC's decision on prostate cancer screening.

7 References

1. Sheffield Uo. Estimating EQ-5D by age and sex for the UK. Available from: <https://sheffield.ac.uk/nice-dsu/methods-development/estimating-eq-5d>.
2. Bass E J PA, Connor M, Gabe R, Padhani A R, Rockall A, Sokhi H, Tam H, Winkler M, Ahmed H U. . A systematic review and meta-analysis of the diagnostic accuracy of biparametric prostate MRI for prostate cancer in men at risk. *Prostate Cancer and Prostatic Diseases*. 2021.24(3):596–611. doi: 10.1038/s41391-020-00298-w
3. London IC. Trial of Randomised Approaches for National Screening FOR Men (TRANSFORM). Identifier: ISRCTN13801649. In: Health Research Authority (HRA) & Research Ethics Committee (REC) [internet]. London: 2025. [cited 5 February 2026] Available from <https://www.isrctn.com/ISRCTN13801649>.
4. Cancer Research UK. Prostate cancer statistics. 2025. Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer>.
5. Dodkins J, Cook A, Mayne E, Parry M, Parry MG, Boyle J, *et al*. Are evidence-based guidelines translating into clinical practice? A national population-based study of the use of treatment intensification in metastatic hormone-sensitive prostate cancer (mHSPC) in England. *European journal of cancer (Oxford, England : 1990)*. 2025.220:115335. doi: 10.1016/j.ejca.2025.115335
6. National Cancer Audit Collaborating Centre. National Prostate Cancer Audit (NPCA) State of the Nation Report. London: October 2025. Available from: <https://www.natcan.org.uk/wp-content/uploads/2025/10/NPCA-SotN-2025.pdf>.
7. Prostate Cancer UK. It's a fact: prostate cancer now the most common cancer in the UK. 2026. Available from: <https://prostatecanceruk.org/about-us/news-and-views/2026/01/prostate-most-common-cancer>.
8. Dodkins J, Cook A, Mayne E, Parry M, Nossiter J, Payne H, *et al*. Geographic, socioeconomic and demographic inequalities in the incidence of metastatic prostate cancer at time of diagnosis in England: a population-based evaluation. *BMJ Oncology*. 2025.4(1):e000643. doi: 10.1136/bmjonc-2024-000643
9. NHS England. Cancer Survival in England, cancers diagnosed 2016 to 2020, followed up to 2021. NHS Digital 2023. [cited 6th February 2026]. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/cancer-survival-in-england/cancers-diagnosed-2016-to-2020-followed-up-to-2021>.
10. Wise J. Prostate cancer: Routine NHS screening is rejected by UK expert committee. *BMJ*. 2025.391:r2524. doi: 10.1136/bmj.r2524
11. Harris M. UK NSC opens consultation on draft prostate cancer screening recommendation. UK National Screening Committee (NSC); 2025. Last updated 28 November. [cited 22 December 2025]. Available from: <https://nationalscreening.blog.gov.uk/2025/11/28/uk-nsc-opens-consultation-on-draft-prostate-cancer-screening-recommendation/>.
12. National Institute for Health and Care Excellence. Suspected cancer: recognition and referral. 2015. Available from: <https://www.nice.org.uk/guidance/ng12/resources/suspected-cancer-recognition-and-referral-pdf-1837268071621>.
13. Harding TA MR, Merriel SW, Jones R, O'Sullivan JM, Kirby M, Olajide O, Norman A, Bhatt J, Hulson O, Martins T. Optimising the use of the prostate-specific antigen blood

- test in asymptomatic men for early prostate cancer detection in primary care: report from a UK clinical consensus. *British Journal of General Practice*. 2024.74(745)
14. Mishra SC. A discussion on controversies and ethical dilemmas in prostate cancer screening. *Journal of Medical Ethics*. 2021.47(3):152–58. doi: 10.1136/medethics-2019-105979
 15. Ilic D, Djulbegovic M, Jung JH, Hwang EC, Zhou Q, Cleves A, *et al*. Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. *BMJ*. 2018.362:k3519. doi: 10.1136/bmj.k3519
 16. European Council of the European Union. Council updates its recommendation to screen for cancer. 2022. Available from: <https://www.consilium.europa.eu/en/press/press-releases/2022/12/09/council-updates-its-recommendation-to-screen-for-cancer/>.
 17. SCHARR (Sheffield Centre for Health and Related Research). Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk. 17 November 2025. Available from: https://nationalscreening.blog.gov.uk/wp-content/uploads/sites/254/2025/11/SCHARR-Report-Phase-3-Prostate-Cancer-Modelling_FINAL.pdf.
 18. HM Treasury. The Magenta Book. 2011. Available from: <https://www.gov.uk/government/publications/the-magenta-book>.
 19. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, *et al*. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research*. 2022.25(1):3–9. doi: 10.1016/j.jval.2021.11.1351
 20. Macdonald G LN, Hanratty J, *et al*. The effectiveness, acceptability and cost-effectiveness of psychosocial interventions for maltreated children and adolescents: an evidence synthesis. *Health Technology Assessment*. 2016.20(69)
 21. UK Government. The AQuA Book. UK Government. 2015. Available from: <https://www.gov.uk/guidance/the-aqua-book>
 22. HM Treasury. Review of quality assurance of Government analytical models. March 2013 2013. Available from: https://assets.publishing.service.gov.uk/media/5a7c7363e5274a5590059f36/review_of_q_a_of_govt_analytical_models_final_report_040313.pdf.
 23. Drummond MF SM, Claxton K, Stoddart GL, Torrance GW. *Methods for the economic evaluation of health care programmes*; 2015.
 24. Ahmed HU, El-Shater Bosaily A, Brown LC, Gabe R, Kaplan R, Parmar MK, *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):815–22. doi: 10.1016/s0140-6736(16)32401-1
 25. Hugosson J, Månsson M, Wallström J, Axcróna U, Carlsson SV, Egevad L, *et al*. Prostate Cancer Screening with PSA and MRI Followed by Targeted Biopsy Only. *New England Journal of Medicine*. 2022.387(23):2126–37. doi: doi:10.1056/NEJMoa2209454
 26. Vickers AJ, Brentnall A. Effect of implementing population-based prostate-specific antigen screening on testing rates and prostate cancer overdiagnosis in England: a statistical modelling study. *medRxiv*. 2026.2026.01.23.26344710. doi: 10.64898/2026.01.23.26344710
 27. Merriel SW, Akter N, Zakkak N, Swann R, McPhail S, Rubin G, *et al*. Factors affecting prostate cancer detection through asymptomatic prostate-specific antigen testing in

- primary care in England: evidence from the 2018 National Cancer Diagnosis Audit. *British Journal of General Practice*. 2025.75(754):e300–e05. doi: 10.3399/bjgp.2024.0376
28. Collins KK, Oke JL, Virdee PS, Perera R, Nicholson BD. Prostate specific antigen retesting intervals and trends in England: population based cohort study. *BMJ*. 2025.391:e083800. doi: 10.1136/bmj-2024-083800
 29. UK National Screening Committee. Bowel Cancer - UK Screening Recommendations. Available from: <https://view-health-screening-recommendations.service.gov.uk/bowel-cancer/>.
 30. Pohl K, Newton L, Anderson R, Taylor C, Randle A, Filby A, *et al*. Evaluating the impact of faecal immunochemical testing (FIT) on suspected colorectal cancer referrals and outcomes in the South West. *Frontline Gastroenterology*. 2026.17(2):111–18. doi: 10.1136/flgastro-2024-102958
 31. Vynckier P, Annemans L, Raes S, Amrouch C, Lindgren P, Májek O, *et al*. Systematic Review on the Cost Effectiveness of Prostate Cancer Screening in Europe. *European Urology*. 2024.86(5):400–08. doi: <https://doi.org/10.1016/j.eururo.2024.04.036>
 32. Patasius A, Krilaviciute A, Smailyte G. Prostate Cancer Screening with PSA: Ten Years' Experience of Population Based Early Prostate Cancer Detection Programme in Lithuania. *Journal of clinical medicine*. 2020.9(12)doi: 10.3390/jcm9123826
 33. Langley S, Uribe-Lewis S, Uribe J, Van Poppel H, Goad J, Bell S, *et al*. Targeted Prostate Health Checks, a Novel Screening System to Identify Men at Risk of Prostate Cancer: Real-world Evidence from More than 18 000 Prostate-specific Antigen Tests. *European Urology Oncology*. 2025.doi: <https://doi.org/10.1016/j.euo.2025.10.007>
 34. Wills L, Nagarwalla D, Pearson C, McPhail S, Hinchliffe R, Sharpless B, *et al*. Estimating surgery, radiotherapy and systemic anti-cancer therapy treatment costs for cancer patients by stage at diagnosis. *The European journal of health economics : HEPAC : health economics in prevention and care*. 2024.25(5):763–74. doi: 10.1007/s10198-023-01623-5
 35. Brodersen J, Schwartz LM, Heneghan C, O'Sullivan JW, Aronson JK, Woloshin S. Overdiagnosis: what it is and what it isn't. *BMJ Evidence-Based Medicine*. 2018.23(1):1–3. doi: 10.1136/ebmed-2017-110886
 36. Carter S, Barratt A. What is overdiagnosis and why should we take it seriously in cancer screening? *Public Health Research & Practice*. 2017.27(3)doi: 10.17061/phrp2731722
 37. Kilpeläinen TP, Tammela TLJ, Roobol M, Hugosson J, Ciatto S, Nelen V, *et al*. False-positive screening results in the European randomized study of screening for prostate cancer. *European Journal of Cancer*. 2011.47(18):2698–705. doi: <https://doi.org/10.1016/j.ejca.2011.06.055>
 38. Ben-Shlomo Y, Evans S, Ibrahim F, Patel B, Anson K, Chinegwundoh F, *et al*. The Risk of Prostate Cancer amongst Black Men in the United Kingdom: The PROCESS Cohort Study. *European Urology*. 2008.53(1):99–105. doi: <https://doi.org/10.1016/j.eururo.2007.02.047>
 39. Lillard JW, Jr., Moses KA, Mahal BA, George DJ. Racial disparities in Black men with prostate cancer: A literature review. *Cancer*. 2022.128(21):3787–95. doi: 10.1002/cncr.34433
 40. UK National Screening Committee. UK National Screening Committee: screening in healthcare. GOV.UK; 2022. Last updated 11 July 2025. [cited 17 February 2026]. Available from: [https://www.gov.uk/guidance/principles-of-population-screening/inequalities#:~:text=Equality%20impact%20assessments%20\(%20EIAs%20\)%20should,to%20mitigate%20against%20health%20inequalities](https://www.gov.uk/guidance/principles-of-population-screening/inequalities#:~:text=Equality%20impact%20assessments%20(%20EIAs%20)%20should,to%20mitigate%20against%20health%20inequalities).

41. NHS. Fit for the Future: The 10 Year Health Plan for England. Government U; July 2025. Available from: <https://assets.publishing.service.gov.uk/media/6888a0b1a11f859994409147/fit-for-the-future-10-year-health-plan-for-england.pdf>.
42. NHS England. Core20PLUS5 Framework. NHS England; 2021. Last updated 2025. [cited 28 January 2026]. Available from: <https://www.england.nhs.uk/about/equality/equality-hub/national-healthcare-inequalities-improvement-programme/core20plus5/>.
43. Williams CD, Bullard AJ, O'Leary M, Thomas R, Redding TSt, Goldstein K. Racial/Ethnic Disparities in BRCA Counseling and Testing: a Narrative Review. *Journal of racial and ethnic health disparities*. 2019.6(3):570–83. doi: 10.1007/s40615-018-00556-7
44. Martin AP, Downing J, Collins B, Godman B, Alfirovic A, Greenhalgh KL, *et al*. Examining the uptake of predictive BRCA testing in the UK; findings and implications. *European journal of human genetics : EJHG*. 2021.29(4):699–708. doi: 10.1038/s41431-020-00783-9
45. National Institute for Health and Care Excellence. NICE health technology evaluations: the manual. 2022. Available from: <https://www.nice.org.uk/process/pmg36/resources/nice-health-technology-evaluations-the-manual-pdf-72286779244741>.
46. HM Treasury. The Green Book. 2022. Available from: <https://www.gov.uk/government/publications/the-green-book-appraisal-and-evaluation-in-central-government/the-green-book-2020>.
47. Martin RM, Turner EL, Young GJ, Metcalfe C, Walsh EI, Lane JA, *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):1460–70. doi: 10.1001/jama.2024.4011
48. Hugosson J, Roobol MJ, Månsson M, Tammela TLJ, Zappa M, Nelen V, *et al*. A 16-yr Follow-up of the European Randomized study of Screening for Prostate Cancer. *Eur Urol*. 2019.76(1):43–51. doi: 10.1016/j.eururo.2019.02.009
49. Hamdy FC, Donovan JL, Lane JA, Metcalfe C, Davis M, Turner EL, *et al*. Fifteen-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer. *The New England journal of medicine*. 2023.388(17):1547–58. doi: 10.1056/NEJMoa2214122
50. National Institute for Health and Care Excellence. Cost Comparison Appraisal - Abiraterone (originator and generics) for treating newly diagnosed high-risk hormone sensitive metastatic prostate cancer (review of TA721) [ID6378] Committee Papers. Available from: <https://www.nice.org.uk/guidance/ta1110>.
51. National Institute for Health and Care Excellence. Prostate cancer: diagnosis and management (NG131). 2021. Available from: <https://www.nice.org.uk/guidance/ng131/resources/prostate-cancer-diagnosis-and-management-pdf-66141714312133>.
52. National Institute for Health and Care Excellence. Resource impact report: Transperineal biopsy for diagnosing prostate cancer (HTG680). 2023. Available from: <https://www.nice.org.uk/guidance/htg680/resources/resource-impact-report-pdf-13069193149>.
53. Gaska I CA, Pajewska M, Partyka O, Deptała A, Badowska-Kozakiewicz A, Czerw N, Mękal D, Sygit K, Wojtyła-Blicharska K, Drobnik J. Direct and Indirect Costs of Prostate Cancer: A Comprehensive Assessment of Economic and Social Impact. *Cancers*. 2025.17(19):3257.
54. Krahn MD ZB, Laporte A, Alibhai SM, Bremner KE, Tomlinson G, Warde P, Naglie G. . Healthcare costs associated with prostate cancer: estimates from a population-based

- study. *BJU International*. 2010.105(3):338–46. doi: <https://doi.org/10.1111/j.1464-410x.2009.08758.x>
55. Smith-Palmer J TC, Valentine W. . Literature review of the burden of prostate cancer in Germany, France, the United Kingdom and Canada. *BMC Urology*. 2019.19(1)doi: <https://doi.org/10.1186/s12894-019-0448-6>
 56. National Institute for Health and Care Excellence (NICE). Prostate cancer: diagnosis and management. NICE; 2019. Last updated 15 December 2021. [cited 29 January 2026]. Available from: <https://www.nice.org.uk/guidance/ng131>.
 57. BAUS. Transperineal Ultrasound-Guided Biopsies of the Prostate Gland. In: The British Association of Urological Surgeons Limited; 2024
 58. Prostate Cancer UK. Policy Position – Transperineal Biopsy of the Prostate. 2019. [cited 6th February 2026]. Available from: <https://prostatecanceruk.org/media/zmmc2xvr/statement-tp-biopsy-2019.pdf>.
 59. National Institute for Health and Care Excellence. Transperineal biopsy for diagnosing prostate cancer. 2022. [cited 6th February 2026]. Available from: <https://www.nice.org.uk/consultations/1235/1/the-diagnostic-tests>.
 60. Nyberg T TM, Antoniou A C. BRCA1 and BRCA2 pathogenic variants and prostate cancer risk: systematic review and meta-analysis. *British Journal of Cancer*. 2021.126:1067–81.
 61. Bratt O DL, Akre O, Garmo H, Stattin P. Family History and Probability of Prostate Cancer, Differentiated by Risk Category: A Nationwide Population-Based Study. *JNCI: Journal of the National Cancer Institute*. 2016.108(10)doi: <https://doi.org/10.1093/jnci/djw110>
 62. Ng A AA, Agarwal A, Panebianco V, et al. . Biparametric vs Multiparametric MRI for Prostate Cancer Diagnosis: The PRIME Diagnostic Clinical Trial. *JAMA*. 2025.334(13):1170–79. doi: 10.1001/jama.2025.27266
 63. Steinkohl F PR, Junker D. Short review of biparametric prostate MRI. *Magazine of European Medical Oncology*. 2018.11(4):309–12. doi: <https://doi.org/10.1007/s12254-018-0458-1>
 64. Strieder de Oliveira G, Altmayer S, Torri GB, Prediger JE, Abreu-Gomez J, Ghai S, et al. Diagnostic Performance of Biparametric versus Multiparametric Magnetic Resonance Imaging for Prostate Cancer Diagnosis: An Updated Systematic Review and Meta-analysis. *European Urology*. 2026.doi: <https://doi.org/10.1016/j.eururo.2026.01.030>
 65. Twilt T J SA, Bosma J S, Ginneken B V, Bjartell A, Padhani A R, Bonekamp D, Villeirs G, Salomon G, Giannarini G, Kalpathy-Cramer J, Barentsz J, Maier-Hein K H, Rusu M, Rouviere O, van den Bergh R, Panebianco V, Kasivisvanathan V, Obuchowski N A, Yakar D, Elschot M, Veltman J, Futterer J J, Huisman H, de Rooij M, PI-CAI Consortium. Evaluating Biparametric Versus Multiparametric Magnetic Resonance Imaging for Diagnosing Clinically Significant Prostate Cancer: An International, Paired, Noninferiority, Confirmatory Observer Study. *European Urology*. 2025.87(2):240–50. doi: 10.1016/j.eururo.2024.09.035
 66. Aus G DJ-E, Khatami A, Lilja H, Stranne J, Hugosson J. Individualized Screening Interval for Prostate Cancer Based on Prostate-Specific Antigen Level: Results of a Prospective, Randomized, Population-Based Study. *Archives of Internal Medicine*. 2005.165(16):1857–61. doi: <https://doi.org/10.1001/archinte.165.16.1857>
 67. Bratt O GRA, Jiborn T, Wallstrom J, Akre O, Carlsson S, Nordstrom T, Thimansson E, Alterbeck M, Zackrisson S, Hugosson J, Bjartell A, Lantz A. . Population-based Organised Prostate Cancer Testing: Results from the First Invitation of 50-year-old Men. *European Urology*. 2024.85(3):207–14. doi: <https://doi.org/10.1016/j.eururo.2023.11.013>

68. Bul M vLPJ, Zhu X, Schroder F H, Roobol M J. . Prostate Cancer Incidence and Disease-Specific Survival of Men with Initial Prostate-Specific Antigen Less Than 3.0 ng/ml Who Are Participating in ERSPC Rotterdam. *European Urology*. 2011.59(4):498–505. doi: doi.org/10.1016/j.eururo.2011.01.001
69. Randazzo M BJ, Huber A, Grobholz R, Manka L, Chun F K, Kluth L A, Wyler S F, Recker F, Kwiatkowski M. . Is further screening of men with baseline PSA < 1 ng ml–1 worthwhile? The discussion continues—Results of the Swiss ERSPC (Aarau). *International Journal of Cancer*. 2015.137(3):553–59. doi: doi.org/10.1002/ijc.29420Digital Object Identifier (DOI)
70. Remmers S BCH, Godtman R A, Carlsson S V, Auvinen A, Tammela T L J, Denis L J, Nelen V, Villers A, Rebillard X, Kwiatkowski M, Recker F, Wyler S, Zappa M, Puliti D, Gorini G, Paez A, Lujan M, Nieboer D, Schroder F H, Roobol M J. Relationship Between Baseline Prostate-specific Antigen on Cancer Detection and Prostate Cancer Death: Long-term Follow-up from the European Randomized Study of Screening for Prostate Cancer. *European Urology*. 2023.84(5):503–09. doi: doi.org/10.1016/j.eururo.2023.03.031
71. Wu G H-M AA, Yen A M-F, Hakama M, Tammela T L, Stenman U-H, Kujala P, Ruutu M, Chen H-H. . The Impact of Interscreening Interval and Age on Prostate Cancer Screening With Prostate-Specific Antigen. *European Urology*. 2012.61(5):1011–18. doi: doi.org/10.1016/j.eururo.2012.01.008
72. Zhu X APC, Andriole G L, Roobol M J, Schroder F H, Vickers A J. . Risk-Based Prostate Cancer Screening. *European Urology*. 2012.61(4):652–61. doi: doi.org/10.1016/j.eururo.2011.11.029
73. Pavlovich C. Prostate Cancer: Age-Specific Screening Guidelines. John Hopkins Medicine; [cited 30 January 2026]. Available from: <https://www.hopkinsmedicine.org/health/conditions-and-diseases/prostate-cancer/prostate-cancer-age-specific-screening-guidelines>.
74. de Carvalho T M HEAM, de Koning H J. . Comparative effectiveness of prostate cancer screening between the ages of 55 and 69 years followed by active surveillance. *Cancer*. 2018.124(3):507–13. doi: <https://doi.org/10.1002/cncr.31141>
75. Dusic EJ, Theorin T, Wang C, Swisher EM, Bowen DJ. Barriers, interventions, and recommendations: Improving the genetic testing landscape. *Frontiers in digital health*. 2022.4:961128. doi: 10.3389/fdgth.2022.961128

Appendix A: Other Critique Considerations

Point of consideration	Page number	Interpretation of justification	YHEC evaluation of consideration	YHEC recommendation
The search strategy is not included in the report	23	No justification provided	It is important to consider the breadth of evidence that was considered as part of the review. If certain evidence was missed as part of the searches being more pragmatic, then it is important to reflect how this may impact the results. It is best practice, even for pragmatic reviews, to provide the search strategy, where possible. Providing a search strategy is common for other large technical reports, including NICE submissions. This allows transparency over the scope of evidence considered. From the searches provided to us, it is clear that important papers were not picked up in the pragmatic review. These papers are referenced throughout Section 3.	Provide an appendix where the search strategy is detailed. It is worth discussing the likelihood of missed evidence in the discussion sections of the report. Papers referenced throughout our report are not identified using SCHARRs search strategy.
The disutility scores for biopsies are applied for one week, but longest symptoms last for 5 days.	72	Generally applied conservatively to account for the fact that some people may have symptoms or impacts for longer.	The disutility scores for biopsy (although low) are likely an overestimate. They are also applied to lots of people, so this could have an significant impact. SCHARR assumes that a disutility of - 0.013 last for one week. However, they also state that (i) "the longest symptoms last for five days", (ii) people who received biopsies "more than recover", implying that their quality of life returns higher than before the biopsy. This might be a valid finding, in that the biopsy provides reassurance and relief from worry which is not reflected. They also state that many people do not have any symptoms.	Adjust the application of disutilities so they only apply for 5 days. If data are available, then SCAHRR should consider the benefit from quality of life improving due to receiving a test.
The source cited for the palliative care costs is incorrect.	79	SCHARR cites Diernberger et al, (2023)[63] in the text but reference 63 is a Diernberger et al, (2021) paper.	We believe the correct source is: Diernberger K, Luta X, Bowden J, Droney J, Lemmon E, Tramonti G, Shinkins B, Gray E, Marti J, Hall PS. Variation in hospital cost trajectories at the end of life by age, multimorbidity and cancer type. <i>Int J Popul Data Sci</i>. 2023 Jan 16;8(1):1768. doi: 10.23889/ijpds.v8i1.1768. PMID: 36721848; PMCID: PMC9871727.	Amend the reference list to cite the correct paper.
Screening strategies with multiple screening tests consider scenarios for risk adjustment. However, this is only reinventing those with a PSA result of 2.5ng/mL or 3ng/mL. There is a range of evidence that suggests people with	N/A	SCHARR explored a range of screening strategies. However, it is not clear if they considered the impact of low PSA test results on future testing within these scenarios.	It is unclear why only those under 3 ng/mL or 2.5ng/mL were selected for scenarios where they are not screened further. Previous evidence still indicates that the risk in these groups of developing prostate cancer is quite high. Therefore, strategies could be considered for those at much lower risk. Clinicians indicated that it would still be useful to test these people every five years, rather than no longer screening them at all.	Adjust the scenarios to only consider reducing follow up testing based on those at lowest risk, not just under 2.5ng/mL or 3ng/mL.

Point of consideration	Page number	Interpretation of justification	YHEC evaluation of consideration	YHEC recommendation
an initially low PSA test results are less likely to go on to develop prostate cancer (less than 1ng/mL) [66-72]				
SCHAAR's modelling generally focuses on screening strategies between age 50 and 60. However, clinical feedback, and evidence from other countries suggest the most effective screening happens between ages of 55-69 [73, 74].	N/A	It is not clear why SCHARR focused screening on ages 50-60.	It is unclear the rationale for many of the screening strategies considered looking at age 50-60. Given evidence from other countries, screening strategies at ages beyond 60 should also have been explored, to understand the impact on the results. For instance, it could be that screening those close to 50 is likely not efficient, or it could be that screening close to 70 is not efficient. However, it is difficult to comment given this was not fully explored.	Consider changing the screening strategies that capture age groups to reflect those used in other countries, based on previous evidence.
Concerns were raised by clinicians that active surveillance methods have changed since 2016-2018. Clinicians raised concerns that the guidelines are out of date, and the costings likely do not reflect current practice.	N/A	SCHARR has based their modelling on the most recent guidelines, and available data they identified.	We acknowledge the challenge of modelling a disease area where the care pathway is changing relatively quickly. However, it is also important that a wide range of clinical experts is consulted to inform modelling parameters and structure, which does not appear to be the case. For example, in the SCHARR report (page 22), an oncologist was not consulted as part of validating the model.	Seek further clinical engagement to discuss current practices in surveillance. This will help shape what can be costed as part of active surveillance costs. It is likely the Wills et al (2024) costs can be adjusted to better reflect current practice, based on clinical advice.
The specific device used for LATP was not specified in the report.	N/A	N/A	NICE guidance outlines the four recommended freehand needle positioning devices for LATP including: ▪ PrecisionPoint ▪ EZU-PA3U device ▪ Trinity Perine Grid ▪ UA1232 puncture attachment Each of these devices is associated with a different cost. These costs can be sourced from the NICE Resource impact report (HTG680) [52].	Consider the specific device used in practice to accurately cost the diagnostic pathway. If this is already accounted for in the average cost, then this should be made clear in the text
The report does not discuss the inequalities associated with knowing BRCA status.	N/A	No justification provided	Knowledge of the BRCA gene mutation requires genetic testing. Genetic services are vulnerable to accessibility barriers that prevent equitable access to services. These difficulties in access disproportionately affect those who are more socially vulnerable due to factors such as socioeconomic status and ethnicity. This is also reflected in a lack of resources and physical access to services [75]. This analysis does not model BRCA gene testing as it falls outside of the project scope. However, it should	The impact of these inequalities should be discussed within the report

Point of consideration	Page number	Interpretation of justification	YHEC evaluation of consideration	YHEC recommendation
			consider the impact of recommending screening for those with known BRCA status on the health equity gap.	

Appendix B: Model Scenario Requests

The document embedded below shows the model scenario requests made and the exchange between YHEC and SCHARR clarifying what would be run.



YHEC SCHARR Model
Scenarios - Response

Following discussion, the final responses for request 3 exchanged further via email were as follows:

YHEC response

We think this comes from trying to overcomplicate the scenario. We are not saying that people from earlier stages won't progress and require SACTs. However, it seems like you are weighing down those diagnosed directly at stage 4 (not a progression), to account for progression (we know you are not modelling this explicitly). This will then underestimate the SACT costs, because this is a one-year snapshot and we cannot entangle where exactly people come from in a snapshot. Specifically, from the data, given the definitions are not the clearest, you cannot necessarily untangle who was a progressed metastatic cancer, and who was a new metastatic cancer. The base assumption would be that it doesn't matter, and that 47% of people who progressed to stage 4 go on to get SACTs, and 47% who were diagnosed immediately at stage 4 get SACT, given there is no distinction between how you got to stage 4.

What we're saying is that 47% should be applied to those who are diagnosed at stage 4, and then those diagnosed at earlier stages the costs can be scaled to account for the fact that some people will progress to stage 4 from earlier stages. The complexity comes in because you are trying to line up progression on a 1-year snapshot of data. Stage 1,2,3 would be working out how many people we expect to progress to stage 4, and 47% of those people who progress will then receive SACT (47% multiplied by the proportion expected to progress to stage 4 in each stage) We know this second step is done implicitly rather than explicitly by weighting treatment costs.

We are not saying that it should be applied to only people diagnosed at stage 4. However, you developed the model around the datapoint that 28% of people received treatment in stage 4. We are saying this should be replaced with 47%, with 47% of people diagnosed at stage 4 receiving SACT, and if done before, working out roughly how many people would progress to stage 4 from earlier stages, and taking that 47% of those would receive SACT too. It was not clear in the original report that you adjusted earlier stages for SACT (based on the fact some people will progress), but it was clear you had used the datapoint of 28%. The assumption was

that the 28% was pivotal to weighting costs before, so we are suggesting replacing it with 47% and spreading this appropriately to capture metastatic disease

Reply from SCHARR

Following several discussions with the UK NSC, I would be grateful if you could confirm whether you agree with this approach for Scenarios 3 and 4, as a summary of all email exchanges, or suggest an alternative approach which is feasible to implement easily within the model structure? SENSS does not have capacity to look for data and recalculate proportion of patients annually progressing across the stages to calculate average weighted costs now, so if this is YHEC suggestion, could you please provide these calculations and references.

SENSS suggestion:

Stage 4 at diagnosis: Allocate SACT treatment costs to 46.88% of men.

Stage 1–3 at diagnosis: Allocate one year of stage 4–related costs to those patients who were diagnosed at stages 1–3 and progressed to stage 4 in the year of their death, under the assumption that progression to stage 4 occurred prior to mortality.

YHEC response

We're aware it is a difficult scenario to run quickly and will take longer to investigate more thoroughly. In that case we're happy to run the scenario suggested.

Appendix C: Scenario Results



final.zip

This zip file contains the information relating to the scenario analysis and updated base case.

Appendix D: Clinical and Expert Advisors

The below table details the 15 clinicians and expert advisors consulted for this critique.

Name	Occupation
Dr Simon Bott	Consultant Urologist, Frimley Park Hospital
Professor Ola Bratt	Professor of Clinical Cancer Epidemiology, University of Gothenburg and Chairman of the National Working Group for Organised Prostate Cancer Testing
Dr Kyle Bryan	Global Head, Oncology Center of Excellence & Chief Medical Officer, IQVIA Biotech
Professor Sigrid Carlsson	Division Head of the Clinical Epidemiology of Early Cancer Detection at DKFZ German Cancer Research Center
Mark Chapman	Former director of HealthTech, NICE
Professor Philip Cornford	Consultant Urologist Bon Secours Cork and Honorary Professor. Chair of EAU Prostate Cancer Guidelines
Professor Simon Crabb	Professor of Experimental Cancer Therapeutics, Southampton School of Cancer Sciences and Honorary Consultant in Medical Oncology, University Hospital Southampton
Professor Harry de Koning	Deputy Head and Professor of Public Health & Screening Evaluation, Department of Public Health, Erasmus MC University Medical Centre
Professor Ruth Etzioni	Program in Biostatistics, Division of Public Health Sciences, Fred Hutchinson Cancer Research Center
Professor Nick James	Professor of Prostate and Bladder Research, Institute of Cancer Research and Royal Marsden Hospital
Professor Stephen Langley	Professor and Clinical Director of Urology at the Royal Surrey County Hospital
Professor Anwar Padhani	Oncological Radiologist, Mount Vernon Cancer Centre and Professor of Cancer Imaging at the Institute of Cancer Research
Professor Prasanna Sooriakumaran	Consultant Urological Surgeon, University College London Hospitals
Dr Andrew Vickers	Attending Research Methodologist, Memorial Sloan Kettering Cancer Center
Pieter Vynckier	Department of Public Health and Primary Care, Ghent University

S65	Mark Buckingham	Bayer PLC	While the recommendation to screen men aged 45-61 with BRCA1 or BRCA2 gene mutations is a step forward, it falls short of including other high risk groups such as Black men and those with a family history despite the significantly higher risks they face. Black men are almost twice as likely as white men to be diagnosed with prostate cancer and 2.5 times more likely to die from it. Men with a father or brother diagnosed before the age of 65 face more than double the average risk. Excluding these groups from the first targeted screening programme raises urgent questions about how we ensure equity in prostate cancer care. Bayer is aware of Prostate Cancer Research's consultation submission and supports the approach PCR are recommending. We support PCR's proposal that the consideration of this screening policy should be extended to ensure the best available modelling is available and considered and that there can be appropriate discussion and understanding of how screening policy for prostate cancer aligns with the Government's focus on moving from treatment to prevention and on addressing health inequalities.
S66	Esther Onyeka	Caribbean & African Health Network	Recognition of progress and policy context The Caribbean & African Health Network welcomes the opportunity to respond to the UK National Screening Committee's consultation on its draft recommendation for screening. We are responding particularly focused on Black African and Caribbean communities, of which Black men are experiencing the highest disparities at double the rate of their White counterparts. The NSC's proposal to introduce targeted screening for men aged 45-61 with BRCA1 and BRCA2 gene mutations, is a positive step towards personalised screening approaches. We acknowledge NSC's viewpoint on population-wide PSA screening not being recommended due to limitations in test accuracy and the risk-benefit balance. The National Cancer Plan pledges to review the final recommendation of the NSC on Prostate Cancer screening and implement a screening programme where the evidence supports it. The Plan also highlights that the NHS will continue to support the TRANSFORM trial to answer outstanding questions on screening effectiveness particularly for Black men and men with family history. The Plan calls for an update to advice to patients, ensuring they are provided with clarity on symptoms and their risk of prostate cancer. The Men's Health Strategy initiatives propose: • Home-based monitoring for men with raise PSA levels • Virtual care pathways

			• Targeted awareness campaigns to encourage early testing and tack disparities for at risk groups • Improved access and equity The Government's Plans and strategies all aligning with the National ten-year health plan focus on prevention, highlighting early screening and improvement of health education on prostate cancer. Black men need new and improved screening and testing measures to tackle the ongoing disparities for African and Caribbean communities. Exclusion of Black Men from Targeted Screening programmes Personalised screening approaches such as the targeted screening for men the BRCA1 and BRCA2 gene mutations are good but do not extend a targeted approach to Black men. CAHN, in solidarity with Prostate Cancer UK and Prostate Cancer Research among other organisations have expressed our disappointment on the recommendation, especially as there is no alternative to improvement of earlier and more effective screening for a highly at risk group. There are a plethora concerns with the sole use of PSA testing due to inaccuracies and not a reliable test when used alone. In order to develop earlier and effective testing for Black men, PSAs should be given along with MRIs to improve accuracy for diagnosis, also reducing the need for unnecessary biopsies. Black men have historically been excluded from involvement in trials and there is still a lack of awareness of risk and access to early testing. The current access afforded to Black men fails to address significant racial inequalities in incidence, stage at diagnosis and mortality. CAHN urges the consideration, design and implementation of a targeted prostate cancer screening programme for Black men that focuses on testing earlier and providing culturally appropriate health education for African and Caribbean communities on symptoms, risk factors and pathway support. A screening programme for Black men must be created and done in collaboration with Black community organisations, condition-specific organisations and community champions. Evidence of inequalities Prostate cancer is the most commonly diagnosed cancer among men in the UK, with the burden unevenly distributed. There are inequalities for Black men, men with family history or those in deprived areas. The lack of a targeted or effective screening programme is exacerbated where health education, access and trust in services are already compromised.

		• Black men are twice as likely to be diagnosed with prostate cancer compared to White men. • Mortality rates are disproportionately higher in Black communities. The NSC's decision must take into consideration that the risk of overdiagnosis and overtreatment do not outweigh the risks of continued harm to Black men due to continued late diagnosis. We are aware of the structural racism in our health system, a severe justified lack of trust from Black communities in health service provision and the increased avoidable mortality rates in Black men. These are all exacerbated without action towards health equity in prostate cancer care. Recommendations • Collaborate with community organisations like CAHN to deliver health literacy and education programmes on prostate cancer for Black communities. Coproduce communication materials with the community. • Increase threshold for trials, pilot programmes and screening studies to improve diversity of sample groups – particularly driving up the representation of Black men. • Develop and implement improved and more effective targeted screening programmes for Black men that are done in collaboration with Black communities. • Ensure equity impact assessments are central to final recommendations. • Update, revise and adapt primary care advice for earlier testing especially where larger groups of Black communities reside. • Improve diagnostic pathways to include MRI testing alongside PSA testing. • Increase clinical understanding of genetic and racial risk across health workforce. • The routine collection and reporting of ethnicity-disaggregated screening and outcome data. Investment in longitudinal outcome data. CAHN stands ready to work collaboratively with the UK NSC, NHS bodies and partners to develop a screening approach that is evidence-based, equitable and effective for Black communities. About CAHN:

		The Caribbean & African Health Network (CAHN) is a Black-led organisation on a mission to eradicate health inequalities and wider disparities for Black Caribbean and African people in the UK. For information about the organisation, please visit https://www.cahn.org.uk/ ----- Dear Secretariat Team, Thank you for the time allocated to submit evidence to this consultation. As previously discussed, please find attached our submission on the prostate cancer screening review. This response reflects our engagement with the Black community Our intention is to support the Committee in reaching a decision that is equitable, evidence led and aligned with national priorities on early diagnosis and health inequalities. The attached final document sets out the collective considerations raised through this engagement and the issues we believe are essential for a proportionate and informed assessment. We would like to be registered on the stakeholder list; please feel free to use ***** email address as the point of contact. Our organisational homepage can be found here: https://www.cahn.org.uk/ We will also review the recommendations page for other conditions and submit appropriate information where relevant. We appreciate the opportunity to contribute to this important process and look forward to hearing a response in the coming weeks. Best Wishes

CAHN UK

National Screening Committee Consultation Response Targeted Prostate Cancer Screening for Black Men

Submitted by Caribbean & African Health Network (CAHN) on behalf of Black communities, Black-majority churches, and national Black health organisations

PART 1

EXECUTIVE SUMMARY

Black men in the UK face the highest risk of prostate cancer: they are twice as likely to develop the disease, more likely to be diagnosed late and more likely to die from it. This represents one of the most severe and persistent health inequalities in the UK.

The UK National Screening Committee's (NSC) decision to recommend targeted screening for BRCA1/2 carriers but not for Black men is inconsistent with the evidence. BRCA mutations are rare and do not explain the elevated risk in Black men. Ethnicity is the strongest predictor of prostate cancer risk.

NICE, the Prostate Cancer Risk Management Programme (PCRMP), NHS England's Core20PLUS5 framework and the NHS Long Term Plan all recognise Black men as a high-risk group and support earlier investigation. The NSC's position contradicts existing national guidance.

Black communities have not been passive. They have led prostate cancer awareness, education and early-detection efforts for years and often without funding. CAHN's weekly Health Hours, Black-majority church PSA days, GM Cancer Alliance outreach and Prostate Cancer UK's StrongMen campaign demonstrate strong community leadership and demand for targeted action.

The TRANSFORM trial will take up to ten years. Black men are dying now. Delaying action will widen inequalities and cost lives.

CAHN recommends a targeted screening programme for Black men, delivered in partnership with Black-majority churches, Black-led community organisations and trusted community health champions.

This is an evidence-based, ethically necessary and community-mandated intervention that aligns with national priorities and would save lives.

1. Introduction And Core Position

CAHN welcomes the NSC's commitment to personalised screening and acknowledges the proposal to introduce targeted testing for men aged 45 to 61 with BRCA1 and BRCA2 mutations.

However, the decision not to recommend targeted screening for Black men represents a serious and harmful omission. It fails to protect the group with the highest risk, the poorest outcomes and the highest mortality from prostate cancer in the UK.

Black men are twice as likely to develop prostate cancer, more likely to be diagnosed at a later stage and more likely to die from the disease. Families across Caribbean and African communities have buried fathers, brothers, uncles, husbands and friends long before their time.

The absence of a targeted screening programme contributes directly to avoidable deaths, preventable harm and growing mistrust in the health system.

2. BRCA1 And BRCA2 Mutations Do Not Explain the Elevated Risk in Black Men

BRCA1 and BRCA2 mutations are rare and are not more common in Black men.

Most Black men who develop prostate cancer do not have BRCA mutations.

Ethnicity is the strongest predictor of prostate cancer risk in the UK.

The NSC's proposal to target BRCA carriers but exclude Black men is inequitable and inconsistent with the principles of population health.

3. Systemic Exclusion and The Reality of Black Men's Experiences

Black men continue to be excluded from targeted screening because of longstanding systemic issues.

Many Black men report being turned away when requesting PSA tests, being told they are too young or that they do not meet criteria.

These experiences reflect structural inequities documented by decades of reports.

This pattern contributes to late diagnosis and higher mortality.

3.1 Governance and Evidence Gaps

There is no evidence that an Equality Impact Assessment was conducted in relation to the NSC's decision not to recommend targeted screening for Black men. Given that Black men experience the highest incidence, the highest mortality and the poorest outcomes from prostate cancer in the UK the absence of an Equality Impact Assessment is a significant omission.

Race is a protected characteristic under the Equality Act 2010, and the Public Sector Equality Duty requires public bodies to have due regard to the need to eliminate discrimination, advance equality of opportunity and reduce inequalities in health outcomes. A decision that directly affects a high-risk protected group should not be made without a formal assessment of its impact. The lack of an Equality Impact Assessment raises concerns that the disproportionate harm faced by Black men has not been fully considered, and that the recommendation may inadvertently widen existing racial health inequalities.

There is also no evidence that the York Health Economics Consortium (YHEC) has conducted an ethnicity-specific economic analysis to assess the cost effectiveness of targeted screening for Black men. YHEC modelling underpins NSC recommendations, yet the available reports do not include any modelling of the impact of earlier detection for Black men, the highest-risk group in the UK. Given these omissions, no decision not to recommend targeted screening for Black men

should be made until the underlying economic modelling has been updated to reflect ethnicity-specific risk, incidence, mortality and diagnostic pathways.

There is also a longstanding paucity of research on Black men's health in the UK, driven in part by limited investment and the lack of dedicated research funding streams. Black men are consistently under-represented in clinical studies, screening trials and epidemiological datasets, and Black-led organisations report significant barriers in accessing research grants to generate the evidence needed to inform policy. This structural under-investment means that the evidence base relating to Black men's prostate cancer risk, diagnostic pathways and outcomes is less developed than it should be, despite the severity of the inequality. The absence of targeted research funding has contributed to gaps in national datasets and modelling and reinforces the need for the NSC to take a precautionary and equity-led approach when making decisions that affect the highest-risk group.

Without an economic assessment that reflects the disproportionate incidence, mortality and late-stage diagnosis experienced by Black men, the NSC cannot be confident that its recommendation represents an equitable or efficient use of resources.

A wide range of national reports reinforce these concerns. The NHS Race and Health Observatory has documented structural inequities in cancer pathways, including delayed diagnosis, inconsistent GP responses and lower access to early detection for Black communities. Cancer Research UK, Public Health England (now OHID) and the Parliamentary and Health Service Ombudsman have all highlighted persistent ethnic inequalities in cancer outcomes, independent of deprivation, and the need for targeted interventions. Independent analyses from the School of Health and Related Research (SCHARR) at the University of Sheffield further emphasise that screening programmes must account for differential risk across population groups and that high-risk groups benefit most from targeted early detection. SCHARR's work on screening, risk stratification and health inequalities highlights that population-level averages can obscure significant disparities and that failure to incorporate ethnicity-specific risk can lead to widening inequalities. Together, these governance and evidence gaps demonstrate that the NSC's current recommendation does not adequately consider the needs of the highest-risk group and risks entrenching existing inequalities.

4. Community Outrage, Lived Experience and the Scale of Engagement

Despite having only a two-week window to gather community insight, CAHN mobilised a significant national response through our established networks. We engaged leaders representing more than one hundred Black majority churches across Caribbean and African communities. We engaged community leaders across Black led organisations. These leaders collectively represent tens of thousands of Black families across the UK. Their endorsement gives this submission a strong national mandate.

Across every engagement activity, one message was repeated with painful consistency. Almost every person we spoke to knows someone who has died from prostate cancer or been harmed by late diagnosis. This is not an abstract policy issue. It is a lived reality in Black families, churches and neighbourhoods.

The community is outraged. Black men and their families told us that the decision to exclude them from targeted screening feels like a continuation of the same neglect that has cost so many lives already. They see friends, fathers, uncles, brothers and community leaders dying unnecessarily. They see men being diagnosed too late. They see families devastated. They see harm that could have been prevented.

This outrage is not emotional overreaction. It is a rational response to decades of disproportionate harm and policy decisions that fail to protect those at highest risk.

The CAHN Black Men's Health Manifesto, published in 2024, identifies prostate cancer as a critical health inequality requiring urgent national action. It calls for targeted screening, earlier detection, culturally competent education, community-based delivery through churches and trusted spaces and better access to PSA testing and diagnostic pathways. This submission directly reflects those priorities.

- Black communities have led prostate cancer awareness and education for years, often without funding.
- CAHN delivers weekly Health Hours; this is a national health literacy programme and without dedicated resource. Prostate cancer is a recurring topic, with clinicians engaging directly with Black men.
- Black-majority churches host prostate cancer awareness days, men's health Sundays, health fairs and PSA education sessions. These are volunteer-led and unfunded.
- Community organisations run workshops, peer-support groups and outreach activities, producing leaflets, videos and culturally relevant materials.

Examples include (also in annex):

- **Prostate Cancer UK's StrongMen campaign**, targeting Black men with culturally relevant messaging.
- **GM Cancer Alliance outreach**, partnering with Black churches and community groups.
- **Local church PSA days**, where clinicians speak directly to men about risk and testing.
- **Black-led health fairs**, offering prostate cancer information alongside other health checks.
- **Movember's Black Men's Health initiatives**, including barber-shop outreach and community conversations.
- **ICS-led community roadshows**, including in Birmingham, London, Manchester and Leeds.

Black media, these include The Voice Newspaper, Keep the Faith magazine and Black-led radio stations, such as legacy, they consistently highlight prostate cancer inequalities and amplify community voices.

Despite this extensive activity, Black organisations receive limited or no funding. The burden of unfunded labour falls disproportionately on Black volunteers, faith leaders and community advocates.

Black communities have demonstrated leadership, commitment and action. What is missing is national support and a targeted screening programme.

5. The UK Evidence Base: Peer-Reviewed Research

The PROCESS studies (Ben-Shlomo et al., 2008; Evans et al., 2010) show significantly higher prostate cancer risk for Black men in the UK.

Jones and Chinegwundoh (2014) confirm higher incidence, earlier onset and poorer outcomes.

Down et al. (2024) show Black men have higher odds of clinically significant cancer even after PSA testing.

Nashwan and Mannethodi (2024) emphasise the clinical implications of this evidence.

Chinegwundoh (2021) highlights mistrust and communication barriers.

Prostate Cancer UK modelling shows Black men would benefit most from targeted early detection.

6. NICE, PCRMP And NHS England Guidance Support Targeted Action

- NICE CKS recognises Black men as a high-risk group and supports PSA testing for asymptomatic men.
- PCRMP states that Black men over 45 should discuss PSA testing with their GP and that GPs must offer a PSA test to any man who requests one.
- NICE NG12 identifies Black ethnicity as a clinical risk factor.
- NHS England's Core20PLUS5 identifies Black communities as a priority population.
- The NHS Long Term Plan commits to earlier cancer diagnosis and reducing inequalities.
- The NSC's position is inconsistent with existing national guidance.

7. The TRANSFORM Trial Cannot Justify Delay

- TRANSFORM will take up to ten years.
- Black men are dying now.
- The evidence base is already strong, consistent and UK-specific.
- Delaying action will widen inequalities and cost lives.

8. CAHN's Role as National Convener

CAHN has national reach across Black-majority churches, community organisations and health networks.

CAHN is prepared to lead a coordinated, culturally competent early-detection programme that is fully resourced, we have the machinery and the reach to deliver this at scale.

9. Consequences Of Inaction

- Black men will continue to die at disproportionately higher rates.

- Late-stage diagnosis will remain common.
- Trust in the NHS will deteriorate.
- Inequalities will deepen.

10. Recommendations

10.1 Introduce a Targeted Screening Pathway for Black Men Aged 45+

Establish a national targeted early-detection pathway for Black men, aligned with the evidence base. Use PSA + MRI as the standard diagnostic sequence. Ensure the pathway is co-designed with Black communities and Black-led organisations.

10.2 Mandate Proactive PSA Conversations in Primary Care

Require GPs to initiate PSA discussions with Black men aged 45+. Embed ethnicity-specific prompts in GP IT systems. Monitor compliance through ICS-level dashboards.

10.3 Commission Black-Led Community Delivery Partners

Fund Black-majority churches, Black-led community organisations and trusted community health champions to deliver outreach, education and navigation. Provide multi-year funding to avoid reliance on unfunded labour.

10.4 Develop a National Communications Campaign for Black Men

Co-produce culturally relevant messaging with Black communities. Use Black media, barber shops, churches, sports clubs and community radio. Ensure messaging addresses mistrust, stigma and previous negative experiences.

10.5 Implement Workforce Training on Culturally Competent Prostate Cancer Conversations

Train primary care teams, cancer navigators and community clinicians. Include modules on racism, bias, communication barriers and trust-building. Ensure training is mandatory for ICS cancer teams.

10.6 Require ICS-Level Equity Impact Assessments

ICSs must demonstrate how they will reduce prostate cancer inequalities for Black men. Include metrics on uptake, stage at diagnosis, and time to treatment. Publish annual progress reports.

10.7 Accelerate Action Ahead of TRANSFORM Trial Results

Do not wait 10 years for TRANSFORM. Use existing UK evidence to implement interim targeted screening. Commit to revising the pathway once TRANSFORM data becomes available.

10.8 Establish a National Prostate Cancer Inequalities Taskforce

Include CAHN, Prostate Cancer UK, NHS England, ICS Cancer Alliances and Black-led organisations. Oversee implementation, monitoring and accountability. Ensure Black men's voices shape every stage.

10.9 Ensure Data Transparency and Ethnicity-Specific Reporting

Require ethnicity coding for all PSA tests, MRI referrals and biopsy outcomes. Publish national dashboards showing uptake and outcomes for Black men. Use data to drive targeted improvement.

10.10 Provide Dedicated Funding for Community Navigation and Support

Fund navigators embedded in Black-led organisations. Support men through testing, diagnosis and treatment. Reduce drop-off between PSA, MRI and biopsy.

11. Final Position

A targeted screening programme for Black men is evidence-based, ethically necessary and community-mandated.

The NSC has an opportunity to correct a longstanding inequity.

ANNEX X – Peer-Reviewed Evidence on Prostate Cancer in Black Men

Introduction to Annex X

This annex provides a comprehensive review of the peer-reviewed evidence on prostate cancer risk, incidence, mortality, diagnostic pathways and outcomes for Black men in the UK. It includes epidemiological studies, cohort analyses, clinical commentaries, modelling studies and systematic reviews. The evidence is consistent, robust and spans more than two decades.

Across all sources, the conclusion is clear:

Black men in the UK face the highest risk of prostate cancer, are diagnosed later, and experience poorer outcomes - independent of socioeconomic status, comorbidities or access to care.

This annex demonstrates:

- The elevated risk is well-established.
- The evidence is UK-specific, not extrapolated from US data.
- The risk is not explained by BRCA1/2 mutations.
- The disparity persists even after adjusting for confounders.
- Black men benefit most from early detection.
- The evidence base is sufficient to justify targeted screening now.

This annex underpins CAHN's recommendation for a targeted screening programme for Black men aged 45+.

1. The PROCESS Studies (Ben-Shlomo et al., 2008; Evans et al., 2010)

The PROCESS studies remain the most important UK-based evidence on prostate cancer risk in Black men.

Key findings:

- Black men in the UK are twice as likely to be diagnosed with prostate cancer.

- They present younger, often under 60.
- They present with higher PSA levels.
- They have more advanced disease at diagnosis.
- These differences persist after adjusting for socioeconomic status.

Why this matters:

PROCESS is the foundation of UK policy discussions on prostate cancer risk. It demonstrates that ethnicity is an independent risk factor and that Black men require earlier detection.

2. Jones & Chinegwundoh (2014): “Update on Prostate Cancer in Black Men in the UK”

This review synthesised UK data and confirmed:

- Higher incidence
- Earlier onset
- Higher mortality
- Lower awareness
- Lower likelihood of early-stage diagnosis

The authors concluded that targeted interventions are necessary to address the disparity.

3. Down et al. (2024): MRI-Based Screening and Ethnic Inequalities

This recent UK study examined MRI-based screening and found:

- Black men had higher odds of clinically significant cancer even when PSA levels were similar to White men.
- MRI detected more aggressive cancers in Black men.
- PSA alone under-detects risk in Black men.

Implication:

A PSA-only approach disadvantages Black men. A combined PSA + MRI pathway is essential.

4. Chinegwundoh (2021): Clinical Commentary on Inequalities

Chinegwundoh, a leading UK urologist, highlights:

- Black men often experience delayed diagnosis.
- Many report dismissals of symptoms or being told they are “too young”.
- There is mistrust due to previous negative experiences.
- Cultural stigma and fear contribute to late presentation.

Implication:

Clinical behaviour and system barriers contribute to late diagnosis. Targeted screening must be paired with culturally competent communication.

5. Prostate Cancer UK Modelling (2020–2023)

PCUK's modelling shows:

- Black men would benefit most from targeted early detection.
- Earlier diagnosis would significantly reduce mortality.
- Targeted screening is cost-effective for high-risk groups.
- Without targeted action, inequalities will widen.

Implication:

The modelling supports a targeted screening programme for Black men.

6. Racial Differences in Tumour Biology (UK and International Evidence)

Several studies indicate:

- Black men are more likely to develop aggressive tumours.
- Tumour biology may differ, contributing to poorer outcomes.
- These differences persist even in equal-access systems.

Implication:

Earlier detection is clinically justified.

7. UK Mortality Data

ONS and Cancer Research UK data show:

- Black men have higher mortality from prostate cancer.
- Mortality is linked to late-stage diagnosis.
- Earlier detection would reduce deaths.

8. UK Studies on Awareness and Health-Seeking Behaviour

Multiple studies show:

- Black men have lower awareness of prostate cancer risk.
- Many do not know they are at higher risk.
- Cultural stigma and fear of diagnosis are common.
- Mistrust of the health system is a barrier.

Implication:

Community-led education is essential - and Black communities are already doing this work, often unfunded.

9. UK Studies on GP Behaviour and Access

Evidence shows:

- Black men are less likely to be offered PSA tests.
- Some are refused PSA tests even when they request them.
- GP knowledge of ethnicity-specific risk is inconsistent.
- System prompts do not flag Black ethnicity as a risk factor.

Implication:

A targeted screening programme must include primary care prompts and training.

10. Evidence on Cost-Effectiveness

Studies show:

- Targeted screening of high-risk groups is more cost-effective than population-wide screening.
- Early detection reduces treatment costs.
- MRI-based pathways reduce unnecessary biopsies.

Implication:

A targeted programme for Black men is economically justified.

11. Evidence on MRI-First Pathways

UK trials (e.g., PROMIS, PRECISION) show:

- MRI-first pathways improve detection of clinically significant cancers.
- They reduce over-diagnosis.
- They are particularly beneficial for high-risk groups.

Implication:

MRI should be part of the targeted pathway for Black men.

12. Evidence on Genetic Risk Beyond BRCA

Studies show:

- BRCA1/2 mutations are rare in Black men.
- They do not explain the elevated risk.
- Polygenic risk scores are less predictive for Black men due to under-representation in genomic studies.

Implication:

Ethnicity remains the strongest predictor of risk.

13. Summary of Peer-Reviewed Evidence

Across all peer-reviewed sources:

- Black men are at highest risk.
- They are diagnosed later.

- They have poorer outcomes.
- BRCA does not explain the disparity.
- MRI + PSA is the most effective pathway.
- Targeted screening is clinically justified, cost-effective, and ethically necessary.

ANNEX Y – Non-Peer-Reviewed Evidence and Community-Led Action

Introduction to Annex Y

This annex presents the extensive non-peer-reviewed evidence demonstrating the scale, consistency and longevity of Black-led prostate cancer awareness, education and early-detection activity across the UK. It includes:

- Community campaigns
- Faith-based outreach
- Black-led media coverage
- ICS and Cancer Alliance initiatives
- Charity-led programmes
- Barber-shop and grassroots interventions
- Testimonies, case studies and lived experience
- Evidence of unfunded labour
- Evidence of demand from Black men themselves

This evidence is crucial because:

1. It demonstrates that Black communities have not been passive, it shows that they have been leading the work for years.
2. It shows that Black men are actively seeking information, testing and support.
3. It highlights the scale of unfunded labour carried by Black volunteers, churches and community organisations.
4. It provides real-world evidence that targeted screening is both needed and wanted.

The NSC must consider this evidence alongside the peer-reviewed literature. Ignoring it would overlook the lived reality of the communities most affected.

1. Black-Led Community Campaigns and Programmes

1.1 CAHN Health Hour (National Weekly Programme)

CAHN's Health Hour is one of the largest and most consistent Black-led health literacy programmes in the UK.

- Delivered every week, nationally, since May 2020
- Prostate cancer is one of the most frequently requested topics.
- Sessions feature Black clinicians, urologists, GPs and cancer specialists.
- Hundreds attend live; thousands watch recordings.
- Delivered without dedicated funding.
- Provides direct Q&A with Black men who often report barriers to PSA testing.

Significance: This is one of the strongest examples of sustained, unfunded community leadership in early detection.

1.2 Black-Majority Church Prostate Cancer Days

Across the UK, Black-majority churches run:

- Men's health Sundays
- Prostate cancer awareness days
- Health fairs
- PSA education sessions
- Testimony-based events
- Family-focused health days

These events:

- Are organised by volunteers
- Often include clinicians speaking directly to men
- Reach men who rarely engage with mainstream health services
- Are culturally safe and trusted
- Have been running for over a decade in some churches

Significance: Faith-based outreach is one of the most effective ways to reach Black men, this is not new and it is already happening at scale but again with no recognised or adequate funding to sustain this activity.

1.3 Barber-Shop Health Conversations

Barber shops are trusted spaces for Black men. Across London, Birmingham, Manchester, Leeds and Bristol, barber-shop prostate cancer conversations have been delivered by:

- Local community groups
- Cancer charities
- Black clinicians
- Movember
- Prostate Cancer UK
- ICS Cancer Alliances

These sessions:

- Reach men who rarely attend GP appointments
- Provide culturally relevant information
- Normalise conversations about prostate cancer
- Often lead to men requesting PSA tests

Significance: Barber-shop outreach is a proven model for engaging Black men in health conversations.

2. Charity-Led Campaigns Targeting Black Men

2.1 Prostate Cancer UK – StrongMen Campaign

This national campaign specifically targeted Black men with:

- Culturally relevant messaging
- Black ambassadors and spokespeople
- Social media content tailored to Black audiences
- Community events
- Partnerships with Black-led organisations

The campaign significantly increased awareness among Black men.

2.2 Movember – Black Men’s Health Initiatives

Movember has delivered:

- Barber-shop outreach
- Community conversations
- Black men’s health panels
- Targeted social media campaigns
- Partnerships with Black influencers

These initiatives highlight the need for culturally competent messaging.

2.3 Macmillan and Cancer Research UK Community Engagement

Both charities have:

- Produced materials tailored to Black men
- Delivered community workshops
- Partnered with Black-led organisations
- Supported ICS-level outreach

Significance: Major charities recognise the need for targeted action, the challenge is that their work is limited without national screening.

3. ICS and Cancer Alliance Initiatives

3.1 GM Cancer Alliance – Black Men’s Prostate Cancer Outreach

GM Cancer Alliance has partnered with:

- CAHN
- Black-majority churches
- Community groups

- Black clinicians

Activities include:

- Community events
- PSA awareness sessions
- Targeted communications
- Engagement with Black men aged 45+

Significance: ICS-level work demonstrates that targeted outreach is feasible and effective.

3.2 North Central London ICS – Community Roadshows

These roadshows include:

- Prostate cancer information
- Engagement with Black men
- On-the-spot conversations with clinicians

3.3 Birmingham and Solihull ICS – Black Men’s Health Events

Events include:

- Prostate cancer talks
- Screening information
- Partnerships with local Black churches

3.4 West Yorkshire Cancer Alliance – Community Engagement

Includes:

- Black men’s health sessions
- Prostate cancer awareness workshops

Significance: ICSs are already doing targeted work - but without national screening, impact is limited.

4. Black-Led Media Coverage

4.1 The Voice Newspaper

The Voice has run:

- Prostate cancer features
- Interviews with Black clinicians
- Awareness campaigns
- Testimonies from Black men

4.2 Keep the Faith Magazine

Regularly covers:

- Prostate cancer awareness
- Faith-based health initiatives
- Black men's health stories

4.3 Black-Led Radio Stations

Stations such as:

- Galaxy Radio
- Colourful Radio
- BBC Radio London (Black-focused shows)
- Community FM stations
- Legacy FM

These platforms:

- Host prostate cancer discussions
- Feature Black clinicians
- Reach older Black men effectively

Significance: Black media has been doing the work that national health systems have not.

5. Testimonies and Lived Experience

Across CAHN Health Hours, church events, barber-shop sessions and community workshops, Black men consistently report:

- Being refused PSA tests
- Being told they are “too young”
- Not being informed of their higher risk
- Not being offered MRI
- Delays in referral
- Fear and mistrust due to previous experiences
- Lack of culturally competent communication

These testimonies are consistent across regions and over time.

6. Evidence of Unfunded Labour

This is one of the most important sections.

Black-led organisations, churches and volunteers have:

- Delivered hundreds of events
- Produced culturally relevant materials
- Organised outreach

- Hosted clinicians
- Provided navigation and support
- Reached thousands of Black men

Almost all of this has been unfunded.

This represents:

- A structural inequity
- A reliance on unpaid Black labour
- A failure of national systems to resource high-risk communities
- A barrier to scaling effective interventions

Significance: The NSC must recognise that Black communities have already built the infrastructure for targeted screening, but they cannot continue to do so without support.

7. Evidence of Demand from Black Men

Across all community settings, Black men consistently:

- Ask for PSA tests
- Seek information
- Want earlier detection
- Express fear of late diagnosis
- Want clarity on their risk
- Want trusted, culturally competent communication

8. Summary of Non-Peer-Reviewed Evidence

The evidence shows:

- Black communities have led prostate cancer awareness for years.
- Outreach is widespread, consistent and effective.
- The work is largely unfunded.
- Black men are actively seeking early detection.
- ICSs and charities recognise the need for targeted action.
- Black media amplifies the message.
- Community infrastructure already exists for a targeted screening programme.

S67	Thomas Lyon	Johnson & Johnson Innovative Medicine	

Johnson & Johnson

Johnson & Johnson Submission to the UK NSC Consultation on Prostate Cancer Screening

Submissions are a maximum of 5,000 words

Johnson & Johnson Innovative Medicine welcomes the UK National Screening Committee's (NSC's) draft recommendation and the Committee's thorough and rigorous review of the available evidence on prostate cancer screening. We recognise the complexity of balancing potential benefits and harms in screening policy and commend the NSC for its careful consideration of emerging data and evolving diagnostic pathways.

Our response focuses on five key themes with recommendations:

1. **Overcoming identification gaps in BRCA1/2-focused screening**
2. **Moving towards a broader, risk-stratified prostate cancer screening approach**
3. **Reviewing the risk–benefit balance of screening considering modern diagnostics**
4. **Updating cost-effectiveness modelling to reflect current thresholds and practice**
5. **Capturing the full clinical and socio-economic value of earlier diagnosis**

1. Overcoming identification gaps in BRCA1/2-focused screening

We recommend that the UK NSC ensures any BRCA1/2-focused prostate cancer screening programme is proactive by design, rather than reliant on self-identification or voluntary presentation by men at risk.

We strongly support the NSC's draft recommendation to introduce screening for men with BRCA1/2 variants, given the compelling evidence that this group faces a significantly elevated lifetime risk of having prostate cancer and experiencing poorer outcomes. We believe that targeted screening for these men has the potential to save lives through earlier detection and treatment and recognise this as a positive first step towards a broader screening programme for other high-risk men.

However, to ensure that this programme reaches its full potential:

- A BRCA1/2-focused screening programme should not rely solely on men coming forward voluntarily.
 - o The recent launch of the National Inherited Cancer Predisposition Register (NICPR) is an important step forward. By capturing data on individuals in England with a confirmed likely pathogenic variant in a cancer susceptibility gene, including BRCA1 and BRCA2, the NICPR provides a national, clinically validated dataset of people at increased inherited cancer risk. This creates a strong foundation for proactive follow-up, audit, and the delivery of targeted screening programmes.
 - o However, an effective screening programme must go beyond those who have already been identified and entered onto national registers. Doing so would maintain the status quo, in which individuals at higher risk are expected both to recognise their own risk and to take proactive steps to mitigate it. This approach has already proven ineffective in the UK's current reactive approach to prostate cancer testing and risks leaving many high-risk men undiagnosed until later stages of the disease.
 - o To be effective, such a programme would need to combine:
 - o Proactive outreach to men already known to carry BRCA1/2 variants, making full use of infrastructure such as the NICPR to ensure consistent invitation, follow-up, and audit;
 - o Comprehensive and systematic testing strategies to identify men with BRCA1/2 variants who are currently unaware of their risk, including those who have never engaged with genetic services.

Johnson & Johnson

- o Measures to ensure it does not exclude a significant proportion of men with late-stage prostate cancer as a result of an arbitrary cut-off on the age of eligibility.
 - o Cascade testing for relatives of BRCA1/2 confirmed men would support case finding and ensure as wide a population as possible is reached.
- o This latter point is particularly important, given polling of the UK public by Johnson & Johnson in 2024 found that only 26% of UK adults have heard of the BRCA biomarker.¹ Low awareness of BRCA risk means that men with a family history of prostate, breast or ovarian cancer are less likely to investigate their risk or participate in PSA testing without proactive engagement.
- o NICPR should be viewed not as a complete solution, but as a support system that must be assisted by proactive case-finding. Without action to improve identification and testing, a BRCA-only screening recommendation risks benefiting only those already well served by existing pathways, while exacerbating inequities in awareness, diagnosis, and outcomes.
- Routine biomarker and genomic testing should be expanded to all men at the point of prostate cancer diagnosis, so inherited BRCA1/2 risk is identified as early as possible, patients are directed onto the most appropriate treatment pathway, and eligible men and their relatives can be fed back into screening and cascade testing pathways. This should deliver on National Cancer Plan² commitments to post-diagnosis genomic testing, with investment to ensure rapid turnaround times and equitable access across regions.
- The NSC should reconsider the evidence base for capping screening at age 61, given modelling demonstrates that a significant proportion of men with BRCA1/2 variants are diagnosed above this age, and the average age of a BRCA2 carrier at the point of prostate cancer diagnosis is 60 years old.³
- Education and awareness-raising should be prioritised to ensure men understand the testing offer and have a clear understanding of what a positive BRCA1/2 result means for them and their families. Improving understanding is essential to reducing anxiety caused by uncertainty and misinformation.
 - o Many men may be unaware of their BRCA1/2 status, and therefore their risk, because it has never been discussed within their families, particularly in communities where men's health has historically been a taboo subject.
 - o Raising awareness in more deprived communities is essential to avoid exacerbating inequalities. Affluent communities tend to have higher levels of health literacy, meaning they are more likely to benefit from a limited screening programme.
 - o The NSC decision should be communicated clearly. Some men may misinterpret the Committee's recommendation as PSA testing being unsafe which may dissuade some from participating.

2. Moving towards a broader, risk-stratified prostate cancer screening approach

We recommend that the UK NSC moves beyond a BRCA1/2-only recommendation and commits to developing a broader, risk-stratified prostate cancer screening approach that explicitly includes other high-risk groups, including Black men and men with a family history of prostate cancer.

While we support the introduction of screening for men with BRCA1/2 variants, we are concerned that a recommendation limited to this group alone does not fully reflect the risk faced by other populations. Excluding Black men and those with a family history of prostate cancer risks reinforcing already well-established inequalities in healthcare access and outcomes. Continued reliance on opportunistic PSA

testing tends to benefit men who are more aware of their health risks and more confident in navigating the healthcare system, while leaving others behind.

We believe that, in addition to men with BRCA 1/2 variants, the NSC should recommend a more ambitious, targeted, risk-stratified approach to prostate cancer screening. In our view, such an approach should prioritise groups at the highest risk. This should include:

- Black men aged 45+
- Men with a family history of prostate cancer aged 45+

All these groups have well-established links to a higher risk of clinically significant prostate cancer. For Black men in particular, the lack of a screening programme is contributing to poorer outcomes. Black men in the UK are two to three times more likely to develop prostate cancer than white men and have double the mortality rate, yet only 20% are aware of their increased risk.⁴ Likewise, men living in more deprived areas are less likely to be aware of their risk and to request a PSA test,⁵ meaning they are also less likely to be diagnosed early and more likely to experience poorer outcomes, highlighting a persistent challenge that is not fully addressed in the current draft recommendation.

By improving early diagnosis through targeted screening and proactive outreach, men at the highest risk are more likely to receive treatment at earlier stages of the disease, leading to improved outcomes.⁶

Moreover, it's important to ensure that available international evidence is appropriately considered within the NSC's final recommendation to ensure that the UK is not falling behind comparator countries. For example, in January 2026, the Croatian Institute of Public Health announced that the success of their two-year pilot programme for prostate cancer screening has enabled the launch of a national prostate cancer screening programme.⁷ Similarly, while the NSC made loose reference to a programme in Lithuania that has been ongoing since 2006, there seemed to be little recognition of the success of this programme. In that time, annual PSA testing for men aged 50 – 70 and aged 45-49 for those with a family history has led to a significant decrease in the diagnosis of prostate cancer at an advanced stage, while also having the added benefit of improving knowledge and awareness of prostate cancer at the population level.⁸

3. Reviewing the risk–benefit balance of screening considering modern diagnostics

We recommend that the UK NSC re-assesses the balance of benefits and harms of prostate cancer screening to fully reflect the impact of modern diagnostic pathways, including mpMRI-first approaches and transperineal biopsy techniques.

A central concern, historically associated with prostate cancer screening, has been the risk of overdiagnosis, overtreatment, and procedure-related harms. However, the diagnostic landscape has evolved substantially in recent years with the widespread adoption of multiparametric MRIs (mpMRI) and transperineal biopsies, which have significantly reduced the risks associated with downstream diagnostic investigations following PSA testing.

Evidence indicates that the use of mpMRIs before a biopsy leads to a nearly 64% reduction in unnecessary biopsies, equivalent to approximately 602 fewer men undergoing a biopsy for every 10,000 men who receive a PSA test.⁹ In addition, transperineal biopsy techniques are associated with a 55% reduction in the number of men who develop sepsis, addressing one of the most serious historic complications of prostate biopsies.¹⁰

Crucially, mpMRI-led diagnostic pathways also substantially reduce the risk of overdiagnosis by improving the specificity of cancer detection. Evidence indicates a nearly 77% reduction in diagnoses of clinically insignificant prostate cancer, as men without suspicious MRI findings can safely avoid biopsy, and low-risk lesions are less likely to be detected incidentally.¹¹ These advances represent a step change in the balance of benefits and harms and should be given greater weight in assessing the overall value of a screening programme.

These are findings that are supported by the patient group community. As stated by Prostate Cancer Research in their response to the draft recommendation, “we agree that screening must be guided by robust evidence. But the reality is clear; the evidence has evolved, the harms caused by unnecessary tests and diagnostic procedures have fallen.”¹²

4. Updating cost-effectiveness modelling to reflect current thresholds and practice

We recommend that the UK NSC revisits its cost-effectiveness conclusions for targeted prostate cancer screening to reflect updated NICE QALY thresholds and contemporary clinical practice.

The cost-effectiveness modelling commissioned by the NSC and carried out by the Sheffield Centre for Health and Related Research (SCHARR) concluded that a screening programme for high-risk men would not be cost-effective. While we recognise the high costs associated with overdiagnosis that have contributed to this conclusion, we believe that some of the assumptions that underpin this modelling are now outdated.

One assumption is the use of a £20,000 per QALY threshold to measure cost-effectiveness, reflecting the National Institute for Health and Care Excellence’s base threshold at the time the analysis was undertaken.

As the Committee will be aware, this threshold is imminently set to increase to a range of £25,000 to £35,000 per QALY.¹³ This change has a material impact on what may be considered cost-effective within the NHS context and could alter conclusions about the viability of targeted prostate cancer screening approaches.

We therefore encourage the NSC to revisit cost-effectiveness conclusions in light of these updated thresholds as it deliberates on a final recommendation to present to the Government.

There are also concerns that the SCHARR modelling did not sufficiently consider what a screening programme would replace in terms of the status quo (i.e., delivering cost-savings by replacing opportunistic PSA testing with targeted screening towards men most at risk). The modelling may also attribute too much weight to the harms of overdiagnosis using insufficiently evidenced assumptions and overlooking the harms of underdiagnosis.

5. Capturing the full clinical and socio-economic value of earlier diagnosis

We recommend that the UK NSC ensures its cost-effectiveness assessment captures the full clinical and socio-economic value of earlier diagnosis, rather than focusing narrowly on direct healthcare costs and QALYs alone.

In addition to re-assessing assumptions around harms and cost-effectiveness thresholds, we believe it is important that modelling captures the full range of benefits associated with earlier diagnosis through screening. This includes not only survival gains and quality-of-life improvements for patients, but also wider socio-economic impacts such as the ability of individuals to remain in work, the reduced burden placed on informal carers, and the downstream savings associated with treating earlier-stage disease.

Analysis conducted by Deloitte UK for Prostate Cancer Research, which takes a more expansive view of the benefits of screening, concluded that a targeted prostate cancer screening programme could generate £54 million in net socio-economic benefits.¹⁴ These gains are driven in part by earlier treatment, reduced treatment intensity, and improved productivity outcomes.

It is also important to note that the NHS already undertakes large volumes of opportunistic PSA testing – around 6-9% of men receive a test each year.¹⁵ This occurs outside a structured screening framework and therefore lacks consistent safeguards, clear pathways, and equitable access. As a result, current practice can be ineffective, inconsistent, and inequitable. A targeted screening programme, centred on men at higher risk, would represent a more efficient and impactful use of spend, without requiring substantial additional investment.

Johnson & Johnson

The UK NSC should consider reviewing cost-effectiveness modelling to ensure that it looks at the following factors:

- The inefficiency of unstructured PSA testing as it currently takes place
- Equity issues in who can currently access testing
- Whether organised screening would offset the current, less efficient spend
- The impact on carers (i.e., reduced carer requirements from earlier stage diagnosis or the psychological/economic impact on carers of reduced late-stage diagnoses)
- Productivity gains from remaining in work and reduced sickness absence
- The economic value of earlier treatment

Summary Recommendations:

We recommend that the UK NSC:

- ensures any BRCA1/2-focused prostate cancer screening programme is proactive by design, rather than reliant on self-identification or voluntary presentation by men at risk.
- moves beyond a BRCA1/2-only recommendation and commits to developing a broader, risk-stratified prostate cancer screening approach that explicitly includes other high-risk groups, including Black men and men with a family history of prostate cancer.
- re-assesses the balance of benefits and harms of prostate cancer screening to fully reflect the impact of modern diagnostic pathways, including mpMRI-first approaches and transperineal biopsy techniques.
- revisits its cost-effectiveness conclusions for targeted prostate cancer screening to reflect updated NICE QALY thresholds and contemporary clinical practice.
- ensures its cost-effectiveness assessment captures the full clinical and socio-economic value of earlier diagnosis, rather than focusing narrowly on direct healthcare costs and QALYs alone

¹ Johnson & Johnson Data on File

² DHSC (2026) National Cancer Plan, available at: <https://www.gov.uk/government/publications/national-cancer-plan-for-england>

³ Ecancer (2025) ESMO 2025: Men with BRCA1 and BRCA2 gene mutations should get annual prostate cancer screening - ICR, available at: <https://ecancer.org/en/news/27145-esmo-2025-men-withbrca1andbrca2gene-mutations-should-get-annual-prostate-cancer-screening-icr>

⁴ Prostate Cancer UK (n.d.). Toolkit for Raising Prostate Cancer Awareness with Black UK Communities. Available at:

<https://prostatecanceruk.org/for-health-professionals/for-my-role/engaging-with-black-communities> [Accessed December 2025].

⁵ Prostate Cancer UK (2024) Our manifesto for the next Government, available at: <https://prostatecanceruk.org/get-involved/campaigning/our-manifesto-for-the-next-government>

⁶ World Health Organisation (n.d) Promoting Cancer Early Diagnosis, available at: <https://www.who.int/activities/promoting-cancer-early-diagnosis>

⁷ Europa Uomo (2026) National screening programme announced in Croatia, available at: <https://www.europa-uomo.org/news/national-screening-programme-announced-in-croatia/>

⁸ Patasius, A., & Smaliyte, G. (2019). Changing Incidence and Stage Distribution of Prostate Cancer in a Lithuanian Population-Evidence from National PSA-Based Screening Programme. International journal of environmental research and public health, 16(23), 4856. Available at: <https://pubmed.ncbi.nlm.nih.gov/31816821/>.

⁹ Prostate Cancer UK (n.d) Tens of thousands fewer men face harm in prostate cancer diagnosis, available at: <https://prostatecanceruk.org/for-health-professionals/for-my-role/fewer-men-face-harm-in-prostate-cancer-diagnosis>

¹⁰ Prostate Cancer UK (n.d) Tens of thousands fewer men face harm in prostate cancer diagnosis, available at: <https://prostatecanceruk.org/for-health-professionals/for-my-role/fewer-men-face-harm-in-prostate-cancer-diagnosis>

¹¹ Prostate Cancer UK (n.d) Tens of thousands fewer men face harm in prostate cancer diagnosis, available at: <https://prostatecanceruk.org/for-health-professionals/for-my-role/fewer-men-face-harm-in-prostate-cancer-diagnosis>

¹² Prostate Cancer Research (2025) The UK National Screening Committee decision falls short of targeted screening recommendation, available at: <https://www.prostate-cancer-research.org.uk/uk-nscc-decision-falls-short-of-targeted-screening-recommendation/>

¹³ Gov.uk (2025) Landmark UK-US pharmaceuticals deal to safeguard medicines access and drive vital investment for UK patients and businesses, available at: <https://www.gov.uk/government/news/landmark-uk-us-pharmaceuticals-deal-to-safeguard-medicines-access-and-drive-vital-investmentfor-uk-patients-and-businesses>

¹⁴ Prostate Cancer Research (2024) Socio-economic Impact of Prostate Cancer Screening, available at: https://www.prostate-cancer-research.org.uk/wp-content/uploads/2024/11/PCR_Socioeconomic_Impact_Prostate_Cancer_Screening_Nov24-v1.0.pdf

¹⁵ Young GJ, Harrison S, Turner EL, et al. Prostate-specific antigen (PSA) testing of men in UK general practice: a 10-year longitudinal cohort study BMJ Open 2017;7:e017729 <https://pubmed.ncbi.nlm.nih.gov/29084797/>

S68	Association of Directors of Public Health	Association of Directors of Public Health	We make the following observations in support of the draft recommendation: The ethics of screening • The benefits of screening are often overestimated, while the potential harms are often underestimated. For example, the impact of invasive biopsy and unnecessary treatment. • As a result of policy, these harms can grow from individual experience to impacting entire populations. • Screening can turn well people into patients, and this is very poorly understood. It means the ethical basis of screening is fundamentally different to the ethics of health care delivery. Therefore, the threshold for the risk/benefit of screening needs to be higher. • Studies can encourage optimistic coverage that misrepresents actual findings, which can in turn shape public, policy, and clinical opinions on screening. • For example, positive headlines on mortality rates were circulated after the follow-up of the European Randomised Study of Screening for Prostate Cancer (ERSPC). • This study seemed to confirm a 'sustained reduction in deaths', stating a 13% relative risk reduction after introducing Prostate Specific Antigen (PSA) tests. • However, the absolute risk reduction was 0.22%, reinforcing that the burden of diagnosis is rarely outweighed by its benefit. • The ERSPC also left out other important variables, like quality of life outcomes, which ignore the 'labelling effect' of diagnosis. This includes harms from overtreatment, such as experiences of impotence and incontinence. • Analysis from the ERSPC also shows little value in screening from the age of 70. • Overpromoting early detection may also increase the risk of harm, where those otherwise living well could encounter harm from both the screening process and during treatment. • Pushing for early detection may also increase diagnoses through case-finding without any concrete impact on health outcomes, which should remain the goal. • Screening is often seen as just the 'test' part of diagnosis. However, screening should be understood as a comprehensive programme, which includes other aspects such as quality assurance and failsafe procedures.

		• Screening ethics should be clearly explained to all audiences, extending beyond prostate cancer screening, and involve discussing potential negative impacts on those who are well. • In addition to the UK NSC infographic, it would be useful to provide a plain English description of when individual screening is appropriate. Shared decision-making • If UK NSC were to recommend screening, it would leave too much work to shared decision-making. • This would require significant resourcing and run the risk that under-resourcing could worsen harmful outcomes. Uneven resourcing across areas could also create a postcode lottery in screening quality, worsening health inequalities. • The reliability of shared decision-making is often overestimated, particularly the ability of clinicians to understand and then communicate statistical probabilities in a complex system. This is critical to informed consent. Men's health • Arguably, the prostate's link to sex has often led to prostate health being thought of and treated as part of men's health, risking overshadowing other important determinants and conditions affecting men. • There are other, more impactful targets for improving men's health. For example, addressing the negative health impacts that harmful products such as alcohol or tobacco have on men or prioritising the improvement of men's mental health. TRANSFORM trial • Proceeding with screening may significantly undermine the TRANSFORM trial, which will provide critical evidence to understand the risk/benefit balance of the contemporary screening question (PSA + MRI + genomic risk). • Screening may cloud the results of the trial, affecting their validity and making them difficult to interpret. • We agree that it is crucial that black men are well represented in the TRANSFORM trial, with Black British men two to three times more likely to receive prostate cancer diagnoses than white British men and twice as likely to die from prostate cancer. Use of resources • Spending money where there is insufficient evidence is unethical, displacing resources away from areas where there is clearer

			evidence of benefit and preventing us from finding out the ideal diagnostic mix for the men in the groups outlined.
S69	Rini Jones	NHS Race & Health Observatory	Dear Team, Please find attached the NHS Race & Health Observatory's response to the UK National Screening Committee's consultation on its recommendations regarding prostate cancer screening. Please do not hesitate to contact us should the Committee require any further clarifying information. Very best, Rini Jones

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name:	Rini Jones, on behalf of the NHS Race & Health Observatory	Email address:	*****
Organisation (if appropriate):	NHS Race & Health Observatory		
Role:	Senior Policy and Delivery Manager		
Do you consent to your name being published on the UK NSC website alongside your response?		Yes	
<u>About the NHS Race & Health Observatory</u>			
The NHS Race & Health Observatory is an independent expert body, established to identify and tackle the widespread inequity experienced in health and healthcare by minoritised ethnic patients, communities, and the workforce in England. We work as a proactive investigator: mobilising robust evidence, enabling impactful policymaking, and implementing long-term, transformational change across the health system. We welcome the opportunity to respond to the UK National Screening Committee's (UK NSC) consultation, recognising the central challenge of identifying potentially fatal, treatable disease, while avoiding the harmful overdiagnosis of incidental cancer. It is encouraging that the UK NSC is actively considering targeted screening for Black men and other high-risk groups, including men with a relevant family history and men with known BRCA1 and BRCA2 gene variants. We are, however, concerned by the UK NSC's decision to, at this stage, not recommend targeted screening for Black men.			
<u>Our key concerns</u>			
→ The draft recommendation to not introduce targeted prostate cancer screening for Black men risks entrenching structural inequity and systemic racism, by reinforcing a long-standing ethnic health inequality that is consistently reported in epidemiological data and through lived experience. Black men in the UK are two to three times more likely to be diagnosed with prostate cancer, and twice as likely to die from it, compared to their White counterparts. They are also more likely to be diagnosed younger and to present with more advanced diseaseⁱ ⁱⁱ. This disproportionate risk is one reason why targeted screening approaches warrant serious consideration.			
→ We identify substantive concerns with the quality of the SCHARR economic model. We contend that the evidence and data on which it relies are inappropriate, statistically flawed, and do not reflect modern care pathways - as a result, the model risks attenuating the benefits and inflating the perceived harms of introducing targeted screening for Black men.			
→ Two critical issues with the SCHARR economic model are (1) its omission of societal costs and the cost offset of late-stage disease management in Black men, and (2) that it relies on evidence which is unrepresentative of Black men - i.e., trials and studies in which Black men are almost entirely absent - to predict the benefits and risks of prostate cancer screening for Black men. This flawed approach not only casts doubt over the accuracy and relevance of the model's findings, it also raises an important question regarding evidentiary thresholds. Why is it considered tolerable to use data that does not represent Black men to model outcomes for them, while ostensibly dismissing a plurality of representative real-world data, qualitative lived experience data, and other evidence sources which outline how targeted screening could reduce inequalities for Black men?			
→ These issues takes on further significance, when accounting for the Public Sector Equality Duty, under which the UK NSC is legally required to consider whether their policies and decisions will have an unequal impact on populations with protected characteristics, and to take proportionate steps to mitigate this impact. While the UK NSC's close collaboration with the TRANSFORM Trial is greatly welcomed, we seriously question whether, in the meantime, it can be proportionate to maintain a recommendation of inaction based on a circular evidence gap in which Black men have been previously under-represented and excluded in prostate cancer trials, which is then used to justify the denial of targeted screening for them.			

→ **The UK NSC risks failing its legal duty to mitigate foreseeable and disproportionate harm: by proposing inaction for several years until the TRANSFORM Trial yields relevant data, while allowing the current opportunistic PSA testing programme to persist in full knowledge that it will continue to entrench inequalities and allow preventable deaths for Black men. We contend that a decision to not implement risk-stratified measures for a population at double the mortality risk constitutes a failure to provide equitable healthcare and may leave the NHS vulnerable to challenges of indirect discrimination.**

Summary of our response

- Circular evidence and under-representation of Black men
 - The data inputs used in the SCHARR economic model are based in evidence from trials and studies that are broadly unrepresentative of Black men, a statistically flawed approach. E.g., cost-effectiveness is significantly determined by predicted screening uptake, which is benchmarked using CAP Trial uptake rates. These benchmarked rates are used despite the very low, unrepresentative inclusion of Black men in the CAP Trial, and emerging indications that Black men's uptake would be higher under an organised offer. This approach risks biasing and underestimating the modelled cost-effectiveness against targeted screening for Black men. This approach also raises questions over the evidentiary thresholds used by the UK NSC, specifically, why unrepresentative data is apparently tolerable for modelling outcomes for Black men, whereas the plurality of evidence indicating that targeted screening would help prevent inequitable outcomes for Black men is not tolerable.
 - The UK NSC risks failing its obligations under the Public Sector Equality Duty to mitigate foreseeable and disproportionate harm to a group with a protected characteristic: by proposing inaction for several years until the TRANSFORM Trial yields relevant data, while allowing the current opportunistic PSA testing programme to persist in full knowledge that it will continue to entrench inequalities and allow preventable deaths for Black men. We contend that a decision to not implement risk-stratified measures for a population at double the mortality risk constitutes a failure to provide equitable healthcare and may leave the NHS vulnerable to challenges of indirect discrimination.
- Conflation of structural inequities with biology
 - US data are used to account for ethnic differentials in disease aggressiveness, with the SCHARR economic model cautioning that higher grade at diagnosis may reflect inequities in access to, and timeliness of, diagnosis, rather than biological differences, undermining generalisability to the UK. It is right that ethnic differentials in disease progression are interrogated in the UK context, a significant evidence gap that the TRANSFORM Trial among others aims to address.
 - We contend, however, that the strength of UK-based evidence of inequities that Black men face in accessing the current prostate cancer pathway does not receive due attention in the SCHARR economic model. Conflating the two affects both baseline risk and stage distribution inputs and amplifies the risk of misspecification, which in turn influences mortality benefits and quality-adjusted outcomes.
- Misalignment between modelled pathways and real-world diagnostics
 - The SCHARR economic model largely relies on trial data in which legacy protocols are used - where an elevated PSA test leads directly to biopsy. To account for this, evidence from 2017 is used to reflect the pre-biopsy mp-MRI pathway, where uptake rates, as previously stated, are based on unrepresentative CAP Trial data. We contend that as a result, the modelling does not truly reflect current care, which has changed significantly since 2017, and since the UK NSC's 2020 review of advances in diagnostic and treatment pathways on which the current recommendations are based.
 - The SCHARR economic model does not seem to account for real-world UK evidence indicating the harm reduction benefits of current mp-MRI-first diagnostic pathways, which significantly reduce unnecessary biopsies, overdiagnosis, and treatment-related harms. As a result, we contend the model risks overstating downstream harms from modelled screening scenarios. Because Black men are more likely to present with late, advance-stage disease, failure to model real-world mp-MRI-based pathways underestimates potential benefits from earlier, more accurate detection.
- Narrow cost perspective and omission of societal and system-wide benefits
 - The SCHARR economic model does not appear to consider the significant economic cost resulting from the exacerbated harms that Black men face in the current, inequitable programme of opportunistic PSA testing; further negatively influencing modelled cost-effectiveness. Focusing predominantly on direct healthcare costs omits substantial downstream savings from the earlier diagnosis of Black men (e.g., reduced late-stage treatment, palliative care in high-cost settings) and broader societal costs (e.g., time spent in paid work, in providing unpaid care), which external economic studies indicate are material. We contend that because Black men are more likely to present late, underestimating the costs of late-stage disease disproportionately undervalues the cost benefits of

targeted screening in modelled outcomes.

- Further, the SCHARR economic model assumes a stable backdrop of opportunistic PSA testing even if a structured screening programme is introduced, and assumes this will have no health economic impact. Given rising awareness and current high volumes of opportunistic PSA testing, this assumption is unlikely to hold and obscures both displacement effects and equity impacts (opportunistic testing disadvantages Black men). We contend that if structured screening partially substitutes opportunistic testing, it could reduce harm caused by inequitable access, altering both costs and health outcomes relative to the model's base case.
- BRCA-focused recommendation without addressing inequities
- Proposed screening for men with BRCA1/2 variants, while welcome, does not account for known inequities in access to genetic testing. The SCHARR economic model assumes knowledge of one's BRCA status increases with age, based on a single study which does not report the ethnicity of participants, casting doubt on the applicability of findings for men with BRCA1/2 variants more broadly, as well as for other high-risk groups, including Black men. Ethnic inequities in access to genomic medicine and genetic testing risk widening disparities if a BRCA-only screening programme proceeds, without concurrent action to address emerging evidence on the genetic risk profile of Black men, and to address existing inequities in opportunistic PSA testing.
- The SCHARR economic model also does not account for the cost of genetic testing. We contend this is a significant oversight which raises further questions regarding the apparent inconsistency of evidentiary thresholds in this review.

Recommended direction of travel

We encourage the UK NSC to work with sector experts in ethnic prostate cancer inequity to reappraise the SCHARR economic model's findings through an equity-sensitive lens which accounts for the impact of structural and systemic racism. This reappraisal should account for evidence of advances in the current post-PSA-testing standard of care, the health and economic costs of existing inequities and harms entrenched by opportunistic PSA testing, ethnic differentials in screening uptake, and broadened cost perspectives. This activity should also interrogate the emerging evidence on the genetic risk profile of Black men, to consider actions to remediate genomic medicine access gaps.

Critically, this will require the UK NSC to work in sustained and meaningful partnership with Black patients and communities and the expert community-led organisations that support them. This will ensure the development of screening recommendations accounts for critical lived expertise and ethnic differentials.

Combined, the UK NSC will be better equipped to re-model the benefits and risks of targeted prostate cancer screening without entrenching circular evidence gaps. This will enable the UK NSC to assess how existing evidence can be mobilised to deliver interim, appropriately risk-stratified screening interventions for Black men ahead of the Transform Trial's results.

Section and/or page number	Text or issue to which comments relate	Comment
		<i>Please use a new row for each comment and add extra rows as required.</i>
General comment	The UK NSC draft recommendation to not introduce targeted screening for Black men The recommendation to not introduce targeted screening for Black men risks reinforcing a long-standing and well-documented health inequality. Throughout the UK NSC's 2025 documents, a lack of sufficient clinical trial data involving Black men is provided as a reason for not recommending targeted screening. We contend that this creates a circular evidence gap: Black men have been historically under-represented and excluded in prostate cancer trials, leading to weaker subgroup-specific evidence, which is then used to justify continued inaction, allowing the current programme of unorganised and inequitable opportunistic PSA testing to continue. This approach risks perpetuating avoidable late diagnoses and excess mortality in a population already known to be at higher risk, which must be given due consideration when balancing the risks associated with overdiagnosis. In response to this draft recommendation, we sought insights from the NHS Race & Health Observatory Stakeholder Engagement Group (RHO SEG). The RHO SEG is a multi-disciplinary advisory group of Black, Asian, and minoritised ethnic patients, healthcare professionals, and community members with lived experience of, or professional expertise in, ethnic health inequity. They underscored that: • From a health equity and human rights perspective, the absence of perfect trial data should not be used to justify policies that produce foreseeable and disproportionate harm to a group with a protected characteristic. Under the Public Sector Equality Duty, public bodies are legally required to consider whether apparently neutral policies have unequal impacts and take proportionate steps to mitigate them. It is questionable that this draft recommendation is proportionate given the well-evidenced and disproportionate risk of avoidably poor prostate	

	cancer outcomes faced by Black men. It is also questionable that this recommendation is aligned with the NHS' stated commitment to reducing racial and place-based health inequalities. - While the UK NSC's close collaboration with the TRANSFORM trial is welcome, it is worth noting that the earliest meaningful findings to inform screening decisions will not be available for two to three years. Ostensible inaction as we await future trial results while known inequalities persist risks indirect discrimination. - Importantly, this issue is not abstract or hypothetical. RHO SEG members highlighted the work of 1in4 Prostate Cancer Support Groupⁱⁱⁱ a Sheffield-based, Black-led prostate cancer support charity, which provides UK-specific, lived experience evidence of these inequities. 1in4 operates within the wider ecosystem of Sheffield African Caribbean Mental Health Association (SACMHA) and exists precisely because mainstream prostate cancer pathways have not adequately met the needs of Black men and their families. The sustained demand for 1in4's services reflect ongoing patterns of late diagnosis, psychological distress, mistrust of statutory services, and poorer outcomes for Black men navigating prostate cancer care. As a community-embedded organisation, 1in4 provides place-based evidence that complements national datasets and highlights how inequities manifest locally. This aligns directly with Patient and Carer Race Equality Framework's^{iv} emphasis on valuing lived experience, VCSE leadership, and culturally competent insight as legitimate forms of evidence for service design and policy development. - RHO SEG members also underscored that the UK NSC's framing of the evidence, and the reasons it provides to not recommend targeted screening, do not appear to be transparent. The purpose of the PSA test is to screen, not to diagnose. As with other screening tests, a PSA test does not automatically trigger treatment, its purpose is to determine whether further diagnostic investigations are needed. The impression given is that is the UK NSC has made the recommendation to reduce the burden of investigations on the NHS, to avoid investment in staff and resources to deliver a targeted screening programme and ensuing diagnostic tests, without sufficient regard to the health and wellbeing of Black men. - Risk-stratified approaches, such as targeted screening, offer clear, proportionate alternatives to both inaction and blanket screening. Inaction could also be prevented with the provision of an interim, evidence-informed pathway for Black men, e.g., with structured prostate cancer risk discussions embedded within NHS Health Checks and by updating NICE Guidelines that prevent GPs from raising PSA testing with patients. Such interventions would support informed choice, earlier detection of disease, and the generation of UK-specific data, while minimising the harms associated with mass screening.
UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative (the 'UK NSC 2025 evidence review') Key inputs (data) into the model; The diagnosis and treatment pathway, Section 4.4., page 11.	<i>After the PSA test, people who screen positive are offered multiparametric magnetic resonance imaging (mp-MRI) before their biopsy. It was assumed that the uptake of the tests within the diagnosis pathway would be higher than the screening test, because people are more likely to take up further testing when they think it will directly benefit them. The uptake of the mp-MRI was assumed to be the same as the uptake of the biopsy, drawn from CAP trial data: 85%. The type of biopsy modelled was a local anaesthetic transperineal prostate biopsy (LATP biopsy), because this is now the more common technique. If the biopsy then identified someone as having prostate cancer, they would either:</i> <i>receive immediate treatment, and move onto a 'surveillance' pathway, with a follow-up PSA test every 6 months for the first 2 years after treatment, and then at least once a year after that; or</i> <i>not receive immediate treatment but instead fall under 'active surveillance,' (or watchful waiting) where they would receive:</i> Accounting for the real-world impact of mp-MRI in reducing avoidable harm post-PSA test: - We are concerned that the narrative of the UK NSC 2025 evidence review does not reflect the evidenced, positive impact of mp-MRI in increasing diagnostic accuracy, reducing unnecessary biopsies, and the associated harms of both biopsy and further treatment. The absence of this contextual framing suggests that a positive PSA test necessarily and immediately leads to a biopsy and future harms. - This apparent elision fails to clarify that in current, real-world practice, a positive PSA test is the start of a sophisticated diagnostic pathway which has been recommended since 2019 by NICE (NG131)^v and widely implemented across the NHS, in which mp-MRI follows a positive PSA test, and does not necessarily and immediately lead to a biopsy. - This is compounded by the approach taken in the SCHARR economic model. Modelling was designed to reflect the screening protocol in the CAP Trial in which mp-MRI was not part of the protocol and in which '<i>all men with elevated PSA levels underwent biopsy directly.</i>' To reconcile this difference, the model was adjusted based on data from Ahmed et al. (2017), in which the final analysis is based on 576 men, 39 of whom were Black or Black

	- In the first 12-18 months: PSA test every 3-4 months in the first-year post-diagnosis, a digital rectal examination (DRE) at 12 months, and an mp-MRI at 12-18 months; then - From 2 years' on: a PSA every 6 months and DRE every 12 months. The treatments for prostate cancer included in the model were surgery, radiotherapy, chemotherapy, and hormone treatment. Each of these treatments has some associated risks. Hormone therapy is associated with lifelong physical and emotional harms such as erectile dysfunction, mood changes, osteoporosis, diabetes and heart disease. Surgery (radical prostatectomy) reports common side effects like blood clots, infection and a much higher risk of urinary incontinence following this treatment. Radiotherapy may lead to a higher risk of bowel incontinence as well as erectile problems particularly in the first 6 months, while chemotherapy can lead to hair loss, mouth sores, and possible nerve damage. Those who do not receive treatment but are under active surveillance may also feel distressed by the impression that they have an 'untreated' cancer.	British^{vi}. 4. The modelled screening scenarios were then compared 'against 'usual care' – in other words, what testing and treatment is happening now in practice, without a national screening programme'. 4.1. We contend that the UK NSC should have considered the real-world evidence indicating that 'usual care' and the use of mp-MRI has changed significantly since Ahmed et al. (2017) and the UK NSC 2020 evidence review on which the 2025 draft recommendations are based; and that these changes in clinical practice have improved outcomes among men with higher-risk localised and locally advanced stages of the disease - with pertinent implications for Black men. 4.2. Studies published in the years since 2020 indicate that modern mp-MRI-first diagnostic pathways can halve overdiagnosis, dramatically reduce unnecessary biopsies (by between 21%-49%), and cut biopsy-related infections by up to 90% in NHS practice^{vii viii ix}. Analysis of real-world data shows that this is being delivered in clinical practice^x. 4.3. This outlines a more accurate post-PSA test diagnostic pathway, with reduced biopsy harms, that either reduces detection of low-risk disease or enables its more accurate stratification. This provides the opportunity for an active surveillance regimen that does not require repeat biopsy and enables the side-effects associated with radical treatments to be delayed or avoided.
SCHARR Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk (the 'SCHARR economic model') Model Validation and technical characteristics; CAP trial, Section 7.2.1, page 81.	The model's screening arm was designed to reflect the screening protocol used in the CAP trial. In the CAP trial, men aged 50 to 69 years from participating general practices were randomised, with screening offered to men in the intervention arm. The median age at screening among attendees was 59 years, so the model simulated a single screening event at age 59 to align with this. Men with PSA levels ≥ 3.0 ng/mL were offered a standard 10-core transrectal ultrasound-guided biopsy. As mpMRI was not part of the CAP trial protocol, the model similarly assumed that all men with elevated PSA levels underwent biopsy directly. PSA and biopsy uptake rates were based on CAP trial data: 36% and 85%, respectively. Although the CAP trial used TRUS, the current model uses LATP biopsy. To reconcile this difference, biopsy accuracy in the model was adjusted based on data from Ahmed et al. (2017), assuming 30% sensitivity for low-grade and 70% sensitivity for high-grade cancers (except for those with stage 4 cancer).	5. Given the evidence that Black men are significantly more likely to be diagnosed late and with advanced forms of cancer, we contend that the UK NSC should consider equity-sensitive modelling and interpretations which account for the specific potential benefits for Black men from changes to real-world post-PSA test diagnostic and treatment practice. 5.1. In equity-sensitive modelling and interpretation, these specific benefits should be measured against the inequitable outcomes opportunistic PSA testing entrenches for Black men in current 'usual care', alongside the broader harms generally associated with PSA testing (which we outline in 22.1. - 22.3.)
UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying	In October 2025, the ERSPC published the results of follow-up at 23 years. The study found that prostate cancer screening reduced deaths by 0.22% in absolute terms among men who were screened compared to those who were not. This means that prostate cancer screening using PSA testing can prevent about one prostate cancer death	<u>The risk/benefit balance of screening for Black men:</u> 6. The ERSPC study follow-up at 23 years indicates that prostate cancer screening using PSA testing has a clear, increasing benefit to prostate cancer-specific mortality reduction over time, when compared to the results of their follow-up at 16 years (in which 1 death was averted for every 628 men screened and for every 18 men diagnosed)^{xi}.

Narrative (the 'UK NSC 2025 evidence review') Section 2.3., page 6.	<i>for every 456 men invited to screening over a 20+ years period, demonstrating a very small benefit. Yet the harms associated with the screening offer would remain high as screening increased the number of men diagnosed with prostate cancer by about 30% of which half are likely to be overdiagnosis which would then lead to overtreatment. The study estimated (at current follow up) that for every 1 prostate cancer death averted there are 12 men overdiagnosed who may have received unnecessary treatments and side effects, and many more men with cancer diagnosed at screening for whom screening does not extend their life. These data were published after the economic model was developed. However, the model predictions were compared with these 23 years of follow-up results and were almost identical in the number of overdiagnoses and the reduction in mortality.</i>	6.1. It has been argued that the results of the follow-up at 23 years indicate that the benefit of reduction in cancer-specific mortality, i.e., that 12 cases need to be diagnosed to avert 1 prostate cancer death, is now nearer to the figures observed in breast cancer screening programmes in which, e.g., 28 cases need to be diagnosed to save 2.5 lives^{xii}. 7. While the harms of overdiagnosis are important to acknowledge, it is worth noting that the original 2009 ERSPC study did not report specific ethnicity data for its participants^{xiii}. The reported ratio at 23 years follow-up (1 death averted per 12 men diagnosed) is likely much more favourable for Black men, because their baseline risk of death is twice as high than for White men. It is not clear how the SCHARR economic model accounted for this, which raises questions over the UK NSC's conclusion that '<i>results [...] were almost identical in the number of overdiagnoses and the reduction in mortality</i>' and how this applies to Black men. 8. Further, mp-MRI was not part of the ERSPC protocol. The SCHARR economic model accounts for this by assuming '<i>the combined diagnostic accuracy of DRE and TRUS to be equivalent to mpMRI to simplify the modelling (with 100% uptake, considering no data on uptake for these tests were reported)</i>' (Section 7.2.2., page 82). 8.1. On this point, we reiterate the contentions outlined in 1 - 5. Indeed, the follow-up study at 23 years highlights that a '<i>stepwise, risk-based approach, guided by risk stratification tools such as risk calculators and magnetic resonance imaging, limits biopsies to men with a confirmed elevated risk, a strategy that breaks the traditional link between elevated PSA and immediate biopsy. Several ongoing, population-based, randomized screening trials that incorporate a risk-based screening approach have shown a reduction in unnecessary biopsies and detection of low-grade prostate cancer while maintaining detection of high-grade cancers. This improved ratio of the detection of high-grade to indolent cancers, as compared with traditional PSA-based screening, suggests a substantial reduction in overdiagnosis.</i>^{xiv} 9. Given the disproportionate, distinctly poor outcomes faced by Black men in the UK, we question the UK NSC's extrapolation of the ERSPC's findings, and whether the conclusion that such a programme demonstrates '<i>a very small benefit</i>' can accurately apply to Black men, or other high-risk groups.
UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative (the 'UK NSC 2025 evidence review')	<i>The model included a data point which suggested that people of Black ethnicity have a greater likelihood of being in a higher GGG (meaning a more aggressive cancer), based on data from the USA. There is uncertainty as to whether these data apply to a UK context. For example, men in the USA may present to healthcare later in their disease progression due to barriers to accessing privately-funded healthcare rather than any natural predisposition to more aggressive prostate cancer, so this trend may not be visible in the UK. This is an area of uncertainty and may mean the model overestimates the aggressiveness of</i>	<u>Acknowledging racism and ethnic inequities in access, diagnosis, and care pathways:</u> 10. Prostate Cancer UK's analysis of the latest data from the 2025 National Prostate Cancer Audit (NPCA) indicates that Black men are more likely than White men to be diagnosed with advanced, Stage 3 or 4 prostate cancer. These NPCA figures demonstrate that in England, Black men are nearly 50% more likely to be diagnosed with late stage prostate cancer, compared to White men^{xv}. 11. Evidence indicates that, when prostate cancer is diagnosed at the same stage and treated comparably, survival outcomes for Black and White men

Key inputs (data) into the model; Disease progression, Section 4.5., page 13.	<i>prostate cancer in Black men and therefore the benefit associated with screening in this group. All other non-White ethnicities were assumed to have the same probability of a GGG as those from a white ethnicity.</i>	are broadly equivalent^{xvi}. This strongly indicates that in the UK, differences in mortality are not inevitable, or necessarily a biological certainty, but are driven by well-known inequalities in access, diagnosis, and care pathways rooted in structural and systemic racism. The disproportionality of advanced presentation, and the driving impact of inequalities, is clear in the UK context.
<u>SCHARR Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk</u> (the 'SCHARR economic model') Data limitations and requirements; Data on Black ethnicity, Section 10.4., page 181.	<i>The model assumed that Black men have a higher probability of presenting with advanced GGG at diagnosis, and - since progression speed in the model is correlated with GGG - a faster disease progression overall. This assumption was informed by US-based data, as no equivalent UK data were identified (see Section 5.5). However, the higher GGG at diagnosis observed in US studies may reflect health inequalities rather than biological differences. Therefore, these data may not be generalisable to the UK context.</i>	12. The SCHARR economic model does not account for the failure of the current prostate cancer pathway to provide equitable outcomes, relying instead, on assumptions from US data. 13. We contend that the strength of UK-based evidence of inequities that Black men face in accessing the current prostate cancer pathway does not receive due attention in the SCHARR economic model. This affects both baseline risk and stage distribution inputs and amplifies the risk of misspecification, which in turn influence mortality benefits and quality-adjusted outcomes.
<u>SCHARR Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk</u> (the 'SCHARR economic model') Modelling results; Men of Black ethnicity, Section 8.2., pages 106 - 120.	Modelling results; Men of Black ethnicity, Section 8.2., pages 106 - 120.	<u>The importance of ethnic differentials in screening uptake:</u> 14. The SCHARR economic model assumed the screening uptake rates used in the UK CAP Trial: <i>'Not everyone who is eligible for prostate cancer screening will necessarily accept their invitation to have a screening test. The model assumed the base case – or benchmark – uptake of prostate cancer screening to be 36%, based on data from the UK CAP Trial.'</i> (Section 4.2.2.). 15. However, the UK CAP Trial, in outlining the limitations of its study, stated that <i>'few Black men, who are at higher risk of prostate cancer, were included'</i>^{xvii}. The CAP Trial had roughly 0.5% - 1% Black representation, as such, using its 36% uptake rate to model a targeted programme for Black men is statistically flawed. This is a key consideration when assessing the determining impact of uptake to the net monetary benefit (NMB) in the SCHARR economic model. 16. Given the difference in NMB exhibited in Section 8.2. of the SCHARR economic model, when comparing scenarios with 100% screening uptake (where NMB is generally positive), to scenarios using the CAP Trial's base uptake (where NMB is generally uncertain or negative), there is a material risk that the SCHARR economic model draws inaccurate conclusions for the cost-effectiveness of targeted screening for Black men and high-risk groups. 17. We contend that the UK CAP Trial's screening uptake rates do not account for ethnic differentials in uptake, and that using them in the SCHARR economic model calls the findings into question. We contend that screening uptake for Black men would likely differ to the UK CAP Trial's rates, given

		the multiple factors that can influence Black and minoritised ethnic groups' health-seeking behaviour (e.g., trust, health literacy, awareness)^{xviii}. Accounting for these differentials could positively impact the cost-effectiveness of targeted screening. 17.1. This is especially relevant considering emerging grey evidence, e.g., in a 2025 nationally representative Healthwatch poll of 3,575 men in England, 79% of all men responded that they would be likely to attend an appointment when invited, if the NHS introduced routine prostate cancer screening; this figure rose to 81% for Black men^{xix}.
SCHARR Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk (the 'SCHARR economic model') Description of screening scenarios, 7.3.4., page 88.	<i>All organised screening scenarios were compared against the standard of care. The standard of care was selected as the sole comparator because reconstructing a true “no screening” scenario was not feasible within the project timeframe and given the available data. In this context, cancer cases detected in the standard care arm represent a mix of cases identified through symptoms, PSA testing performed during investigations for other conditions (i.e. incidental findings), and opportunistic screening. Modelling the comparator arm as a combined group of cancers detected under the standard of care is not expected to substantially affect the cost-effectiveness outcomes. This is because, in the model, average costs, utilities, and survival are assigned to each detected cancer case instead of pathway-specific follow-up strategies; consequently, the overall impact reflects the mean outcomes across these diagnostic pathways. The decision to include only one comparator—the standard of care—was also driven by practical considerations. Modelling a “no screening” scenario would have required calibration to pre-PSA era data, which are outdated (see the calibration section). Moreover, the absence of reliable information on 89 opportunistic screening uptake makes it difficult to accurately construct either a “no screening” or a “current care” scenario.</i>	<u>Accounting for the impact of a screening programme on opportunistic PSA testing:</u> 18. The SCHARR economic model assumes that such a screening pathway would sit on top of, rather than replace, the current opportunistic approach in which men aged over 50 can request a PSA test from their GP, in line with the Government's Prostate Cancer Risk Management Programme. 19. The knock-on assumption made in the model is that the number of men voluntarily asking their GPs for tests would not change if a new screening protocol was introduced. We contend that this is a significantly uncertain - arguably unrealistic - assumption, especially when as of 2026, prostate cancer has now surpassed breast cancer as the most diagnosed cancer across the UK. This has been driven by much greater awareness of the disease, which has encouraged more men to query their risk profile and come forward for PSA tests^{xx}. 20. The NHS already pays for large volumes of opportunistic PSA testing; but without the safeguards of a structured pathway for Black men, it remains ineffective, inconsistent and inequitable (which we detail in 22.1. - 22.3.) 21. We question the assumption that the introduction of the UK NSC's draft recommendation to introduce screening for men with the BRCA1 and BRCA2 variants would not drive greater awareness for other men, including Black men, to request PSA testing; and that the impact on opportunistic PSA testing uptake would '<i>not [be] expected to substantially affect the cost-effectiveness outcomes</i>' of the SCHARR economic model. 22. The SCHARR economic model does not account for the further cost implications arising from the inequities entrenched by the current opportunistic PSA testing programme. Unlike other structured screening programmes, opportunistic PSA testing advantages men who are more health literate and from less deprived backgrounds - disadvantaging Black men, who are more likely to live in deprived areas and for whom we know that health literacy and engagement is lower^{xxi}. The inequities that opportunistic PSA testing entrenches are well-evidenced: 22.1. Men living in more deprived areas are more likely to be diagnosed with metastatic prostate cancer^{xxii}. Black men are disproportionately more likely to live in more deprived neighbourhoods^{xxiii}, which

		compounds the risk they face. 22.2. It is worth noting that ethnic prostate cancer mortality disparities persist at every level of deprivation, which underscores the role of structural and systemic racism, inequalities in access, and other factors^{xxiv}, e.g., a survey of 2,000 Black individuals found that 62% of respondents believed that racial discrimination stopped them or a loved one from being screened for prostate cancer^{xxv}. 22.3. In most cases, PSA testing is only accessible via GPs, and through over-stretched GP resources - troubling in light of the repeated lived experience testimony of men who are not taken seriously when requesting a PSA test, and evidence indicating that 1 in 3 people from minoritised ethnic backgrounds require three or more GP visits before being diagnosed with cancer^{xxvi xxvii}.
<u>SCHARR Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk</u> (the 'SCHARR economic model') Costs estimation, Section 6.11., page 72.	Costs estimation, Section 6.11., page 72.	<u>Accounting for the cost savings incurred through early diagnosis, to the healthcare system and to society more broadly:</u> 23. We contend that the SCHARR economic model underestimates the cost benefit of targeted screening for Black men through its near-singular focus on direct healthcare and public social services costs; it does not account for the cost-offset of late-stage disease management and it omits societal costs. The model therefore fails to consider how diagnosing and treating Black men earlier could save costs elsewhere in the healthcare system and to society. 24. Black men are disproportionately represented in late-stage (Stage 3 and 4) diagnoses. The economic burden of managing metastatic castrate-resistant prostate cancer, including high-cost drug regimens (e.g., Abiraterone, Enzalutamide), frequent hospitalisations for skeletal-related events, and end-of-life palliative care is significantly higher than the one-off costs of radical treatment for localised disease. By failing to model the cost-offset generated by shifting Black men from late-stage to early-stage diagnosis, the SCHARR economic model artificially inflates the perceived cost of a screening programme. 25. Given that Black men are often diagnosed younger, often in their 50s, the societal cost of premature mortality and morbidity is substantial. This includes the loss of economic productivity, reduced tax contributions, and the informal care burden placed on families and community networks. A targeted screening programme that preserves life years in this working-age cohort offers a high return on investment that is currently invisible in the SCHARR economic model's framework. 26. In 2024, independent modelling by Deloitte UK commissioned by Prostate Cancer Research^{xxviii} accounted for the costs to individuals (e.g., out of pocket costs), to the healthcare system (e.g., additional costs to other parts of the system incurred through late or missed diagnosis), and to society (e.g., lost working hours, informal caring hours, etc.). It showed that: 26.1. Late-stage treatment averages £127,000 per patient versus £13,000 for early-stage. This disparity also raises questions over the

		SCHARR economic model's estimation of palliative care costs (Section 6.11.7., page 79), in which costs were assumed to equate to roughly 12 months of care. Black men are more likely to be diagnosed with prostate cancer at advanced stages and they are less likely to receive the best treatments available when their prostate cancer is found to be incurable. It has also been evidenced that terminally ill Black and minoritised ethnic people are much more likely to receive palliative care, and die, in hospital^{xxix} - which costs 5 times more than in primary, community health, and hospice care settings^{xxx}. The absence of consideration of the cost impact of ethnic differentials in palliative care in the SCHARR economic model raises further questions over the NMB findings for Black men. 26.2. Introducing a 5-year screening programme for Black men aged 45-69, using the current diagnostic and treatment pathway, would yield a net £7m net positive socioeconomic impact over 30 years. This is driven by lower diagnosis costs due to high prevalence as well as improved survival outcomes and life expectancy. 27. 2025 modelling by Carnall Farrar commissioned by Prostate Cancer Research^{xxxi} indicates the practicality and affordability of targeted prostate cancer screening. Findings suggest that a programme for Black men and men with a relevant family history will cost the NHS roughly £25m annually - 0.01% of the NHS budget; involve a roughly 23% increase in the number of PSA tests, mp-MRIs, and biopsies delivered; require an uplift in NHS workforce FTE roles from 0.01% - 0.4%; and reduce entrenched inequalities for Black men, those with a relevant family history, and those in areas with high levels of deprivation. 28. These models, which account for real-world data and current practice, present a compelling economic case, opening a path to increased capacity within existing resources. We encourage the UK NSC to include a sensitivity analysis that specifically weighs the high-intensity cost of late-stage treatment in Black men against the upfront costs of a targeted, mp-MRI-supported screening pathway. This would acknowledge that for the Black population, the dominant fiscal driver quantifying harm is the cost of inaction (treating preventable, advanced diseased), rather than solely the cost of treating overdiagnosed patients.
SCHARR Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk (the 'SCHARR economic model') Model population; Known BRCA1,2	Model population; Known BRCA1,2 status, Section 6.4.2., page 31.	<u>The need to consider ethnic inequities in access to genetic testing</u> 29. The SCHARR economic model assumed that knowledge of one's genetic status would increase with age. In outlining its limitations, it also did not <i>'incorporate a correlation between ethnic familial history because of no data describing three-factors correlations: BRCA carrier, familial history and ethnicity'</i> as the <i>'limitation was considered to be minimal in the model, since the RR of Black ethnicity was not adjusted for familial history in the used literature.'</i> (Section 10.3., page 179). 29.1. That the evidence on which this age-specific assumption appears to be based on single, West England-focused study - Forde et al.

status, Section 6.4.2., page 31.		(2020) - raises questions about its generalisability and the accuracy of the conclusions drawn by the UK NSC^{xxxii} 30. We are concerned that this assumption does not account for known ethnic inequalities in access to genetic testing attested to in the evidence base, including by the NHS Race & Health Observatory's review on ethnic inequity in genomics and precision medicine^{xxxiii}, and reflected in the model's own limitations: '<i>UK Biobank is not representative of the general UK population and that it underrepresents individuals of Black ethnicity. Since both ethnicity and BRCA1/2 mutations are genetically inherited, reliance on Biobank data may underestimate BRCA mutation prevalence.</i>' (10.3., page 179). 30.1. Without addressing inequalities in who is offered and able to access BRCA testing, this approach risks benefiting a narrower and more advantaged subset of the population. 30.2. We contend that this is an oversight, in light of the potential impact that such consideration could have on mutually strengthening the harm reduction- and cost-effective cases for targeted screening for Black men, men with known BRCA 1 or BRCA 2 status, and men with a higher familial risk.
SCHARR Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk BRCA carriers: Conclusion, Section 10., page 175.	<i>This study did not evaluate the cost-effectiveness of BRCA testing itself, which should be examined separately. In addition, because prostate cancer-specific data for BRCA carriers are limited, the model assumed similar costs, utilities, and stage-specific survival to those of other groups, adding uncertainty to projections for this population.</i>	<u>Accounting for the cost of BRCA - and wider genetic - testing</u> 31. We agree that the absence of consideration of the cost-effectiveness of BRCA testing itself raises questions over the SCHARR economic model's findings. We contend that it also raises questions over: 31.1. Rationale, especially given the model's recognition that further work should be undertaken to account for broader health and economic implications of testing, and that this represents an important opportunity for higher-risk groups (Section 10.3, page 179). 31.2. The thresholds for inclusion and consideration of evidence in the modelling for other high-risk groups, as it is not clear why such a critical cost would be excluded for this group, or why this uncertainty is tolerable over others. 32. We agree that further work should take place to determine the health impact and cost-effectiveness of BRCA - and wider genetic - testing, for the reasons we have detailed, but also because of new evidence ^{xxxiv} ^{xxxv} shedding light on the specific genetic factors driving Black men's prostate cancer risk.
<u>Recommended direction of travel</u> We encourage the UK NSC to work with sector experts in ethnic prostate cancer inequity to reappraise the SCHARR economic model's findings through an equity-sensitive lens which accounts for the impact of structural and systemic racism. This reappraisal should account for evidence of advances in the current post-PSA-testing standard of care, the health and economic costs of existing inequities and harms entrenched by opportunistic PSA testing, ethnic differentials in screening uptake, and broadened cost perspectives. This activity should also interrogate the emerging evidence on the genetic risk profile of Black men, to consider actions to remediate genomic medicine access gaps. Critically, this will require the UK NSC to work in sustained and meaningful partnership with Black patients and communities and the expert community-led organisations that support them. This will ensure the development of screening recommendations accounts for critical lived expertise and ethnic differentials. Combined, the UK NSC will be better equipped to re-model the benefits and risks of targeted prostate cancer screening without entrenching circular evidence gaps. This will enable the UK NSC to assess how existing evidence can be mobilised to deliver interim, appropriately risk-stratified screening interventions for Black men ahead of		

- ⁱ Dee EC et al. 2025. *Racial disparities in prostate cancer in the UK and the USA: similarities, differences and steps forwards*. Nat Rev Urol 2025;22:223-34. doi:10.1038/s41585-024-00948-x pmid:39424981
- ⁱⁱ Butler EN et al. 2020. *Fatal prostate cancer incidence trends in the United States and England by race, stage, and treatment*. Br J Cancer 2020;123:487-94. doi:10.1038/s41416-020-0859-x pmid:32433602
- ⁱⁱⁱ 1 in 4 Sheffield Prostate Cancer Support Group. Available at: <https://www.1in4spsg.org/>
- ^{iv} NHS England. *Patient and carer race equality framework (PCREF)*. Available at: <https://www.england.nhs.uk/mental-health/advancing-mental-health-equalities/pcref/>
- ^v NICE. 2019. *Prostate cancer: diagnosis and management NICE guideline*. Available at: <https://www.nice.org.uk/guidance/ng131/resources/prostate-cancer-diagnosis-and-management-pdf-66141714312133>
- ^{vi} Ahmed et al. 2017. *Supplementary appendix, 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
- ^{vii} Norori N et al. 2024. *Using real world data to bridge the evidence gap left by prostate cancer screening trials*. ESMO Real World Data and Digital Oncology, Volume 6, 2024, 100073, ISSN 2949-8201, doi: 10.1016/j.esmorw.2024.100073
- ^{viii} Hugosson J et al. 2022. *Prostate Cancer Screening with PSA and MRI Followed by Targeted Biopsy Only*. N Engl J Med. 2022 Dec 8;387(23):2126-2137. doi: 10.1056/NEJMoa2209454.
- ^{ix} Tesfai A et al. 2024. *The impact of pre-biopsy MRI and additional testing on prostate cancer screening outcomes: A rapid review*. BJUI Compass. 2024; 5(4): 426–438. <https://doi.org/10.1002/bco2.321>
- ^x Norori N et al. 2024. *Using real world data to bridge the evidence gap left by prostate cancer screening trials*. ESMO Real World Data and Digital Oncology, Volume 6, 2024, 100073, ISSN 2949-8201, doi: 10.1016/j.esmorw.2024.100073
- ^{xi} Hugosson J et al. 2019. *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. PMID: 30824296; PMCID: PMC7513694.
- ^{xii} Duffy SW et al. *Absolute numbers of lives saved and overdiagnosis in breast cancer screening, from a randomized trial and from the Breast Screening Programme in England*. J Med Screen. 2010;17(1):25-30. doi: 10.1258/jms.2009.009094. Erratum in: J Med Screen. 2010 Jun;17(2):106. PMID: 20356942; PMCID: PMC3104821).
- ^{xiii} Schröder FH et al. 2009. *Screening and Prostate-Cancer Mortality in a Randomized European Study*. New England Journal of Medicine, 360(13), pp.1320–1328. doi:<https://doi.org/10.1056/nejmoa0810084>.
- ^{xiv} Roobol, MJ et al. 2025. *European Study of Prostate Cancer Screening — 23-Year Follow-up*. New England Journal of Medicine, 393(17), pp.1669–1680. doi:<https://doi.org/10.1056/nejmoa2503223>.
- ^{xv} Prostate Cancer UK. 2021. *The odds are stacked against you': Black men more likely to be diagnosed at later stage*. Available at: <https://prostatecanceruk.org/about-us/news-and-views/2025/01/black-men-more-likely-to-be-diagnosed-at-later-stage>
- ^{xvi} Butler EN et al. 2020. *Fatal prostate cancer incidence trends in the United States and England by race, stage, and treatment*. Br J Cancer 2020;123:487-94. doi:10.1038/s41416-020-0859-x pmid:32433602
- ^{xvii} Martin RM et al. 2024. *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. PMID: 38581198; PMCID: PMC10999004.
- ^{xviii} NHS Race & Health Observatory. 2025. *Patient Experience and Trust in NHS Primary Care Patient Experience and Trust in NHS Primary Care*. Available at: <https://nhsrho.org/wp-content/uploads/2025/03/TRUST-IN-PRIMARY-CARE-REPORT.pdf>.
- ^{xix} Healthwatch. 2025. Available at: <https://www.healthwatch.co.uk/blog/2025-10-08/men-would-come-forward-prostate-cancer-screening>
- ^{xx} Thomas T. 2026. *Prostate cancer is most commonly diagnosed cancer across UK, study finds*. The Guardian. Available at: <https://www.theguardian.com/society/2026/jan/20/prostate-cancer-is-most-commonly-diagnosed-cancer-across-uk-study-finds>
- ^{xxi} Marmot M et al. 2010. *The Marmot Review*. Available at: <https://www.instituteofhealthequity.org/resources-reports/fair-society-healthy-lives-the-marmot-review>
- ^{xxii} Dodkins J et al. 2025. *Geographic, socioeconomic and demographic inequalities in the incidence of metastatic prostate cancer at time of diagnosis in England: a population-based evaluation*. BMJ Oncology. 2025 Apr;4(1):e000643.
- ^{xxiii} UK Government. 2020. *People Living in Deprived Neighbourhoods*. Available at: <https://www.ethnicity-facts-figures.service.gov.uk/uk-population-by->

[ethnicity/demographics/people-living-in-deprived-neighbourhoods/latest/](#)

xxiv National Voices. 2025. Available at: <https://www.nationalvoices.org.uk/blogpost/advancing-racial-health-equity-the-prostate-cancer-uk-experience>

xxv Dodd V. 2024. *Majority of Black people think racism played role in failure to test for prostate cancer*. The Guardian. Available at: <https://www.theguardian.com/society/2024/sep/26/majority-of-black-people-think-racism-played-role-in-failure-to-test-prostate-cancer>

xxvi Prostate Cancer Research. 2024. *Socioeconomic impact of prostate cancer screening*. Available at: https://www.prostate-cancer-research.org.uk/wp-content/uploads/2024/11/PCR_Socioeconomic_Impact_Prostate_Cancer_Screening_Nov24-v1.0.pdf

<https://www.prostate-cancer-research.org.uk/wp-content/uploads/2025/10/Prostate-Cancer-Screening-The-Impact-on-the-NHS-Report.pdf>

xxvii Nuffield Trust. 2024. *Cancer diagnosis – QualityWatch*. Available at: <https://files.nuffieldtrust.org.uk/qualitywatch/cancer-diagnosis/>

xxviii Prostate Cancer Research. 2024. *Socioeconomic impact of prostate cancer screening*. Available at: https://www.prostate-cancer-research.org.uk/wp-content/uploads/2024/11/PCR_Socioeconomic_Impact_Prostate_Cancer_Screening_Nov24-v1.0.pdf

xxix Davies JM et al. 2026. *Ethnic inequality in place of death: Analysis using 'gold standard' self-reported ethnicity data from the Census Longitudinal Study*. Palliat Med. 2026 Feb;40(2):273-277. doi: 10.1177/02692163251395455. Epub 2025 Dec 4. PMID: 41342480; PMCID: PMC12852481.

xxx Cummins L et al. 2025. *Public expenditure in the last year of life*. Research report, Nuffield Trust and Health Economics Unit for Marie Curie

xxxi Prostate Cancer Research. 2025. *Prostate Cancer Screening: The Impact on the NHS*. Available at: https://cdn.prod.website-files.com/66c43323facd99575ff6737b/6912fcd99d155b775c79ea4b_Prostate-Cancer-Screening-The-Impact-on-the-NHS-Report-v2.pdf

xxxii Forde C et al. 2021. *Uptake of pre-symptomatic testing for BRCA1 and BRCA2 is age, gender, offspring and time-dependent*. Journal of Medical Genetics.

xxxiii NHS Race and Health Observatory. 2024. *Ethnic inequities in genomics and precision medicine*. Available at: <https://www.nhsrho.org/wp-content/uploads/2024/06/RHO-Genomics-Report-June-2024.pdf>

xxxiv Chen F et al. 2025. *Integrating Pathogenic Variants, Polygenic Risk Score, and Family History for Prostate Cancer Risk Estimation in Men of African Ancestry*. *European Urology*. doi:<https://doi.org/10.1016/j.eururo.2025.09.416>

xxxv Conti, DV et al. 2021. *Trans-ancestry genome-wide association meta-analysis of prostate cancer identifies new susceptibility loci and informs genetic risk prediction*. *Nat Genet* 53, 65–75.

S70	James Gibson	Healthwatch England	Consultation Response: Prostate Cancer Screening Submitted by Healthwatch England Introduction Healthwatch England welcomes the opportunity to respond to the consultation on prostate cancer screening. As the statutory champion for people using health and social care services in England, we bring forward evidence from our recent national research into men's health experiences, attitudes and behaviours. Our findings are directly relevant to the Committee's consideration of prostate cancer screening, particularly in relation to inequalities, access, public confidence, and likely uptake. Prostate cancer is now the most commonly diagnosed cancer in the UK. One in eight men will develop prostate cancer in their lifetime, rising to one in four among Black men, who are also more likely to develop the disease at a younger age. While overall incidence is lower in more deprived areas, rates of metastatic disease are higher in these communities. Given the significantly poorer prognosis associated with metastatic prostate cancer, this pattern risks exacerbating existing health inequalities. Any decision regarding screening must therefore be considered not only through a clinical and economic lens, but also through an equity lens. Men's health research The evidence presented here is drawn from Healthwatch England's national men's health research project. Quantitative data were collected through nationally representative polling commissioned from Savanta and conducted online in June 2025. The total sample comprised 7,407 adults in England, including 3,575 men and 3,832 women. Within the overall sample, 1,124 respondents (17%) identified as belonging to an ethnic minority group, including 515 ethnic minority men. All figures (other than sample sizes) were weighted to ensure representativeness of adults aged 18 and over in England. Statistical significance was tested at the 95% confidence level ($p < 0.05$). This quantitative work was complemented by qualitative insights from across the Healthwatch Network. We drew on recent local Healthwatch research exploring men's experiences of health and care services, as well as direct feedback and case studies submitted by members of the public. This mixed-method approach provides statistical robustness and depth of lived experience. Public Attitudes Towards Prostate Screening Our research demonstrates strong stated support for an NHS-led prostate screening programme.

		Our research differs significantly from the data cited in the ‘Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk’ report, which was derived from the UK CAP trial. The reported cited uptake of prostate cancer screening was 36%. However, in our polling, when asked about the likelihood of attending a prostate screening appointment if invited, 79% of men said they would be likely to attend, including 53% who said they would be “very likely.” Only 7% reported that they would be unlikely to attend. Importantly, Black men (who face significantly higher lifetime risk) were among the most likely to say they would attend (81%). Overall, 71% of ethnic minority men said they would be likely to attend, though there was variation between groups. Older men and men who were financially comfortable were more likely to report that they would attend, mirroring patterns observed in PSA request behaviour. The qualitative findings add further nuance. A recurring theme was that some men are reluctant to initiate contact with health services but would respond to a direct invitation. Several participants described themselves as unlikely to “take the initiative,” but willing to act if formally called. This behavioural insight is relevant, and a structured invitation model may mitigate some of the barriers inherent in the current system. At the same time, it is important to recognise that willingness to attend does not eliminate the need to weigh benefits against harms. Evidence indicates that PSA-based screening may offer only modest mortality reductions over a ten-year period and carries risks of false positives, overdiagnosis, unnecessary biopsy, and treatment-related harms. Healthwatch England does not seek to substitute public preference for clinical evidence. Rather, we emphasise that patient perspectives, behavioural realities, and equity implications form an essential part of a comprehensive assessment. Savanta Prostate Cancer Screening Question: Q. Prostate screening is a blood test that looks for signs that you may have a prostate condition. If the NHS introduced prostate screening routinely for every man of a certain age, how likely would you be to go for an appointment when invited? Very likely 1,895 (53) Somewhat likely 928 (26) Neither likely/nor unlikely 396 (11) Somewhat unlikely 142 (4)

		Very unlikely 105 (3) NET: Likely 2,823 (79) NET: Unlikely 247 (7) Access to PSA Testing Under the Current System Though men aged 50 and over may request a prostate-specific antigen (PSA) test from their GP even if asymptomatic, our findings suggest that reliance on individual initiation creates substantial inequalities. Among men aged 50 and over, only one-third (33%) reported that they had requested and received a PSA test. Uptake was strongly associated with age and socio-economic position. Older men were more likely to have requested testing, as were men who described themselves as financially comfortable and those working in professional or managerial occupations. By contrast, men who reported that they were “just getting by” or “really struggling” financially were markedly less likely to have requested a test. These findings suggest that the current opt-in model may advantage men who are more confident navigating healthcare systems, more health literate, or better resourced. Men in routine or manual occupations and those experiencing financial hardship appear less likely to access testing. Given that metastatic prostate cancer is more prevalent in deprived areas, this is a matter of concern. In addition, seven percent of eligible men in our polling reported that they had requested a PSA test but were refused. Local Healthwatch research has echoed these experiences, including reports from men with a family history of prostate cancer who felt discouraged or denied testing. While there may be legitimate clinical reasons for declining a PSA test, men consistently reported confusion about their rights and about the basis on which decisions were made. National guidance is not consistently understood. Some materials imply that men over 50 who have considered balanced information may access testing, while other guidance emphasises that men may request, rather than obtain, a test. Current Department of Health and Social Care guidance advises GPs not to proactively promote PSA testing to asymptomatic men. At the same time, men attend primary care less frequently than women and may delay help-seeking. This creates a system in which individuals must both initiate discussion and navigate uncertainty around entitlement. Qualitative accounts suggest that this ambiguity can undermine trust. Some men reported feeling that they had to exaggerate symptoms in order to secure testing. Others interpreted clinical caution as discouragement. Inconsistent messaging and reliance

		on opportunistic presentation may therefore entrench inequalities and generate avoidable frustration. “Initially I was told that I could not be tested unless I had symptoms. As my father had prostate cancer when he passed away, and my younger brother has an enlarged prostate I decided to get tested and said that I had symptoms even though I didn’t [just to get a test]” Story shared by Healthwatch Birmingham Inequalities and High-Risk Groups Our findings underscore the importance of considering inequalities explicitly in any final recommendation. The present system appears to favour those who are more affluent, older, and more engaged with healthcare services. Meanwhile, men in more deprived circumstances, who may already face higher risks of late-stage diagnosis, are less likely to access opportunistic testing. The particularly high stated willingness among Black men to attend screening is notable, given their substantially elevated lifetime risk. To avoid perpetuating avoidable disparities, any targeted approach to prostate cancer screening must ensure clear communication, proactive engagement, and accessible pathways. “I’m reluctant to take the initiative to get checked for anything. The thing that would change that is someone telling me to. So, if you’re this age then you need to get checked.” Story shared with Healthwatch Coventry Recommendations Healthwatch England recommends that the Committee consider men’s lived experience alongside clinical and economic modelling when reaching its final decision. Our research suggests that there is both strong public appetite for structured screening and evidence of inequality in the current access model. Irrespective of the ultimate recommendation on a national screening programme, there is a clear and immediate need for consistent national guidance on asymptomatic PSA testing. This guidance should clarify whether men aged 50 and over are entitled to a consultation about testing, how decisions are reached, and what options exist if a request is declined. Clarity is essential for maintaining trust and ensuring equitable access. Finally, there is a need to strengthen public awareness of prostate cancer risk factors, particularly among higher-risk groups such as Black men, and to reinforce messages about early help-seeking. Awareness initiatives must be designed in ways that reach men who are less likely to attend primary care proactively.

S71		British Association of Urological Surgeons	Dear UK NSC Consultation Team, On behalf of the British Association of Urological Surgeons (BAUS), please find attached our response to the consultation on targeted prostate cancer screening for higher-risk groups. We welcome the opportunity to contribute to this important work and would be pleased to engage further if helpful. Please let me know if any additional information is required. Best regards,

BAUS Response to Draft NSC Prostate Cancer Screening Consultation document

BAUS welcomes the opportunity to engage with, and help shape, the National Screening Committee's proposal for targeted prostate cancer screening in men at higher genetic risk (including pathogenic BRCA1/2 variants). We support the direction of travel toward a risk-adapted approach, but emphasise that success will depend on whether it is **deliverable in routine NHS systems, equitable by design, and resourced end-to-end**, from primary care and genetics, through MRI and biopsy capacity, to treatment, surveillance and survivorship.

In parallel, our review of the SCHARR prostate cancer screening model highlights several structural choices that may **understate the potential benefits** and **overstate some harms** of modern, MRI-era, risk-targeted strategies, particularly when headline findings are summarised over short time horizons. This matters for high-risk cohorts: benefits from metastasis and mortality prevention accrue later, while harms are counted immediately and discounted heavily, risking an unbalanced portrayal of contemporary pathways.

Taken together, BAUS recommends that policy development proceeds with:

- (1) clear, operational mechanisms for identifying eligible men
- (2) explicit EDI protections to prevent widening existing disparities (including for Black men and those in deprived communities)
- (3) safeguards to protect access to informed PSA testing for higher-risk men outside genetic registries
- (4) workforce and diagnostic capacity planning that is fully costed and nationally consistent and
- (5) continued investment in research and model refinement to reflect MRI-first practice, modern biopsy safety, active surveillance, and longer-term outcomes.

1. BAUS position on targeted screening for BRCA1/2 and other high-risk groups

BAUS welcomes the opportunity to engage with, and help shape, the National Screening Committee's recent proposal regarding targeted prostate cancer screening. We recognise this as a potentially important step toward a future risk-adapted screening strategy and appreciate the committee's focus on individuals with pathogenic BRCA1 and BRCA2 variants. However, several fundamental implementation and equity issues must be addressed before such an approach can deliver meaningful population-level benefit.

- **Targeted PSA screening should be offered from age 40–69 for people with prostates who carry pathogenic BRCA1/BRCA2 variants, with annual PSA testing rather than 2 yearly** (supported by IMPACT study data showing higher incidence and earlier onset in BRCA carriers).
-

1. Identification of eligible individuals

Lack of routinely available data and national genomic repository – opportunities and limitations

Identification of eligible individuals is currently not feasible within routine NHS systems. While ethnicity is generally well coded in primary care, BRCA status and family history are not systematically recorded, and there is no existing national mechanism to reliably identify BRCA-positive men.

There has been a recent NHS England announcement regarding the development of a national inherited cancer predisposition register (a “national genomic repository”) intended to capture individuals with pathogenic variants in cancer-predisposition genes, including BRCA1 and BRCA2. While this is welcome, it is important to recognise that such a repository will only include individuals who have already undergone germline testing through existing NHS Genomic Medicine Service or clinical genetics pathways. It will therefore not, in its current form, identify undiagnosed carriers or individuals who have never met referral thresholds for testing. It is also unclear whether this infrastructure is sufficiently mature or operationally ready to support population-level targeted screening.

Complexity of current genetic referral pathways

Current genetic referral pathways are complex, heterogeneous, and largely cancer-site-specific. If selective screening based on BRCA status is to be pursued, an important question is whether existing referral criteria for germline testing should be broadened and simplified to ensure a more complete and representative capture of individuals with pathogenic BRCA variants. Without expansion and standardisation of germline testing pathways, any downstream repository will inevitably reflect only a subset of true carriers.

2. Equity

The current proposal risks further alienating groups who already experience poorer access to healthcare and worse prostate cancer outcomes, particularly men of Black ethnicity and those from socio-economically deprived communities. A selective screening model focused

solely on BRCA status does not address the well-established regional and demographic patterns of metastatic presentation seen across England, including in predominantly white, non-BRCA, and asymptomatic populations.

3. Safeguarding access to informed PSA testing

BAUS is concerned about unintended consequences of the current proposal. Any new framework must not make it harder for men with recognised risk factors (e.g., first-degree family history, Black ethnicity, or personal concern) to access PSA testing through primary care. Clear national guidance should accompany the NSC position, reaffirming that informed PSA testing remains appropriate in higher-risk individuals who present requesting assessment.

4. Workforce understanding, education, and resource implications

System readiness and resource impact require careful consideration. A selective screening approach will place additional burden on primary care, urology services, diagnostics, imaging, and downstream treatment pathways. Without ring-fenced funding, workforce expansion, and training, implementation risks worsening existing pressures and widening geographical inequities.

Widespread education and engagement of urologists, primary care clinicians, and genetic services will be required. Many clinicians currently have limited familiarity with genetic testing criteria, variant interpretation, and management of unaffected BRCA-positive men.

5. Evidence generation and hybrid models

Evidence generation should run in parallel with policy development. Large-scale studies, such as TRANSFORM, are likely to provide critical data to inform future risk-stratified screening strategies. Investment in such research may represent a higher-yield use of public funds at this stage.

BAUS supports exploration of hybrid approaches, whereby organised, research-driven screening initiatives operate alongside improved opportunistic testing, with consistent data capture, governance, and evaluation.

2. Methodological considerations: SCHARR screening model and implications for policy

We recognise the SCHARR model as a complex and carefully constructed piece of work. Our concern is not that it is 'wrong' in a narrow technical sense, but that several structural and value-laden assumptions appear to lean in the same conservative direction—high overdiagnosis, modest apparent mortality benefit (especially in high-risk groups), and constrained cost-effectiveness, when evaluating modern MRI-first, risk-stratified screening.

- Definition of 'familial high risk' is very broad in the model, potentially diluting truly high-risk families and reducing the apparent value of targeted familial screening.
- International data show that individuals of African ancestry have roughly double the incidence of prostate cancer compared with those of European ancestry (multiple global epidemiology studies). Modelling for Black men uses patchwork sources and yields counter-intuitive benefit–harm estimates, reinforcing the importance of consistent assumptions and UK-specific calibration.
- Recent UK evidence (BMJ 2025) indicates that men of African ancestry can present with more aggressive prostate cancer, highlighting the need for robust UK calibration in subgroup modelling.
- MRI accuracy has improved over the last 5–10 years, with PROMIS and PRECISION showing better detection of clinically significant cancer and fewer unnecessary biopsies (PROMIS 2017; PRECISION 2018).
- Biopsy detection and safety have improved, with MRI targeted and transperineal biopsy increasing significant cancer detection and reducing sepsis to <0.1% (PRECISION 2018; BAUS TP biopsy data).
- Overdiagnosis and harms are treated in a blunt way that may not reflect contemporary active surveillance pathways and evolving treatment-related morbidity; harms are counted immediately while benefits (metastasis and death avoided) accrue later and are heavily discounted.
- Validation is heavily anchored to ERSPC/CAP-era trial behaviour; the model is less strongly challenged against modern UK MRI-era data and risk-stratified registry patterns.
- Economic analysis emphasises lower thresholds (£20k/QALY base, plus £15k sensitivity) with limited exploration of £30k/QALY or subgroup-specific willingness-to-pay considerations for small, high-risk cohorts.

Policy implications

For decisions about targeted screening in BRCA carriers and other high-risk groups, we recommend that model outputs are interpreted with careful attention to (a) appropriate time horizons (lifetime/ ≥ 25 years alongside shorter budget horizons), (b) MRI operating points and diagnostic pathways representative of contemporary practice, (c) modern management of low-risk disease (active surveillance), and (d) robust UK-specific subgroup calibration for ethnicity and family history. These refinements are likely to provide a more policy-relevant estimate of the benefit–harm balance for modern risk-stratified programmes.

3. Summary and Invitation to collaborate

BAUS appreciates the direction of travel toward risk-adapted prostate cancer screening but emphasises that success depends on deliverable mechanisms to identify individuals with pathogenic BRCA variants; explicit EDI-focused design, including protection of access to informed PSA testing for higher-risk men who have not been identified as BRCA variant carriers; adequate resourcing across the entire care pathway; and continued investment in high-quality prostate cancer screening research. We would welcome continued engagement with the NSC and APPG to co-develop a practical, equitable, and evidence-based roadmap, and would be pleased to contribute clinical, methodological and service-delivery expertise, particularly around identifying eligible men, safeguarding PSA access, and ensuring that screening policy does not widen existing geographic and demographic inequities.

S72	Rowan Ellis Hollins	Yorkshire Cancer Research	Hello, Please find attached Yorkshire Cancer Research's response to the UK NSC prostate cancer screening consultation. Best wishes, Rowan

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name:	Rowan Ellis Hollins	Email address:	*****
Organisation (if appropriate):	Yorkshire Cancer Research		
Role:	Public Affairs Officer		
Do you consent to your name being published on the UK NSC website alongside your response?		Yes	
Section and / or page number	Text or issue to which comments relate	Comment <i>Please use a new row for each comment and add extra rows as required.</i>	
'Next Steps' Pages 1-20	Comments refer to the 'Next steps' section in the 'UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document (Pages 19-20).	The conclusions made by the UK National Screening Committee (UK NSC) highlight a stark need for a more accurate test for prostate cancer as well as improved data availability. It is important that the UK NSC work closely with current and future trials to ensure that the gaps outlined in this review are filled. Yorkshire Cancer Research currently funds IMProVE, a clinical trial designed to understand whether a new screening approach could work safely and effectively within the NHS. This trial will investigate whether a programme that combines PSA (Prostate-Specific Antigen) blood tests with MRI scans could improve prostate cancer diagnosis, saving lives and if so, how it can be organised to reduce health inequalities. The trial will initially involve 4,500 men in Sheffield and Leeds and may be expanded to other parts of the region. As a pilot study, IMProVE aims to inform the design of a future, larger trial. Its key objectives include assessing the acceptability of the screening approach and determining how best to engage people from Black and socially disadvantaged backgrounds, who are disproportionately affected by prostate cancer. The UK NSC Research and Methodology Group (RMG) has reviewed IMProVE to ensure the study is designed and delivered in a way that will generate evidence valuable to the UK NSC. IMProVE should therefore be referenced in the 'Next steps' section alongside TRANSFORM, given its potential to help address uncertainties highlighted by the model, inform future research and contribute to improved prostate cancer screening strategies. The UK NSC concluded that whole-population prostate cancer screening using current tests is not recommended because it is unlikely to be cost-effective and may deliver more harm than benefit. IMProVE aims to address these concerns by piloting a risk-stratified, MRI-enhanced screening approach designed to reduce overdiagnosis and improve cost-effectiveness. Unlike PSA-only	

		strategies, IMProVE combines PSA testing with MRI to identify clinically significant cancers while avoiding unnecessary biopsies, thereby minimising harm. The trial incorporates a comprehensive health-economic model to evaluate cost per QALY, net monetary benefit and resource use across different screening strategies, providing UK-specific evidence on affordability and efficiency. In addition, IMProVE will assess psychological outcomes and model benefits and harms such as impact on life years (lifetime), stage shift, false-positivity rate and overdiagnosis, addressing uncertainty around whether screening improves overall health outcomes. This trial will also directly address critical uncertainties identified by the UK NSC regarding targeted prostate cancer screening for Black men. IMProVE contributes by generating UK-specific evidence on psychosocial and behavioural factors influencing PSA screening uptake among Black men and those from deprived backgrounds, areas where current knowledge is largely US-based. Through focus groups and co-design workshops, the trial will identify barriers and facilitators to participation and develop tailored recruitment strategies. These findings can inform feasibility, acceptability and equity considerations around prostate cancer screening. While results from this pilot cannot be directly extrapolated to a population screening programme, IMProVE remains a critical component of the evidence base needed to inform a prostate cancer screening programme and will directly shape a future, larger trial. Importantly, IMProVE and TRANSFORM were developed to complement each other to avoid duplication and ensure that a wide range of evidence is generated. The two research teams are in regular contact to share progress and learning and where possible to standardise reporting across the two studies. For these reasons it is important that both IMProVE and TRANSFORM are included in the 'Next steps' section and utilised to fill the remaining gaps in evidence highlighted in this review. The UK NSC should liaise directly with both trials to ensure that evidence collected will contribute effectively to future reviews and larger research trials and enable more accurate modelling of prostate cancer screening. Where additional information may be required to support decision making on prostate cancer screening, that falls outside the remit of the IMProVE and TRANSFORM trials, this should be identified at the earliest opportunity and steps taken to obtain such data. Yorkshire Cancer Research also recommend that the UK NSC formally call for further research into the possibility of identifying other tests that could either replace the PSA test or be used in combination with it to reduce levels of overdiagnosis.
Overdiagnosis, overtreatment and active surveillance	<i>Comments refer to the 'UK National Screening Committee (UK NSC) Screening for prostate cancer' document (Pages 4-6) and the 'UK National</i>	Overdiagnosis, which can lead to overtreatment, is one of the key reasons given for the UK NSC's recommendation against whole population screening, targeted screening for Black men and targeted screening for men with a relevant family history. Part of the issue with overtreatment lies with the active surveillance pathway. The review identifies that half of men who start on active surveillance will move on to have more radical treatments such as

	Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document (Page 15).	surgery or radiotherapy over 15 years. This is often due to rising PSA levels. However, rising PSA levels do not necessarily indicate the advancing of cancer and usually reflect the ageing of the prostate. This can result in men unnecessarily opting for treatment. To enable a future prostate cancer screening programme that does not result in men unnecessarily undergoing treatment which could have potential harms, there is a clear need to ensure men remain on the active surveillance pathway for as long as is safe. Yorkshire Cancer Research are currently funding the FINESSE trial. This trial will look at whether Finasteride, an existing medication known to slow prostate growth, can increase adherence and reduce the need for extensive surgery or radiotherapy in men on the active surveillance pathway. A minimum of 227 men will be randomised into two arms; one arm will receive finasteride and the other usual care. All men will receive active surveillance including PSA testing and MRI scanning. Theoretically, due to slowed prostate growth, men receiving Finasteride will be less likely to opt for radical treatment. By potentially improving adherence to the active surveillance pathway this trial could be critical for the feasibility of a future prostate cancer screening programme. Yorkshire Cancer Research therefore recommend that the results of this trial should be considered in future reviews to inform considerations around the impact of prostate cancer screening on overtreatment.
'Uptake of the PSA test' (Page 10, Section 4.2.2)	Comments refer to Page 10 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document	This section outlines that the model assumes the uptake of the PSA testing using data from the UK CAP trial, putting the uptake of prostate cancer screening at 36%. The UK CAP trial recruited through primary care practices, randomising men aged 50 to 69 in each primary care practice into the intervention and control groups. The intervention group received a single invitation to a nurse-led clinical appointment where men were given information about PSA testing and then offered the PSA test. The control group received standard NHS management and information about PSA testing was only provided to men who requested it. In this study, 36% of men within the intervention group accepted the offer of a PSA test. PSA testing within the control group was assumed to be approximately 10%-15%. Yorkshire Cancer Research request clarity on the assumption that in a screening scenario the uptake would remain at 36%. The UK CAP trial is run in a primary care scenario, amongst a population where asymptomatic PSA testing is already available. As a result, a proportion of men who declined the screening offer may have done so because they had already been tested opportunistically, and some may have been ineligible for trial participation for the same reason. Yorkshire Cancer Research request further information on whether opportunistic screening for asymptomatic men would stop in a screening scenario and therefore whether the uptake of PSA testing in men invited to screening is likely to be higher than 36%. By applying UK CAP trial uptake rate directly, the model may exclude a group of men who currently seek opportunistic screening. These men are likely to have higher levels of health literacy and proactive health seeking behaviour, suggesting they may have above average uptake in a formal screening programme. Their inclusion could feasibly increase overall uptake beyond 36%. Yorkshire Cancer Research would welcome further justification for the use of the UK CAP trial to model uptake of prostate cancer screening given it is likely to miss out the men currently proactively request PSA tests,

		and for the UK NSC to consider what impact this increased uptake may have in the different screening scenarios explored.
'The usual care scenario' (Page 11, Section 4.3)	Comments refer to Page 11 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document	The model assumes usual care to include both PSA testing for symptomatic presentation and asymptomatic testing due to PSA test request via GP. However, as stated in the previous comment, Yorkshire Cancer Research would like clarity on whether 'PSA testing via request to their GP' would stop if a national screening programme was rolled out. Men may no longer need to proactively seek a PSA test if all men were invited to screening. Yorkshire Cancer Research understands that currently the lack of differentiated coding in primary care means it is unknown what proportion of men are PSA tested due to opportunistic screening, symptomatic testing, active surveillance monitoring or PSA testing following prostate cancer treatment. This is acknowledged as an area of high uncertainty within the model, resulting in the model relying on one current care scenario which combines multiple routes to PSA testing. Yorkshire Cancer Research recommend that the final UK NSC report recommends that data collection in primary care is improved to make future modelling more accurate. Without the ability to separate opportunistic screening, symptomatic testing, active surveillance monitoring or PSA testing following prostate cancer treatment the model lacks a true 'non-screening' arm to compare against. Separate primary care record codes should be used to differentiate between symptomatic and opportunistic PSA testing, as well as PSA testing done as part of follow-up care following prostate cancer treatment or as part of active surveillance. This would help inform conclusions around overdiagnosis. It is currently unclear how frequently the PSA test is used in different scenarios and how the patient outcomes differ following tests in these different scenarios. Crucially, this data should be made available so it can be used to inform research and future screening programmes.
'The diagnosis and treatment pathway' (Page 12, Section 4.4)	Comments refer to Page 12 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document	The document notes that, at the time the modelling was undertaken, data from the Stockholm3 test was not yet available. Yorkshire Cancer Research recognises that it is now too late for this evidence to be incorporated into the current modelling. However, as data from the Stockholm3 trial has since become available (as of October 2025), Yorkshire Cancer Research recommends that the UK NSC commit to including this evidence in future reviews, alongside any other emerging developments, to ensure the modelling reflects the most up to date and comprehensive evidence base.
'Definition of Black ethnicity' (Page 18, Section 5.2.1)	Comments refer to Page 18 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document	This page identifies the lack of available ethnicity data for people of mixed ethnicity as a limitation, grouping all people of mixed ethnicity together. This means the model is unable to differentiate between different mixed ethnic groups or identify which of those men were of mixed Black ethnicity. Ahead of the next review UK NSC should work with partners to ensure there is improved data and proxy measures to enable the modelling to include men of mixed Black ethnicity.
'Definition of BRCA1/2 gene	Comments refer to Page 18 of the UK National	The accompanying narrative document states that 'someone's knowledge of their BRCA status' is modelled using a study that looked at the 'uptake of genetic testing' among apparently healthy relatives

variant carriers’ (Page 18, Section 5.3.1) ‘Actual BRCA1,2 status allocation’ (Page 30-32, Section 6.4.2)	Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative’ document and Pages 30-32 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk,	of people with confirmed BRCA mutations’. It is unclear how, or if, this estimate of ‘known BRCA status’ for people with a BRCA gene mutation has then been applied to the modelled impact of screening, as section 8.4.5 of the SCHARR report models the impact of screening all BRCA1/2 mutation carriers (based on prevalence estimates of 1 in 381 for BRCA 1 and 1 in 277 for BRCA 2). Yorkshire Cancer Research would like to see clarification regarding how or if this model of ‘known BRCA status’ for people with a BRCA gene mutation has then been applied to the modelled impact of screening. If this estimate of ‘known BRCA status’ has been used in the model, the Charity has a few potential concerns regarding the use of the Forde et al. study for this purpose. This study measured the uptake of pre-symptomatic genetic testing among relatives of individuals with confirmed BRCA1/2 mutations to derive age-specific probabilities that individuals know their BRCA1/2 status (assuming they are carriers). Based on the study, the model assumes that, for the 45 to 61 age group, known BRCA status is between 33% and 35% (SCHARR report, Page 32, Section 6.4.2, Table 2). This assumes that the proportion of men with an affected relative who accepted an offer of testing reflects the proportion of the population with a BRCA gene mutation who are aware of their BRCA status. In the Forde et al. study there is no stated estimate of BRCA1/2 mutation prevalence following this testing – only that they have accepted BRCA testing. Being tested for a BRCA gene mutation is not the same as being a confirmed carrier, and therefore it is Yorkshire Cancer Research’s understanding that a proportion of those in the Forde et al. study will have been found not carry a BRCA gene mutation. Additionally, uptake of testing among relatives cannot be used to infer the proportion of BRCA positive individuals in the wider population who know their status. Relatives of identified carriers have strong behavioural incentives to seek testing, whereas the general population typically learn their BRCA status only following a cancer diagnosis, proactive self-referral, referral due to family history, or participation in genetic research. Despite rising levels of genetic testing and awareness of BRCA1/2 status, as noted in the paper, it is unlikely that knowledge of having a BRCA gene mutation among those affected is as high as estimated using the Forde et al study as this study does not indicate whether people are confirmed carriers and applies to a specific population with higher behavioural incentives than the general population. If this estimate has indeed been applied, further justification is required for using this study to infer BRCA awareness in a population where genetic testing is not routinely offered and where many carriers will have no known affected relative.
‘Definition of BRCA1/2 gene variant carriers’ (Page 18, Section 5.3.1)	Comments refer to Page 18 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative’ document	This section of the accompanying document states that there is no reason to suspect that BRCA1/2 mutations are more likely to occur in people of one ethnicity compared to another. Yorkshire Cancer Research recommend the UK NSC call for future research into potential differences in BRCA gene mutation prevalence between different ethnic groups.
‘Modelling results’	Comments refer to Page 8 and Page 19 of the UK	The accompanying narrative document (Page 19) states ‘the most cost-effective strategy for screening men with a confirmed BRCA1/2 gene mutation is screening every 2 years, from age 45 to age 61’. In

(Page 19, Section 5.3.2) <i>'Building the economic model for prostate cancer screening' (Page 8, Section 3.2)</i> <i>'Actual BRCA1,2 status allocation' (Page 30-32, Section 6.4.2)</i>	<i>National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document and Pages 30-32 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk</i>	addition, Page 8 of the accompanying narrative document states the focus of the economic model is on “men with a known BRCA1 and/or BRCA2 gene mutation”, that is only those that know they have a BRCA gene mutation. However, this wording appears misaligned with the SCHARR model which indicates that all potential individuals with a BRCA1 or BRCA2 mutation are included in the model rather than only those with a known mutation. On Page 30 of the SCHARR report, it states that BRCA status was allocated to people within the relevant dataset based on assumed prevalence rates (1 in 381 for BRCA1 and 1 in 277 for BRCA2), that is, an estimate of all individuals with a BRCA gene mutation, whether or not they are aware of it. The language used between these documents appears misaligned and therefore Yorkshire Cancer Research request the language across the documents is updated to make it clear that the modelling for BRCA-related prostate cancer screening was done based on estimated population prevalence of BRCA1 and BRCA2 mutations.
<i>'Additional screening costs' (Page 74, Section 6.11.3)</i>	<i>Comments refer to Page 74 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk</i>	The modelled invitation costs are based on the invitation costs for bowel cancer screening, including invitation letters, reminder letters for non-responders, helpline services, postage, staff time and overheads. However, Yorkshire Cancer Research request the UK NSC provide further justification for this decision and provide information detailing how the costs of the two programmes are comparable.
<i>'BRCA carriers: impact of screening scaled to the population of England' (Page 149, Section 8.4.5)</i>	<i>Comments refer to Page 149 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk</i>	Yorkshire Cancer Research welcomes the recommendation to offer prostate cancer screening to men with a BRCA gene mutation. However, given some studies have indicated 97% of people in the general population who are estimated to have a BRCA gene mutation have not yet been identified and that the modelled benefits of a targeted screening programme rely on the assumption that all eligible men have undergone BRCA testing, it is extremely important that before the roll out of a targeted screening programme, more must be done to identify people that would be eligible.¹ This can ensure the programme will be cost effective, bring benefit to those that are screened and achieve the modelled level of impact. Yorkshire Cancer Research is funding PROTECT-C, a £3.8 million trial, led by Professor Ranjit Manchanda at Queen Mary University of London. The trial will investigate the risks, benefits and feasibility of introducing genetic testing for all women, regardless of whether they have a relative with cancer. It will also help determine how many people accept the offer of genetic testing and, of them, how many are found to have a genetic change. Crucially, it will assess if and how offering genetic testing to all people can be affordable on the NHS. While this trial is only investigating genetic testing for women, it illustrates key areas for consideration in relation to the recommendation to use BRCA status as a way to target a prostate cancer screening programme. Yorkshire Cancer Research request clarity on the mechanism by which people with a BRCA gene

		mutation will be identified as being eligible for prostate cancer screening and subsequently invited to screening. Yorkshire Cancer Research welcomed the introduction of the National Inherited Cancer Predisposition Register (NICPR) last year and request further information on whether the UK NSC plan to work with NDRS and use this platform within the recommended prostate screening programme for men with a BRCA gene mutation. Without using a centralised database such as the NICPR, it is unclear how this type of targeted screening programme would work from a logistical perspective.
Data limitations and requirements (Page 180, Section 10.4)	Comments refer to Page 180 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk	In general, the model requires much more up to date and UK applicable data. For example, the model is based on 2018 incidence data (Page 217). It is likely that this is an underestimation of the current UK incidence and does not capture the spike in testing and diagnosis associated with the 'Fry Turnbull' effect. It seems 2018 data was chosen to align with HSE data used elsewhere within the model (Page 225). However, this could mean that estimates of the additional number of people that might be diagnosed through screening become less relevant as more asymptomatic people are already being diagnosed through usual care. The costing data used is also based on outdated numbers. These have been inflated but only to 2022/23 costs. This is done without any acknowledgement that the inflation rate has changed since 2022/23. Any conclusions made on the basis of these costs are likely to be outdated. It is clear there are significant gaps in the data which could impact the conclusions of the model. The UK NSC should work with researchers conducting trials on prostate cancer and prostate cancer screening, as well as the NHS to ensure the necessary, high quality, UK data is collected and available to use in future reviews.
'Building the economic model for prostate cancer screening' (Page 8, section 3.2).	Comments refer to Page 8 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document	This section outlines that the UK NSC requested submissions for economic modelling for the following groups: population screening in all men (regardless of their risk level), targeted screening in Black men, targeted screening in men with a known BRCA1 and/or BRCA2 (BRCA1/2) gene mutation (or variant) and targeted screening in men with a relevant family history. Based on this modelling it was concluded that the Committee could only recommend targeted screening in men with a known BRCA1 and/or BRCA2 (BRCA1/2) gene mutation. In line with the SCHARR report's suggestion (Page 186) that it is worth exploring targeted screening of men with multiple risk factors, Yorkshire Cancer Research recommend that future reviews also look at combined risk factor groups such as Black men who also have a relevant family history. While it may not currently be cost effective for either of these groups alone, there may be sufficient evidence for screening those who fall under multiple categories.
'Modelling results: PSA screening with threshold	Comments refer to Pages 93 - 150 of the SCHARR report: Cost-effectiveness of Prostate Cancer	This section outlines the modelling results for PSA screening with threshold 3ng/ml for general population, men of Black ethnicity, men with familial risk and BRCA carriers. However, the graphs in this section are not always clearly labelled and the necessary information is not always provided. For example, Figure 24 and Figure 39 show the equivalent graph for different populations, that is the

3ng/ml' (Pages 93 – 150, Section 8)	Screening for Men of Average and High Risk	overdiagnosis rate with repeated screening in general population and men of Black ethnicity respectively. However, Figure 24 has labelled bars and Figure 39 does not, making it difficult to compare overdiagnosis rates between these populations. This makes it difficult to follow the model and understand how conclusions of the model are reached. Yorkshire Cancer Research recommend that an updated report is published, providing a comparison table for all modelling scenarios that look at the impact of screening scaled to the population of England across the different groups outlining additional cases/fewer deaths, estimated overdiagnosis rates, and net monetary benefit (NMB) etc. The general population modelling is the clearest with the overdiagnosis rates clearly labelled (Figure 24) and additional cases/fewer deaths set out for the probabilistic and deterministic analysis of the impact of screening scaled to the population of England. The men of Black ethnicity modelling section requires more detail and data labelling of Figures throughout to bring it in line with the labelling provided in the general population section. The NMB and overdiagnosis rates are not stated for screening Black men at ages 50 to 62 every 4 years which is outlined in the 'impact of screening scaled to the population of England' section as the preferred scenario. Figures 38 and 39 do include this scenario, but these graphs lack the necessary data labels to be able to follow the conclusions made on their basis. Justification is needed for why this scenario is chosen given the NMB is not the highest for this group, nor is the overdiagnosis rate the lowest. Further it is unclear if any adjustments have been made to the assumptions made to the data displayed in Figure 47 as the percentage change between each step of screening in this population is different to that of the general population data displayed in Figure 29. It was not possible to calculate percentage change for every step for men of Black ethnicity due to lack of data labels provided however using the few values provided in the corresponding text it seems the percentage change is not equivalent between steps for men in the general population compared to Black men. The corresponding text for Figures 29 and 47 refers to the number of 'follow-up mpMRI procedures'. To calculate the percentage change between each step for men of Black ethnicity the Charity has assumed 'follow-up mpMRI procedures' refers to the number of positive mpMRI despite the wording between the two statements not aligning. This assumption is made on the basis of the Figure 29 and its corresponding text. Overall, more justification would be valuable for not recommending screening for Black men. The NMB data in Figure 36 is very similar, if not more favourable to that displayed in Figure 72 for the BRCA population. Also, the overdiagnosis rates in Figure 37 are again similar to those in Figure 73 for the BRCA population. Whilst there is an acknowledged level of uncertainty in the data supporting the modelling for Black men, there remains a clearly identifiable population who can self-identify as eligible for screening in contrast to the BRCA scenario, which first requires men with a BRCA gene mutation to be identified. Yorkshire Cancer Research request that additional data to underpin the model for prostate cancer screening in Black men is acquired as a priority to ensure screening is not being withheld from a population that could greatly benefit. The lifetime risk of prostate cancer in Black men is 1 in 4 while the lifetime risk in White men is 1 in 8, highlighting the increased need in this population. Further it will be critical to understand data relating to stage at diagnosis, aggressiveness of disease and survival for Black men and how this differs to White men in England.

		The modelling for men with familial risk also lacks clarity. For example, NMB and overdiagnosis rates are not stated for screening men with familial risk at ages 58 and 60. Figures 56 and 57 do include this scenario, but again these graphs lack the necessary data labels to be able to follow the conclusions made on their basis. It is therefore unclear why it has been decided to use this scenario in the modelled impact of screening scaled to population of England. Furthermore, Figures (such as Figure 65) need data labels adding to align with the equivalent Figures in the general population section. Additionally, the Accompanying Narrative document (Page 19) states that “A family history was taken to mean any first-degree relative with breast, ovarian or prostate cancer”. Yorkshire Cancer Research request to see the other definitions of family history considerations and the rationale behind the decision to go with the stated definition. Finally, the modelling for men with BRCA1/2 mutations lacks some of the necessary details to understand the recommendation. For example, Figures 74 and 75 lack data labels needed to read the NMB and overdiagnosis rates. On the basis of this model it is recommended that a targeted screening programme should be pursued for men with a confirmed BRCA1 and BRCA2 variant every 2 years, from age 45 to age 61. However, at no point in the text (only on the graphs which are unlabelled) does the model state the NMB nor overdiagnosis rate for screening BRCA carriers biennially from ages 45 to 61. For the data displayed in Figure 83, again it would be helpful to understand the assumptions upon which these numbers are based as the percentage change between each step of screening in this population is different to that of the general population data displayed in Figure 29.

Please return your completed form to the UK NSC Inbox UKNSC@dhsc.gov.uk by 11.59pm GMT on 20 February 2026.

S73	Professor Francis Chinegwu ndoh MBE	Cancer Black Care	Cancer Black Care is a longstanding registered charity, based in Brent, but outward-looking. We support cancer sufferers and their families, in particular those from minority ethnic groups. The majority of the men are suffering with prostate cancer. Many diagnosed with advanced disease. What they ask is, could these have been found earlier, when they reing a lise they are incurable? The answer to their question is yes, had the NHS run a prostate cancer screening programme. The reality is that the men we deal with lack knowledge about prostate cancer and so would not know about the psa blood test, yet alone see the GP for the blood test. Even those who can access their GP often face a refusal on request for a psa. Screening would eliminate these barriers to early diagnosis. Whilst Cancer Black Care would support a national screening programme for all men, our particular focus is on black men. It is recognised that black men are twice as likely to be diagnosed with prostate cancer and have twice the mortality. This is an inequity which we do not think that the National Screening Committee (NSC)have adequately considered. We don't think you need a randomised screening trial of black men to run for 20 years to surmise that screening black men for prostate cancer would save lives. That screening saves lives is undisputed from the European Randomised Screening Study, which has reported 23 years out. It is not a stretch to extrapolate what would happen if black men were screened. Would the benefits outweigh the harms? We think so. We do not think that the NSC paid enough notice to the harms of late diagnosis. The black community is strongly in favour of prostate cancer screening. We feel that the harms of screening are overblown compared to the benefits. Black patients consistently report a less favourable experience of cancer care. The NSC recommendation against screening in the high risk group of black men has given the message that the system does not care about us. Caring and trust are linked as we saw during Covid, when there was vaccine hesitancy in the black community. Much

			work went into reversing that trend. We are a risk of losing that improvement in Trust. Maternal mortality is much higher in black women than white women. Another example of what is is the NHS doing for its black community. On the grounds of equity, being responsive to the black community, preserving trust and increasing health literacy, We feel men can decide for themselves if they wish to take up a screening opportunity. The current NSC recommendation is overly paternalistic. Cancer Black Care strongly supports a national screening programme now for black men as a high risk group. Now, not waiting for the TRANSFORM study, much as we welcome that research. We believe that screening would be cost-effective, given the reduction in late stage prostate cancer and the huge costs of drug treatments. Other organisations we are sure will make cogent cases for screening with more facts and figures. We support the Prostate Cancer Research submission, which has been shared with us. We share their concerns over deficiencies in the SCHARR modelling.
S74	Sarah Owen MP	Labour Men and Boys Steering Group	Prostate cancer is the most commonly diagnosed cancer in the UK – with more than 64,000 men diagnosed, and 12,000 men dying, from the disease every year. Around 1 in 8 men will be diagnosed with prostate cancer in their lifetime, but incidence doubles in black men to 1 in 4. Awareness, education and screening can all save lives. There remains a sense of stigma and shame around men and boys discussing health-related issues, both physical and mental, that can prevent men from getting the diagnosis and treatment they require due to feeling anxious or embarrassed about going to see their GP. Regular screening for other types of cancers such as breast, cervical, bowel and lung, catches disease when it is early enough to treat successfully and save lives. Charities such as The Prostate Project have called for a form of screening programme, particularly one targeted as black men owing to their higher risk, expanded from the current recommendation of screening men with the BRCA gene variant. The recent Lancet commission on prostate cancer argued strongly that with improving longevity and age structures, prostate cancer prevalence is likely to increase, and that earlier diagnosis and treatment will improve outcomes for those who suffer from it. Existing research has overwhelmingly focussed on men of

		European origin, and much less has focussed on black men, despite much higher prevalence. The risk of overdiagnosis from the potential inaccuracy of a PSA test is mitigated by further screening and a longer diagnostic process, preventing an overwhelming of biopsy labs. To not screen black men, despite the known higher risk and prevalence of cancer in this community, will further deepen healthcare inequalities and race-based discrepancies in life expectancy. The National Prostate Cancer Audit in 2025 showed that black men and men in deprived areas were more likely to be diagnosed late, and die, from prostate cancer. A national screening programme is therefore necessary to ensure more men get tested, and that black men in particular get early diagnosis and treatment. Though there is a risk of over-diagnosis, under current trends and trajectories the combination of social stigma and a lack of screening of high-risk groups such as older black men may combine to lead to more deaths from prostate cancer. The Labour Men and Boys steering group would encourage the NSC to consider a screening programme, particularly targeted at black men.
S75	Robert Calvert MA MD FRCS(Uro l)	The draft recommendations are largely based on the SCHARR Prostate Cancer Screening model. I commend the NSC for considering modelling evidence which I believe is entirely appropriate in this process. Nevertheless, while this model is technically careful, it is structurally conservative and a model whose scope of validity is narrower than implied: • It describes reasonably well what CAP/ERSPC-style screening might have achieved in a modern NHS context; • It is much less well equipped to describe what a deliberately designed, MRI-era, risk-stratified programme could achieve, especially over appropriate time horizons and using a more flexible economic threshold. That distinction is crucial when interpreting its conclusions for future policy. Below is a methodological review of the model.: Methodological Review of the SCHARR Prostate Cancer Screening Model and its Policy Implications This review focuses on structural and methodological features of the SCHARR prostate cancer screening model which, taken

		together, are likely to understate potential benefits and overstate some harms in modern, risk-targeted screening strategies. It is organised into eight main areas: 1. Definition of “familial high risk” 2. Time horizons used to present benefits and harms 3. How overdiagnosis and harms are defined and weighted 4. Choice of MRI specificity and diagnostic operating point 5. Assumptions about sojourn time in the MRI era 6. Validation strategy and reliance on ERSPC/CAP 7. Modelling of Black men 8. Choice of QALY threshold and limited exploration of £30k/QALY The model is complex and sophisticated and the result of considerable work. The concern is not that it is “wrong” in a narrow technical sense, but that several key structural and value-laden choices all point in the same direction: high overdiagnosis, modest apparent mortality benefit, and conservative economic thresholds, especially for high-risk subgroups. 1. The definition of “familial high risk” 1. 1 Very broad definition The model defines “familial risk” extremely broadly: • Any first-degree relative with breast, ovarian or prostate cancer is counted. • Age at diagnosis is often not constrained (so late-onset breast cancer in a mother may be treated similarly to early-onset prostate cancer in a father). • The age pattern of “known family history” is partly imported from colorectal cancer work (MiMiC-Bowel) rather than prostate-specific family-history data. By the model’s own numbers, this leads to roughly one-third of men in their late 50s/early 60s being classified as having “familial risk”. That is much closer to “any family cancer signal at all” than to what most clinicians would call “familial high risk”. 1. 2 Dilution of true high-risk families Because such a large proportion of the cohort is labelled as “familial risk”, the average risk elevation in this group is only modest. It mixes together:

		• Men with a single elderly relative with breast cancer, and • Men with multiple first-degree relatives with early-onset, aggressive prostate cancer. In effect, the group becomes: “Slightly above average risk”, not “high risk” in any meaningful sense. 1. 3 Consequences for modelled cost-effectiveness This design choice has predictable consequences: • Targeted familial screening appears only marginally more favourable than general-population screening, because the “familial” group is so large and only slightly higher risk. • The model estimates overdiagnosis fractions in familial-risk strategies that are similar to, or only slightly better than, those in the general population. • Crucially, the model provides almost no insight into what most clinicians actually care about: men with truly strong family histories, such as: - o ≥ 1 first-degree relative with prostate cancer diagnosed <60; - o ≥ 2 first-degree relatives affected at any age; - o Dense clustering of aggressive disease. 1. 4 What ought to have been done A more clinically realistic approach would: • Define tiers of familial risk, for example: - o Moderate FH: one first-degree relative with prostate cancer any age. - o High FH: ≥ 1 first-degree relative with prostate cancer <60, or ≥ 2 first-degree relatives at any age, or combined prostate + breast/ovarian clustering. • Calibrate each tier separately, with different hazard ratios and potentially different screening strategies. • Focus policy evaluation on the truly high-risk tier, rather than smearing risk thinly across a third of the male population. As it stands, the “familial” analyses in the model largely answer the wrong question. They show that screening a very large, mildly elevated group is not dramatically better than general screening –

		which tells us almost nothing about targeted screening for genuinely high-risk families. 1. Time horizons limits in national scaled results 1. 1 Use of a 15-year horizon for headline “England-scaled” results Many of the key “impact” tables in the report – particularly for the risk-stratified scenarios (familial risk and Black men) – present results over 15 years from the start of the programme. For example: • For a man first invited at age 50, outcomes are only counted to about age 65. • Extra cancers detected by screening in the early years count fully. • Deaths prevented that occur after year 15 are not counted in those summaries. This is especially important because: • Prostate cancer is often slow-moving, and • The main mortality benefit of early detection generally emerges 15–25+ years after diagnosis, particularly for men screened in their 40s or early 50s. 1. 2 Bias against high-risk and younger groups For high-risk groups screened earlier (e.g. Black men 50–62; BRCA carriers 45–61; “familial risk” starting in the 50s): • The programme generates additional diagnoses and treatment in the first 5–10 years. • Many of the deaths averted will occur in the 15–30-year window after first screen, not just within 15 years. Truncating the horizon at 15 years therefore: • Inflates the apparent ratio of “extra cancers” to “deaths prevented”, because all of the early overdiagnosis is counted but a substantial fraction of mortality benefit is deferred beyond the time window. • Hits high-risk groups particularly hard, as they are more likely to benefit from early detection over a longer remaining lifespan. 1. 3 Better practice For a condition like prostate cancer, and especially for screening starting before 60, it is more appropriate to:

			• Present lifetime or at least 25-year horizons for the primary benefit–harm analysis; and • Where a shorter horizon is also used (e.g. 15 years for budget planning), explicitly show both 15-year and lifetime outcomes side by side. Without that, the headline results risk over-emphasising near-term harms and under-representing long-term benefits, particularly in younger, high-risk men. 1. How overdiagnosis and harms are defined and weighted 1. 1 Definition of overdiagnosis Overdiagnosis in the model is defined mechanically as: Excess incidence in the screening arm, divided by the number of screen-detected cancers i.e. the proportion of screen-detected cancers that would never have been diagnosed before death in the no-screening arm. This is a standard definition in screening modelling, but in prostate cancer in 2025 it is too blunt for several reasons: • It does not distinguish between: - o A man labelled with low-risk cancer and managed on active surveillance with minimal physical harm; and - o A man who undergoes unnecessary radical surgery or radiotherapy with lifelong impact on urinary and sexual function. • It treats all “excess incidence” as a binary harm, regardless of the intensity of treatment, surveillance, or impact on quality of life. Given that modern practice aims to manage many low-risk cancers conservatively, this risks over-penalising any screen-detected cancer that would not have presented clinically, even if it is managed with relatively low morbidity. 1. 2 Utility decrements and treatment era The QALY framework in the model relies on utility decrements for: • Cancer diagnosis and “label”; • Biopsy; • Radical prostatectomy; • Radiotherapy and systemic therapies.

		These are largely derived from older-era studies, often from periods when: • Radiotherapy planning and delivery were less precise; • Nerve-sparing and continence-preserving surgical techniques were less widely adopted; • Active surveillance protocols were less mature. There is a real risk that these decrement values overstate the long-term disutility of contemporary treatments and understate the benign nature of well-run active surveillance, particularly in high-volume centres. 1. 3 Under-valuation of non-fatal benefits The model attempts to compress all benefits into QALYs, but some key non-fatal outcomes are not well represented: • Reduced incidence of metastatic presentations (spinal cord compression, pathological fractures, etc.). • Avoidance of emergency presentations and unplanned admissions. • Potential improvements in quality of death (less late-stage uncontrolled pain, fewer crisis events). These are either counted weakly or only indirectly via QALYs, and are then heavily discounted (see QALY section), reducing their apparent value. 1. 4 Net effect Bringing this together: • Harms such as biopsies, diagnoses, and treatment side-effects are: - o Counted immediately, - o Treated largely as fixed, substantial decrements, and - o Applied generously to any “excess incidence”. • Benefits involving avoidance of metastasis and death are: - o Delayed (often beyond 15 years), - o Converted into discounted QALYs, and - o Judged against a conservative £20k (or £15k) per QALY threshold.

		In combination with a long sojourn time (see below), this tends to produce high overdiagnosis percentages and modest net QALY gain, even in groups where many clinicians would intuitively expect screening to be beneficial. 1. The choice of MRI specificity and diagnostic operating point 1. 1 The chosen MRI performance In the model, mpMRI performance for clinically significant prostate cancer (csPCa) is set to roughly: • Sensitivity ~0.88 • Specificity ~0.45 These figures are essentially a slightly softened version of the PROMIS trial (Ahmed et al.), which reported high sensitivity but relatively low specificity when using a low threshold (any Likert ≥ 3 lesion counted as “positive”). That is a defensible choice if one’s goal is to reproduce PROMIS-like behaviour in a diagnostic accuracy context. 1. 2 Why this may be pessimistic for screening However, PROMIS was: • Conducted in referred symptomatic/suspected men, • Early in the mpMRI adoption curve, • Using template mapping biopsy as the reference standard, • Deliberately using a low threshold to avoid missing csPCa. In a screening or organised risk-stratified programme, one would reasonably expect to: • MRI-lesion targeting rather than template mapping biopsy sacrificing a little sensitivity to improve specificity; • Combine MRI with PSA density and/or risk calculators to avoid biopsying low-risk lesions – especially for PIRADS 3 lesions; • Benefit from better scanner quality and greater radiologist experience than in early PROMIS-era practice. These features move the operating point towards higher effective specificity (fewer false positives and fewer unnecessary biopsies) than 0.45, while maintaining acceptable sensitivity for csPCa. 1. 3 Interaction with sojourn time and overdiagnosis In the SCHARR model, MRI operates on top of a CAP-era natural history with a long sojourn time. Given that structure:

		• Setting MRI specificity at 0.45 means: - o A large proportion of men without csPCa have “positive” MRIs, - o Many undergo biopsy, and - o More low-risk or indolent lesions are detected than might be the case with a higher threshold. • Under the model's definition of overdiagnosis (excess incidence), each additional low-risk cancer found in this way is classified as overdiagnosed, and carries a disutility. If, by contrast, one assumed a more typical modern MRI operating point (e.g. sensitivity 0.80–0.85, specificity 0.65–0.75 for csPCa in a triage role): • Fewer false positives and biopsies, • Fewer low-risk lesions brought to light, • Lower overdiagnosis fractions, and • A better harms:benefits balance. The SCHARR model does not meaningfully explore this trade-off. It effectively fixes MRI at a high-sensitivity, low-specificity setting that maximises false positives in a natural history which already contains a large reservoir of latent, screen-detectable disease. 1. 4 Consequence for the conclusions This is not a “wrong” assumption numerically – it is consistent with PROMIS. But in the context of evaluating future organised screening, it is arguably on the pessimistic side, and it interacts with the long sojourn time to: • Overstate the frequency of MRI-positive, biopsy-negative men, • Overstate the number of low-risk cancers detected, and therefore • Make it difficult for MRI-first strategies to demonstrate the degree of overdiagnosis reduction that many clinicians now see in practice. At minimum, one would expect to see sensitivity analyses across a range of MRI operating points, explicitly showing how higher specificity (with modestly reduced sensitivity) would affect biopsy rates, overdiagnosis, and cost-effectiveness. That is largely absent. 1. The setting of a long sojourn time 1. 1 What the model assumes The model's natural history includes a “pre-clinical, screen-detectable” state. The sojourn time is the amount of time a cancer

		spends in this state – detectable by screening, but not yet clinically diagnosed. In this model: • The calibration target for men aged 50–69 is a mean sojourn time of about 13.4 years ($\pm 10\%$), taken from CAP-era analyses. • When the model is fitted to incidence and mortality targets, the best-fit parameter sets imply a mean sojourn time of roughly 9–11 years in this age band – still long, and clearly rooted in PSA+TRUS-era natural history. 1. 2 Why sojourn time is critical For a given test and screening interval: • Longer sojourn time → more cancers reside in the detectable-but-silent pool → more cancers that screening can pick up. • Crucially, many of these cancers in older men will never become clinically diagnosed before death from other causes → these are classified as overdiagnosed. Sojourn time is therefore one of the dominant drivers of: • How many additional cancers screening detects; and • What proportion of those are labelled overdiagnosis in the model. A CAP-era mean sojourn of ~10–13 years implies a very large reservoir of screen-detectable but clinically indolent prostate cancer. 1. 3 Mismatch with an MRI-first era Modern prostate cancer diagnosis typically uses an MRI-first pathway, in which: • Many small, low-grade (GG1) lesions are not MRI-visible and are not routinely biopsied. • The screen-detected pool is enriched for MRI-visible, clinically significant ($GGG \geq 2$) disease. • Active surveillance is widely used for low-risk disease when it is detected. In this context, the relevant sojourn time for the cancers we actually detect and act on has changed: • Many ultra-indolent lesions effectively never enter the screen-detectable state (for screening purposes) because they remain MRI-invisible throughout life and are not biopsied.

		• For MRI-visible, clinically significant cancers, the window from “MRI-detectable” to “clinical diagnosis without screening” is likely shorter and more closely tied to the biology of genuinely important disease. Anchoring sojourn time to a CAP-era estimate effectively treats MRI-based screening as if it were still sampling the full CAP reservoir of latent disease, including many lesions that we now deliberately ignore. 1. 4 Consequences for overdiagnosis This choice helps explain why: • Overdiagnosis fractions in the model remain very high (often ~40–60% for repeat screening strategies, and rising to 80%+ for one-off screening at older ages). • MRI, in the model, appears mainly as a way of reducing biopsy numbers and adjusting stage mix, not as a tool that genuinely lowers overdiagnosis by excluding many indolent lesions from the detectable reservoir. In other words, the model's overdiagnosis estimates are consistent with its own assumptions, but those assumptions are set such that MRI-era programmes cannot fully realise the potential reduction in overdiagnosis that many clinicians believe exists. 1. 5 What would be needed instead A more realistic MRI-era treatment of sojourn time would: • Re-estimate sojourn time de novo using MRI-era data (PROMIS, PRECISION, NPCA in the MRI period), rather than imposing CAP. • Explicitly model MRI-invisible ultra-low-risk disease as effectively never screen-detectable. • Use separate sojourn distributions for: - o MRI-invisible micro-GG1 (no meaningful sojourn); - o MRI-visible GG1 (shorter sojourn, often managed with AS); - o MRI-visible GGG$\geq$2 (key determinant of mortality benefit). • Provide sensitivity analyses showing how shorter MRI-era sojourn durations change overdiagnosis and cost-effectiveness. Without this, the model's very high overdiagnosis fractions should be regarded as upper-bound, conservative estimates, not precise forecasts of what a deliberately modern, risk-targeted programme could achieve. 1. Structural problems related to validation

		1. 1 Heavy reliance on ERSPC and CAP The model reports “external validation” by running: • A CAP-like scenario (single PSA at 59, TRUS-era biopsy); and • An ERSPC-like scenario (PSA 3.0, 4-yearly, ages 55–69). In these runs, the model reproduces the ERSPC 23-year incidence and prostate-cancer mortality rate ratios very closely, and approximates CAP. On one level, this is reassuring. On another, it means that: • The model is considered “valid” precisely when it behaves like late-1990s/early-2000s PSA+TRUS trials, with known contamination, older treatments and no MRI. • The natural history and screening effect size are de facto anchored to the ERSPC/CAP benefit–harm space, even though clinical practice has moved on. 1. 2 The DRE+TRUS $\approx$ mpMRI assumption in ERSPC mimic A particularly striking assumption is made in the ERSPC mimic: • Although ERSPC used PSA, DRE and evolving TRUS biopsy protocols, the model treats the combined diagnostic accuracy of DRE+TRUS as equivalent to mpMRI, for the purposes of matching trial outcomes. This simplification: • Effectively “upgrades” 1990s diagnostic work-up to modern mpMRI-level accuracy in the validation step. • Narrows the apparent gap between ERSPC-style screening and a modern MRI-first pathway. • Helps ensure that when you run an “ERSPC-like” schedule with the model’s diagnostic machinery, you still get an ERSPC-like result. In combination with the CAP-anchored sojourn time and the low MRI specificity, this makes it structurally difficult for the model to show that truly modern MRI-based screening could yield a substantially better benefit–harm ratio than those trials. 1. 3 Lack of modern, risk-stratified validation By contrast, there is very limited validation against: • MRI-era UK data (e.g. PROMIS, PRECISION, or NPCA in the mpMRI period) for:

		- o Distribution of GGG1 vs GGG$\geq$2 in screen-detected cancers; - o Biopsy rates per 1,000 men; - o Real-world reductions in low-risk detection. • Ethnicity- or family-history–specific registry patterns (for Black men or strong familial risk). • Other models (e.g. CISNET) via common scenario comparisons. The overall effect is that: The model is judged “valid” when it matches CAP and ERSPC, but is not strongly challenged to match modern UK MRI-era behaviour, nor the specific characteristics of high-risk subgroups. 1. Structural problems related to modelling Black men 1. 1 Patchwork data sources For men of Black ethnicity, the model combines: • A hazard ratio for onset (~2.6 vs White men) from UK Biobank. • A shift towards higher-grade disease based on US Medicare data, reflecting more Gleason 7–10 disease at diagnosis. • The same stage-specific survival, utilities and costs as for the general population – no ethnicity-specific survival modelling. There is no explicit calibration step ensuring that the model reproduces UK Black-specific incidence and mortality curves by age, nor any UK-based calibration of stage or grade distributions at diagnosis by ethnicity. 1. 2 “Strange” outputs The resulting outputs for Black men are, in several respects, counter-intuitive: • For a repeat screening strategy such as 4-yearly 50–62, scaled to England, the model projects: - o Roughly 571 additional prostate cancer cases; - o Only about 11 prostate-cancer deaths prevented over 15 years (deterministic run). - o This implies ~52 extra cancers per death averted. • By comparison: - o General-risk “58 & 60” strategy: ~19 extra cancers per death averted.

		o Familial-risk best strategies: roughly mid-teens extra cancers per death averted. So, paradoxically, a group known to be higher-risk (twice the incidence and mortality) is shown to have a worse benefit–harm ratio (more extra cancers per death prevented) than lower-risk groups. Overdiagnosis percentages themselves (as a fraction of screen-detected cancers) are very similar to those in general and familial-risk groups, despite the higher baseline risk. 1. 3 Authors' own caveats The report itself acknowledges that: • The assumption of more aggressive disease in Black men is based on US data, and may reflect health-system inequalities rather than biology. • If this assumption is wrong, the model may mis-estimate (often over-estimate) the cost-effectiveness of screening in Black men. • There is a need for better UK data on Black men, including incidence-to-mortality ratios and uptake patterns. Taken at face value, these caveats already imply that modelled outcomes for Black men are highly uncertain. 1. 4 Interpretation When you combine: • A general-population, CAP-era natural history (long sojourn, high overdiagnosis), • A Black-incidence multiplier from UK Biobank, • A “more aggressive” grade distribution from US data, and • No ethnicity-specific calibration to UK mortality, it is not surprising that the model produces strange, internally inconsistent results: • A high-risk group whose screening appears to generate more harm per benefit than lower-risk groups; • Overdiagnosis fractions that fail to reflect the intuitive expectation that a higher proportion of screen-detected cancers in Black men would be genuinely clinically important. 1. 5 How modelling of Black men could have been better approached

		Even with limited data, a more robust Black-men submodel was possible. In particular, the modellers could have: 7.5.1 Anchor to UK incidence and mortality by ethnicity Rather than just multiplying incidence by a hazard ratio and importing a US “aggressiveness” effect, the model should have been calibrated to both: • Age-specific incidence of prostate cancer in Black vs non-Black UK men, and • Age-specific mortality by ethnicity. This would enforce a realistic incidence-to-mortality ratio in Black men and make it much harder to end up with patterns like “many extra diagnoses but very few deaths averted”. 1. * 2 Use UK (or UK-constrained) stage/grade data, and minimise unvalidated structural differences Where possible, UK data should guide: 2. Stage at diagnosis by ethnicity (localised vs advanced vs metastatic), and 3. Any available grade/GGG distribution differences. US data on “more aggressive disease” could be treated only as a weak prior, allowed to shift if it does not fit UK incidence and mortality. Sojourn time and stage-specific survival should default to being the same as for non-Black men, unless UK data clearly demand otherwise. 1. * 3 Make uncertainty explicit and avoid over-reliance on a 15-year snapshot Given sparse evidence, the Black-men results should be presented with: 2. Wide uncertainty ranges and explicit alternative scenarios (e.g. “higher incidence but no extra aggressiveness”; “equal incidence:mortality ratio to non-Black men”). 3. Lifetime or ≥ 25-year outcomes alongside any 15-year “impact on England” tables, to avoid short-horizon summaries underplaying deaths averted in a younger, high-risk group. 4. Problems related to the choice of QALY threshold and limited exploration of £30k/QALY

			1. 1 Conservative base-case threshold The base-case economic evaluation uses: • A £20,000/QALY threshold; • 3.5% annual discounting for both costs and QALYs (NICE reference case). £20k is the lower bound of NICE's conventional £20–30k/QALY range, not the midpoint. For a preventive, long-horizon intervention like cancer screening, one could reasonably argue that decisions should lean closer to the mid-range of that band. Indeed, since the publication of this model, NICE have increased the QALY range by £5K. 1. 2 Additional Green Book–style scenario at £15k The model also provides a scenario using: • A Green Book–style approach to discounting; • A £15,000/QALY threshold, which is even more conservative. There is no systematic exploration of: • A £30k/QALY threshold; • Higher thresholds for small, high-risk subgroups where budget impact is modest but equity concerns are strong (e.g. Black men, strong FH, BRCA2). 1. 3 Implications for high-risk groups For relatively small but high-risk categories: • Men of Black ethnicity; • Men with strong familial risk; • BRCA2 carriers, the absolute budget impact of a targeted screening programme is limited, and there is a strong equity argument that society may be willing to pay more per QALY to address a clearly higher baseline risk. By fixing the main decision rule at £20k (and exploring only £15k as a sensitivity), the model: • Systematically biases against interventions with modest but clinically meaningful benefits, especially when those benefits appear later in life.

		• Risks sending the message that lives in high-risk groups are “worth less” at the margin, in purely economic terms. A more balanced analysis would have: • Presented cost–effectiveness acceptability curves up to £30k–£40k/QALY; • Explicitly explored subgroup-specific thresholds; • Examined how conclusions change if one adopts £25–30k/QALY, particularly for targeted high-risk strategies. Even with the limitations described in previous sections various prostate cancer screening as modelled by SCHARR compares favourably to other established screening programmes such as AAA or risk-stratified lung cancer screening. These NMB figures would likely show significantly improve cost benefit realisation with lower harms should the model be modified in line with suggestions and focus on more carefully selected familial risk groups. 1. Overall assessment Taken individually, each of these modelling choices can be defended as “reasonable” or at least “pragmatic” given data limitations. Taken together, they point consistently in one direction: • A very broad familial-risk definition dilutes true high-risk families and makes targeted familial screening look weak. • Short time horizons (15 years for key results) under-represent long-term mortality benefit, particularly in younger and high-risk men. • A blunt overdiagnosis definition, conservative utility assumptions, and a low-specificity MRI operating point overweight the harms of diagnosis and treatment relative to later avoidance of metastasis and death. • CAP-era sojourn times ensure a large reservoir of latent disease, so overdiagnosis remains high even with MRI. • An ERSPC/CAP-centred validation strategy, including the DRE+TRUS≈mpMRI assumption, locks the model into an older trial benefit–harm space. • The Black-men submodel relies on patchwork data and produces counter-intuitive benefit–harm ratios that can be improved upon. • A £20k/QALY (and £15k) focus, with limited exploration of £30k/QALY, is an overly austere economic lens certainly for small, high-risk groups.

			The net result is a model that is technically careful but structurally conservative and a model whose scope of validity is narrower than implied: • It describes reasonably well what CAP/ERSPC-style screening might have achieved in a modern NHS context; • It is much less well equipped to describe what a deliberately designed, MRI-era, risk-stratified programme could achieve, especially over appropriate time horizons and using a more flexible economic threshold. That distinction is crucial when interpreting its conclusions for future policy.
S76	Callum Metcalfe-O'Shea and Jessica Turner	Royal College of Nursing	Royal College of Nursing Response UK National Screening Committee (UK NSC) Consultation on the Draft Prostate Cancer Screening Recommendation Draft recommendation The UK NSC's draft recommendation is to: • offer a targeted national prostate cancer screening programme to men with confirmed BRCA1 or BRCA2 gene variants every 2 years, from age 45 to age 61 • not recommend population screening • not recommend targeted screening of Black men • not recommend targeted screening of men with family history • collaborate with the Transform screening research trial team to: - o answer outstanding questions on screening effectiveness for black men and men with a family history – as soon as trial data becomes available - o await results of the study to develop and trial a more accurate test than PSA alone, to improve the balance of benefit and harm of screening Consultation comments The RCN welcomes the opportunity to respond to this consultation and to highlight the essential role nursing staff play in supporting patients to understand prostate cancer risk, testing options, and shared decision-making. As a professional and trade union body, our contribution focuses on the implications for nursing practice, workforce, and equitable access to appropriate care. In developing this response, we engaged closely with the Royal College of Nursing Cancer Forum and Public Health Forum committees to ensure that the views reflected here are grounded in frontline

		experience and professional expertise. A short survey was also circulated to forum members, enabling practising nursing staff across a range of settings to contribute their perspectives on prostate cancer screening, risk stratified approaches, and the practical implications for patient communication and service delivery. Their insights have helped shape the balance of this response, particularly in relation to the realities of shared decision making, the challenges of explaining overdiagnosis, and the need for equitable access to screening opportunities for higher risk groups. As an organisation, we support the recommendation to offer a targeted national prostate cancer screening programme for patients with confirmed BRCA1 or BRCA2 gene variants, with screening offered every two years from age 45 to 61. We recognise that this targeted approach is intended specifically for individuals with a confirmed genetic variant associated with higher risk, and we welcome the opportunity to ensure that nursing perspectives inform how such a programme is communicated, delivered, and evaluated. However, the proposed strategy is not clear on how patients from other high-risk groups—particularly Black patients, who experience significantly higher incidence and mortality from prostate cancer will be considered. It is important that this is clarified in the strategy to ensure that Black patients are not overlooked in a genetically targeted model and assurance is given that equity will be maintained and will not be disadvantaged. Further clarity is also required on how this population will be supported to access appropriate risk assessment and screening opportunities. In addition, we support the decision to await the results of ongoing research aimed at developing and testing a more accurate screening method than PSA, ensuring that any future screening approach is designed to optimise benefit while reducing avoidable harm. A central challenge in prostate cancer screening remains the detection of high-risk, clinically significant cancers while avoiding unnecessary investigations and treatment for slow growing cancers that may never become life limiting. Current screening methods, particularly PSA testing, have not demonstrated consistent reductions in prostate cancer mortality. There are also important harms to consider, including overdiagnosis and overtreatment. Any screening programme, whether national or targeted, will rely heavily on the nursing workforce. Nursing staff are often the first point of contact for patients seeking information about prostate cancer risk, symptoms, and testing options. They are also pivotal in helping patients understand: • The difference between high risk and low risk cancers. • The potential benefits of early detection. • The risks of overdiagnosis and overtreatment.

			• The side effects associated with invasive investigations and treatment. • The implications of genetic testing for individuals and families. Nursing staff are uniquely positioned to support personalised, balanced conversations that help patients make informed choices aligned with their values and risk profile. Any future screening strategy must therefore include investment in training, resources, and time for nursing staff to deliver high-quality, evidence-based discussions. Summary Nursing staff will be fundamental to delivering safe, person-centred conversations and ensuring patients are supported to make informed decisions. Promoting equity in screening for those at greatest risk, such as Black patients, will depend on clear, culturally informed public health messaging that supports appropriate risk awareness and encourages timely engagement with assessment and screening opportunities. The upcoming Transform trial will be pivotal in shaping the future direction of prostate cancer screening, and policy decisions should remain flexible until its findings are available.
S77	Nikhil Mayor	Imperial College London	Dear UK NSC, Please see attached a response to the public consultation on prostate cancer screening prepared by: Dr Nikhil Mayor, Imperial College London Professor Rhian Gabe, Queen Mary University of London Professor Hashim U Ahmed, Imperial College London Warm regards, Mr Nikhil Mayor

UK National Screening Committee

Consultation Comments Pro-forma

Screening for prostate cancer modelling study

Name:	Nikhil Mayor	Email address:	*****
Organisation (if appropriate):	Imperial College London		
Role:	Urology Resident Doctor, PhD Student and Clinical Research Fellow		
Do you consent to your name being published on the UK NSC website alongside your response?		Yes	
Section and / or page number	Text or issue to which comments relate	Comment <i>Please use a new row for each comment and add extra rows as required.</i>	

Please return your completed form to the UK NSC Inbox UKNSC@dhsc.gov.uk by 11.59pm GMT on 20 February 2026.

National Prostate Cancer Screening Survey: Urologists in England

*Report prepared for the UK National Screening Committee consultation
19th February 2026*

Authors

Nikhil Mayor, PhD Student and Clinical Research Fellow^{1,2}

Rhian Gabe, Professor of Biostatistics and Clinical Trials³

Hashim U Ahmed, Professor and Chair of Urology^{1,2}

Affiliations

1. Imperial Prostate, Department of Surgery & Cancer, Imperial College London, Hammersmith Hospital Campus, Du Cane Road, London, W12 0HS
2. Urology Department, Imperial College Healthcare NHS Trust, Charing Cross Hospital, Fulham Palace Road, London, W6 8RF
3. Centre for Evaluation and Methods, Barts Clinical Trials Unit, Wolfson Institute of Population Health, Queen Mary University of London, Charterhouse Square, London, EC1M 6BQ

Executive Summary

Background

The UK National Screening Committee (NSC) published draft recommendations on prostate cancer screening in November 2025 which are currently open to public and professional consultation. To contribute to the consultation process, a national survey was conducted to capture the views of urologists in England.

Survey

A cross-sectional survey was distributed to 819 urologists with valid email addresses across England. Responses were anonymous. A total of 204 responses were received (response rate 24.9%) from across the seven NHS regions in England. Most respondents reported direct involvement in prostate cancer care (90% in diagnosis; 73% in treatment).

Key findings

Whole population screening

75% (153/204) agreed with the recommendation not to introduce population screening. Most respondents rated the supporting evidence as moderate to strong.

Targeted screening in Black men

67% (128/191) disagreed with the recommendation not to offer targeted screening to Black men. Confidence in the supporting evidence was lower, with 41% rating the evidence as weak or very weak.

Targeted screening in men with any family history of prostate cancer

64% (123/191) disagreed with the recommendation not to offer targeted screening to those with any family history of prostate cancer. Evidence strength was similarly rated as weak or very weak by 43% of respondents.

Targeted screening in those with known BRCA1/2 mutations

89% (169/190) agreed with the recommendation to offer targeted screening. Most respondents rated the supporting evidence as strong or very strong.

Conclusion

Amongst responding urologists in England, there was broad agreement with the draft recommendations relating to population-wide screening and BRCA-targeted screening. In contrast, the majority disagreed with the recommendations not to offer targeted screening to Black men or to men with any family history of prostate cancer and these recommendations were associated with lower perceived confidence in the supporting evidence. These findings may help inform the ongoing consultation and highlight areas where further engagement or evidence may be valuable.

Report

1. Background

The UK National Screening Committee (NSC) is responsible for advising ministers and the NHS on the introduction, modification, or cessation of national screening programmes. Prostate cancer screening has been periodically reviewed in light of evolving evidence relating to PSA testing, diagnostic pathways, and risk-stratified approaches.

In November 2025, the NSC published draft recommendations on prostate cancer screening and opened these for public and professional consultation. The draft recommendations included proposals not to introduce population-wide screening, not to offer targeted screening to Black men or to men with a family history of prostate cancer, and to offer targeted screening to men with confirmed BRCA1 or BRCA2 mutations. In view of the potential implications for clinical practice, this survey was conducted to capture the perspectives of urologists in England during the consultation period.

2. Methods

2.1 Study design

We conducted a cross-sectional survey of urologists in England to capture professional views on the NSC draft recommendations on prostate cancer screening.

2.2 Participants

A near-complete list of practising urologists in England was compiled using publicly available professional information and institutional contact details. Duplicate entries were removed and email addresses were verified where possible prior to distribution. A total of 819 urologists with valid email addresses were invited to participate.

Survey invitations were distributed via personalised email links generated through the Qualtrics platform. Each invitation was associated with a unique survey link tied to the recipient's email address, preventing duplicate submissions and restricting access to invited participants only. The survey link was not publicly accessible. Invitations were sent on 4th and 5th February 2026, with three reminder emails sent to non-respondents. Responses were collected until 18th February 2026. Participation was voluntary and no incentives were offered. Invitations stated that a report would be shared with the NSC.

2.3 Survey

The survey addressed the primary recommendations made in the NSC draft report published in November 2025.

2.3.1 Whole population screening (mandatory)

Respondents were asked whether they agreed with the NSC's draft recommendation not to offer population-wide prostate cancer screening.

2.3.2 Targeted screening (optional)

Respondents were asked whether they agreed with the NSC's draft recommendations relating to targeted screening in:

- Black men
- Men with any family history of prostate cancer
- Men with confirmed BRCA1/2 mutations

Respondents were also asked to rate the perceived strength of the evidence underpinning each recommendation on a five-point Likert scale (very weak to very strong). A free text box was provided for respondents to provide additional comments.

2.3.3 Respondent characteristics (optional)

Information was collected on respondents' professional role, NHS region of practice, years working as a urologist, and involvement in the diagnosis and treatment of prostate cancer.

The survey was designed to be completed in approximately 2-3 minutes.

2.4 Data collection and confidentiality

Responses were collected anonymously. No identifiable personal data was collected and IP addresses were not stored. Completion of the survey was taken as implied consent for responses to be analysed in aggregate and included in a report shared with the NSC.

2.5 Analysis

Results were analysed descriptively. Categorical variables are reported as counts and percentages. Likert-scale responses are presented as frequency distributions. No additional statistical analyses were planned, as the purpose of the survey was to summarise professional opinion rather than test hypotheses.

2.6 Ethical considerations

The survey collected professional opinions from healthcare professionals and did not involve patients, interventions, or the collection of sensitive personal data, therefore formal NHS Research Ethics Committee approval was not required.

3. Results

3.1 Response rate

A total of 204 responses were received from 819 invited urologists, giving an overall response rate of 24.9%.

3.2 Respondent characteristics

Of the respondents who provided role information, 185/187 (99%) were consultant urologists and 2/187 (1%) were SAS doctors.

Respondents were distributed across the seven NHS England regions including London (n=46); Midlands (n=20); East of England (n=19); North East and Yorkshire (n=35); North West (n=18); South East (n=27) and South West (n=20).

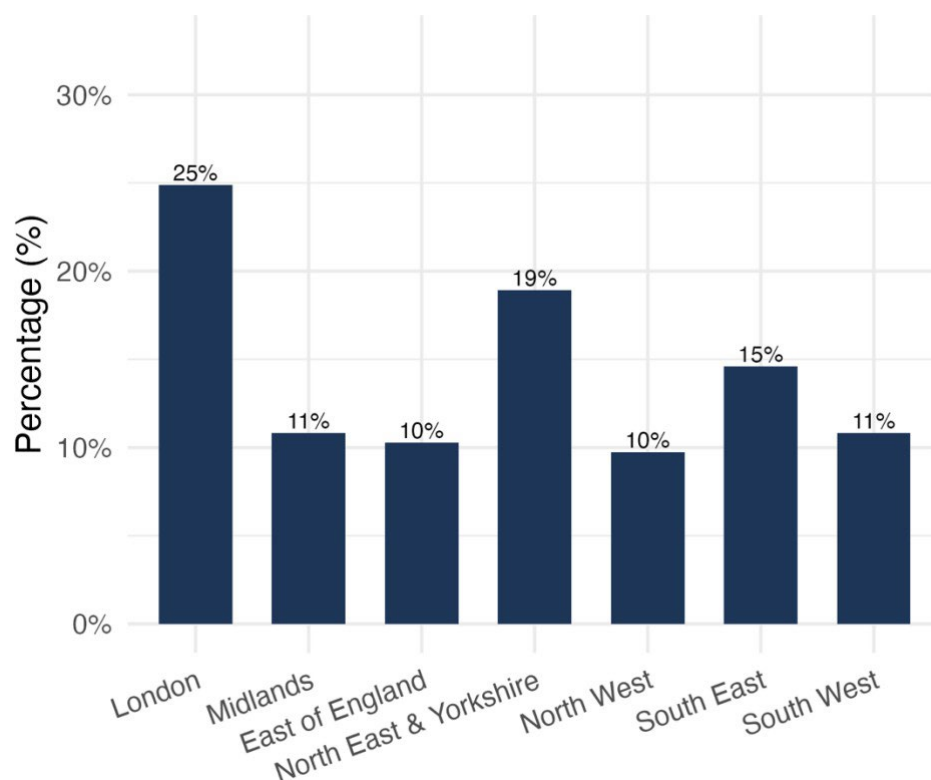


Fig 1. Bar chart showing geographical distribution of responses to survey.

Most respondents reported being directly involved in prostate cancer care:

- 170/188 (90%) involved in prostate cancer diagnosis
- 137/188 (73%) involved in prostate cancer treatment

104 respondents reported years in practice, with a mean of 13.1 years (standard deviation 4.8).

3.3 Survey outcomes

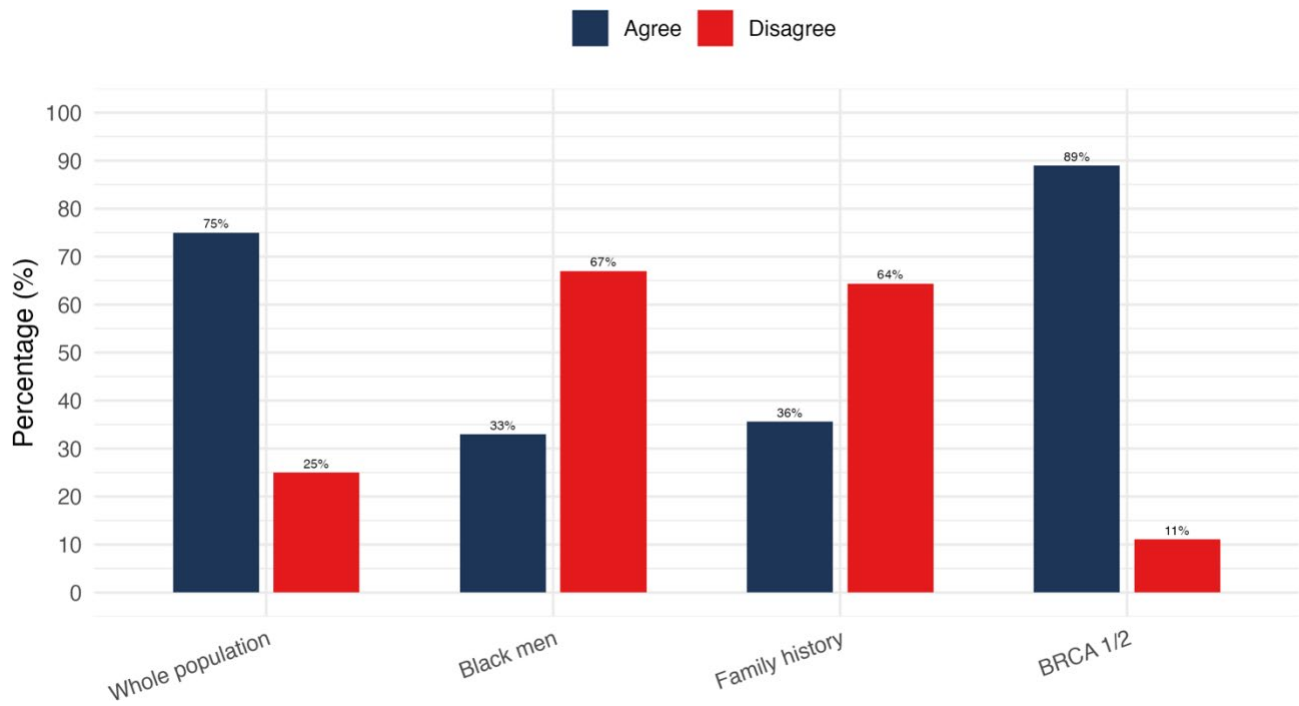


Fig 2. Bar chart showing agreement with each NSC recommendation.

3.3.1 Whole population screening

The majority of respondents agreed with the NSC's recommendation not to offer whole population screening:

- Agree: 153/204 (75%)
- Disagree: 51/204 (25%)

Perceptions of the evidence base were varied:

- Strong or very strong: 90/202 (45%)
- Moderate: 76/202 (38%)
- Weak or very weak: 36/202 (18%)

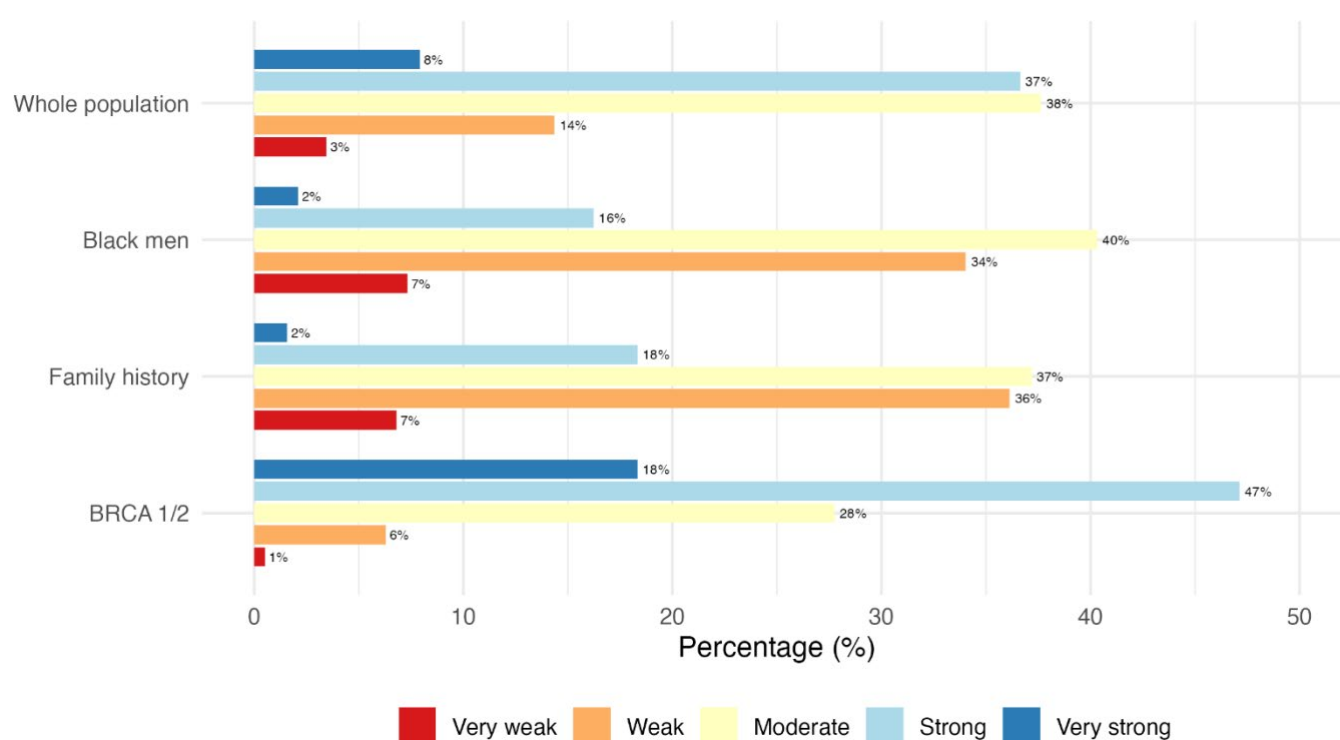


Fig 3. Stacked bar chart showing urologists' perceptions of evidence underpinning each NSC recommendation.

3.3.2 Black men

Two-thirds of respondents disagreed with the recommendation not to offer targeted screening.

- Agree: 63/191 (33%)
- Disagree: 128/191 (67%)

Confidence in the strength of evidence underlying this recommendation was lower:

- Strong or very strong: 35/191 (18%)
- Moderate: 77/191 (40%)
- Weak or very weak: 79/191 (41%)

3.3.3 Family history

Similarly, two-thirds of respondents disagreed with the recommendation not to offer targeted screening for men with any family history of prostate cancer:

- Agree: 68/191 (36%)
- Disagree: 123/191 (64%)

Again, respondents rated the strength of the evidence for this recommendation as low-moderate:

- Strong or very strong: 38/191 (20%)
- Moderate: 71/191 (37%)
- Weak or very weak: 82/191 (43%)

3.3.4 BRCA 1/2

There was strong agreement with the recommendation to offer targeted screening to men with known BRCA1/2 mutations.

- Agree: 169/190 (89%)
- Disagree: 21/190 (11%)

Respondents rated the strength of the evidence base underpinning this recommendation as strong:

- Strong or very strong: 125/191 (65%)
- Moderate: 53/191 (28%)
- Weak or very weak: 13/191 (7%)

3.3.5 Additional comments

The full list of additional comments provided by respondents is attached alongside this report,

Overall, respondents demonstrated broad agreement with the draft recommendations relating to whole population screening and BRCA1/2-targeted screening, but disagreement with recommendations not to offer targeted screening to Black men and to men with any family history of prostate cancer.

4. Implications

4.1 Overview

This survey provides a snapshot of urologists' views on the draft NSC recommendations on prostate cancer screening which are currently open for public and professional consultation. Responses were from consultant urologists across all seven NHS regions in England and the majority reported direct involvement in prostate cancer diagnosis and treatment, indicating that the findings reflect the views of clinicians directly engaged in prostate cancer care. According to NHS Digital workforce statistics, there were approximately 1,061 consultant urologists in England in August 2023. The 819 urologists invited therefore represent a substantial proportion of the national workforce.

Across the four draft recommendations, responses demonstrated a clear and strong pattern: broad agreement with recommendations against whole population screening and for targeted screening in men with known BRCA1/2 mutations, and majority disagreement with recommendations against targeted screening of Black men or those with any family history of prostate cancer.

4.2 Whole population screening

A clear majority of respondents agreed with the recommendation not to offer population-wide prostate cancer screening, and most rated the supporting evidence as moderate to strong.

4.3 Targeted screening of high-risk subgroups

In contrast, most respondents disagreed with the draft recommendations not to offer targeted screening to Black men and to men with any family history of prostate cancer. These areas of disagreement were accompanied by lower confidence in the strength of the supporting evidence, with a substantial proportion of respondents rating the evidence as weak or very weak.

This pattern does not necessarily imply that respondents consider the evidence in favour of targeted screening to be strong. Rather, it may reflect uncertainty regarding whether the current evidence base is sufficient to support a definitive recommendation against targeted screening in these higher-risk groups. The findings may therefore indicate areas where clearer communication of the evidence base, further modelling, or additional research could help address areas of professional uncertainty.

There was strong agreement with the recommendation to offer targeted screening to men with confirmed BRCA1/2 mutations, alongside high confidence in the supporting evidence. These responses suggest broad professional support for risk-stratified screening approaches in men with clearly defined high-risk genetic predispositions to

prostate cancer, where the evidence base for screening is perceived by respondents to be comparatively strong.

4.4 Implications for the consultation

Taken together, the findings suggest a distinction in respondents' views between:

- Population-wide screening, where there is broad agreement with the draft recommendation; and
- Risk-stratified screening in certain higher-risk groups, where there is greater professional uncertainty and lower perceived confidence in the evidence base.

These findings may be relevant to the ongoing consultation by highlighting areas where further engagement with clinicians, clarification of the evidence base, or additional research may be beneficial.

5. Limitations

This survey represents the views of responding consultant urologists rather than the entire urology workforce. Although the response rate of 24.9% is comparable with other national clinician surveys, participation was voluntary and it is possible that those with stronger views were more likely to respond. A substantial number of respondents reported direct involvement in prostate cancer diagnosis and treatment, suggesting that the findings reflect the views of clinicians actively engaged in prostate cancer care. Urologists whose practice is less focused on prostate cancer may have been under-represented, and their views may differ from those captured in this survey.

The survey was limited to urologists practising in England. The NSC recommendations apply across the UK, and the views of clinicians practising in Scotland, Wales and Northern Ireland were not captured in this survey.

Other professionals involved in prostate cancer care and diagnosis such as clinical nurse specialists, radiologists, and oncologists were not included. The findings therefore reflect the perspectives of urologists specifically, rather than the full multidisciplinary prostate cancer workforce.

Finally, the survey was designed to capture high-level professional opinion and did not explore in detail the reasons underlying individual responses, though additional comments were allowed and are provided alongside this report.

Please provide any additional optional comments on the UK NSC's draft recom...

Unclear as to BRCA screening. Agree to screen known carriers but is committee proposing to screen whole population for BRCA status? Seems excessive

I do appreciate that general screening is currently not evidence based. However, I believe we have enough evidence to support opportunistic screening; in those at high risk.

We work in an under-resourced system, and even if the evidence supported population screening, the tax-payer would not be able to afford it.

PSA based screening is inherently flawed as it is not a tumour marker.

The NSC has been entirely sensible and has not been swayed by 'public' opinion.

We do need to have PCa screening, but it should not be PSA based.

You need to think about the number of men having invasive investigations and over treatment. It's not about finding all the cancer - that is impossible.

There are a lot of poor decisions made regarding low volume, low risk prostate cancer.

We know the impact of prostate cancer treatment on quality of life and with the CAP/PROTEC 15 year data suggesting minimal OS benefit in treatment then were clearly over treating the disease of aging.

More men diagnosed, more men's life ruined with treatment.

The current status of unorganised testing is doing more harm and focuses on the wrong group of men. By offering the test to high risk group, the inequity can be reduced and the Message to society would be stronger.

my impression is from straw polls amongst colleagues that the majority of urologists in the UK do not check/know their PSA

Please provide any additional optional comments on the UK NSC’s draft recom...

Affirmative action to offset under-representation of black men in research might be justified, in view of higher risk and societal disadvantages they face, by offering screening in this group.

Family history is poorly coded in primary case so screening this group might not be feasible, although desirable. Family history of lethal prostate cancer might be more useful than any family history.

I am, in general, not a great fan of prostate cancer screening as it would currently run - huge resource and overdiagnosis issues. As a urologist in his 50s, I have not had my PSA checked.
However, even I was surprised at how very restrictive the recommendations were.

The scientific evidence shows that screening would only make a significant population based difference if BRCA positive men are screened. There is still not enough evidence to recommend the correct test to use on the correct men to role out national level screening.
The issue with BRCA positive men is exactly how to identify them. Government funds should be allocated to support studies like TRANSFORM and other prostate cancer diagnostic research to firstly identify the best screening test to use. That can then be applied to the correct/best population base. There also needs to be funding for a national genome repository or linked access to BRCA breast cancer databases to be able to identify BRCA positive men.

None

Is it proposed that testing for the BRCA 1/2 gene will be offered to ALL men from a certain age, in order to determine who to offer targetted prostate cancer screening to?

Where will men access this test?

Black men are a higher risk group - they should surely be offered targetted screening (?)

Re. screening men with BRCA1/2 mutations, the NSC has suggested that testing would only be performed in men who 'know that they are BRCA1/2 carriers'. Unfortunately many men don't know their status or have not been tested. Some men with a strong family history of prostate cancer, breast cancer or Lynch-related cancer will harbour the genes, yet the NSC has explicitly recommended against patients with a strong family history, which is counter-intuitive. The position on BRCA1/2 carriers also risks disadvantaging less educated men, leading to a potential socio-economic bias, in a group who already have poorer prostate cancer outcomes.

I agree at present that whole population screening isn't fully justified, however may in the future.
I do think those at high risk should be screened as they have more aggressive disease than the general population

Considering whole NHS, disproportionately high national health resources are used for a low mortality screen detected/ opportunistic prostate and breast cancer. National resources to be used for highly lethal cancers.

- The vast majority of men with BRCA gene mutations are unaware. A parallel screening of testing for this would be required if this is the only group for screening.

- Much of the evidence used to inform the recommendations is historical- the use of MRI, transperineal LA biopsy and better active surveillance regimes have all been improved in recent years in favour of screening.

Not necessarily “national screening.”

Instead:

A. Structured Informed Offer at 50

Rather than:

PSA available if you ask

Shift to:

At 50, men are informed about prostate cancer risk and PSA testing.

Not automatic testing.

But an active offer with standardised counselling.

That alone would change behaviour significantly.

B. Earlier Structured Offer for High-Risk Men

At 45:

Black men

Strong family history

Currently this is inconsistent across regions.

Standardisation would reduce inequality.

C. Risk-Based Recall

After a baseline PSA:

Very low PSA → long interval (5–8 years)

Moderate PSA → shorter interval

Abnormal PSA → MRI pathway

Right now, follow-up is inconsistent and GP-dependent.

Need to support and deliver Transform to provide evidence to potentially change guidance

Overall they seem very sensible and pragmatic

We would need costing analysis for such a programme and opportunity cost on what services we will remove to potentially accommodate such a programme.

I think it is reasonable. As aver compared with what. If the question is deferring a decision and proceed with large scale screening trial I think reasonable if trial cancelled or fails to recruit then at risk groups should be reconsidered but dont support generalised screening

Please provide any additional optional comments on the UK NSC’s draft recom...

The introduction of a screening programme is the only way to reduce deaths. Using PSA alone at current cut points, even with MRI as a pre biopsy triage is not good enough. The TRANSFORM study is clearly the vehicle to get to the best screening intervention at our disposal. I think the government should review the pilot data from the TRANSFORM study, once available, and invest further in it under the umbrella of a UK prostate cancer screening development group for the UK. scaling up this study will give the greatest power for iterative learning about optimal screening strategies, allow more screening interventions to be tested (Stockholm3, high frequency US instead of MRI etc) and avoid contamination of the control groups by recruiting before attitudes change. There is political element to this and if the government agrees to set up screening in a step wise evidence based way, with all activity providing evidence, there could be a win win for tax payers, providers and men at risk.

The NSC report fails to account for the fact a national screening program would mean the cessation of opportunistic screening by primary care. This would dramatically change its analysis and the outcomes/ recommendations.

I think very reasonable document. Screening studies are based on white population and black men present with higher grades and later. I think reasonable that we do more research in this population.

Re Family Hx - really need several first degrees to make it more likely.

How many 45-61 men have had BRCA testing!! Honestly. That said the evidence is out there for them.

Harms outweigh the benefits with current tests for offering screening to all men over the age of 50. There is also longstanding evidence to show that huge numbers of cancers are not clinically significant and this uses NHS funds to generate mass anxiety

There is a lack of data regarding screening directed at targeted at risk groups.
Family history may be impossible to verify

It will be difficult to identify patients at risk based on BRCA mutation since routine testing is currently not in place.

Black men have double the risk of prostate cancer than white men and in my opinion should be offered PSA tests at least every 2 years from the age of 50 with a sensible cut off after 80
It is even more important to offer PSA at a younger age to men with 1 or more direct relatives with prostate cancer (especially if diagnosed under the age of 60) as their cancer risk is significantly raised

Please provide any additional optional comments on the UK NSC's draft recom...

ignoring the ERSPC trial is one of the favourite sports of some Urologists in UK

None

GP training on prostate cancer diagnosis will be paramount. Funding will need to be available to help manage the significant increase pressure on MRI scans that will be more prevalent if any form of risk adapted screening is considered.

This survey reflects very badly on British Urology. NSC has an expertise that we do not have. We would not accept advice from them in theatre. Just declaring that we have a conflict of interest does not permit us to act in a self serving manner.

Erspsc and newer studies show the benefits of screening in a larger population. A baseline biparametric MRI and PSA to help calculate psa density and lesions would help to risk stratify men along with family history, ethnicity and genetic factors. Screening investigations could start at age 50 in low risk, 45 in high risk men (FH, black, BRCA). After further stratification (MRI/PSA), low risk men could have a PSA every 4-5 years, moderate risk have PSA every 2 years, high risk could either be 6-12 months. Once PSAD is known, the decision whether to progress to treatment is easy.

Should we look at screening with MRI?

Maybe a combination of risk should be favoured

Please provide any additional optional comments on the UK NSC’s draft recom...

Decisions on screening should not be based on opinions, but instead on data and pragmatism. There is a clear agenda in this survey and I am unsure how much benefit can be gained from this type of question for a population screening issue that has to be data driven.

Demographics stored in primary care are completely insufficient to identify patients with significant family history, so screening on that basis is not possible. Similarly our experience of identifying patients based on ethnicity is also challenging.

Although the BRCA +ve population is only a small group, these patients are easily identifiable so can be screened safely

the BRACA gene question is a fudge as BRACA gene testing is limited across the country and not routine. We therefore are not capturing these patients so we don't screen them despite the recommendation.

The propaganda especially from PCUK needs to be strongly rebutted. All urologists associated with PCUK should take a strong line and represent the profession not self interest

the assessments of screening are were made on single rather than repeat risk assessed screening modelling and probably factored in the economics and the resources available to underwrite screening

also the fact that the age of the population that commonly currently has prostate cancer is often no longer a contributor economically to society could be a factor so any economical assessment of healthcare costs are based mainly on the savings in decreasing treatment costs of more advanced disease and palliative care which as much of this is charitable or borne by the patient and thus maybe seen as cheaper than the costs of diagnosis and radical treatment

I would screen men who have young prostate cancer in the family but also look at breast, ovarian, uterine and bowel cancers too.

Please provide any additional optional comments on the UK NSC’s draft recom...

I feel that population based screening is already happening on an ad hoc basis and this is not a satisfactory situation. Many GPs apparently (according to my patients) are reluctant or refuse to do the PSA. This is causing a lot of confusion in men. Despite the lack of evidence, personally as a urologist of 30 years experience, I feel that a properly organised and funded national screening process would be a much better option.

The team have looked at the evidence. Just because celebrities get prostate cancer isn't a reason to have national screening. Most doctors treating prostate cancer are conflicted. Equally, if people want a PSA let them have one. We have to move away from the 'you have a duty to be tested' type mentality that screening can induce. .

Black men >50 and men with close male relatives with prostate cancer should be offered screening

Good document

The screening test (PSA) has to be specified in the questionnaire.

I support the committee’s continued position not to implement whole-population PSA screening at this time, given the persistent risk of substantial overdiagnosis and downstream harms (biopsy complications, overtreatment, long-term urinary/sexual side-effects), and the limitations of PSA as a stand-alone screening test. We need further data, specifically from the TRANSFORM trial and others currently working in this area.

Screening for BRCA 1/2 should be more frequently than every two years

They are evidence-based

Please provide any additional optional comments on the UK NSC’s draft recom...

Large randomised screening trials, particularly ERSPC and CAP, have demonstrated that PSA-based screening can reduce prostate cancer mortality, with the mortality benefit increasing over longer follow-up in ERSPC. Although the absolute reduction in death is modest at a population level, these trials confirm a genuine stage-shift effect, with fewer men presenting with metastatic disease. Importantly, the balance of benefit and harm has evolved since these studies began: contemporary diagnostic pathways now incorporate routine pre-biopsy MRI, transperineal biopsy techniques with lower sepsis risk, and more selective use of radical treatment, with greater uptake of active surveillance for low-risk disease. In parallel, surgical and radiotherapy morbidity—particularly rates of severe incontinence and erectile dysfunction—has declined compared with historical cohorts, and treatment costs have become more predictable within modern NHS pathways. While modelling for the general population suggests that organised PSA screening is unlikely to be cost-effective at the £20,000 per QALY threshold and would require substantial NHS resource through large volumes of PSA tests, MRI scans, biopsies and downstream treatments, the real-world benefit–harm and cost profile in 2025 may be more favourable than that reflected in earlier eras of practice, raising the question of whether current UK guidance fully captures contemporary clinical outcomes.

Recommend targeted screening. Against a national screening programme.

They didn't look at the addition of other tests like Stockholm3 that will reduce the over MRI and over diagnostics hence reducing the harm of a national screening program
They just looked at MRI and PSA and I agree the evidence isn't quite there yet for these 2 but add in Stockholm 3 and other tests and it would change the stats

Like breast cancer screening and colorectal - no screening process will be ideal and fit all the WHO criteria but prostate cancer is highly voluminous and emotive as well a significant disease process in many cases. With MRI improvements present studies should be linked to a national targetted screening trial now rather than later.

Better markers and diagnostic techniques are needed before any effective screening programme can be implemented

Fully agree with this recommendation and brings sanity to an otherwise overhyped risk from proponents of screening

Even with very high risk patients, the screening is biannual rather than annual.

Needs more data

Please provide any additional optional comments on the UK NSC’s draft recom...

Using BRCA as a guide to screening seems daft and unworkable in any meaningful way. I feel we should offer screening to high risk men defined as FH or black men

The elephant in the room here is doing PSA only in the community. we need to roll out the gallileo genome screen, PCA3, 4K, stockholm 3 or urine DNA with a PSA>. The blood test needs to be better, PSA is just too non-specific to sensibly screen the nation.

Screening should be offered to those at high risk such as those with a positive family history and black ethnicity.

Nil

We have to do something for black men, they make up so little of the populations in the screening trials so that evidence is far less relevant.

Nil

Following should have screening;

Black men, FH of Pca and BRCA

Please provide any additional optional comments on the UK NSC's draft recom...

Population prostate cancer screening carries more downside for men than benefit, and would divert valuable resource away from other conditions that have far greater need

I do not particularly embrace the value of economic models, when we are dealing with a screening process, which could save lives, even if we are dealing with a benefit which is far <1%. The argument of over-diagnosis/over-treatment in 30% of the screened population is vague, as this depends on the quality of the health providers, and it reflects the better or worse implementations of current evidence on the management of low and intermediate risk prostate cancer. Aiming for screening at least in the 3 predominant target groups is according to my opinion the minimum acceptable strategy for a patient centred health system

Localised prostate cancer is asymptomatic. It is only ever detected by screening. PSA testing of "symptomatic" men is ridiculous as the men are not symptomatic of localised prostate cancer (by definition). If prostate cancer screening is ineffective, then it is because your treatments are ineffective in too many cases (which they are). Nearly all of the prostate cancer management paradigm is based on faulty logic and wishful thinking driven by clinicians with a vested interest in the status quo.

The best-conducted study of PSA screening for PCa was the ERSPC study, which continues to show a large benefit. Risk-adapted screening can increase the margin of benefit for the patient and the cost of screening for society. It needs to be done.

I think the cat is out of the bag.
random PSAs are occurring with resulting over treatment.
PSA tests are being withheld based on the guidance. and so men who may benefit are presenting late.
Current recommendations don't do what it says on the tin.
I think Afro-Caribbean patients (those at high risk of cancer) and patients with a family history should eb encouraged to present for screening.

The numbers speak for themselves. The technology has advanced from the time we used to do biopsies blindly, over one's finger. This delay in screening is purely cultural and the lack of it is criminal.

The targetted screening of high risk groups - black men, family history - may develop as more data available

The reason I agree is that most of the country has poor quality MRI in terms of imaging and reporting quality, the prostate biopsies are haphazardly done with extremely variable quality, and most of the treatments offered, whether it is surgery, radiotherapy, or focal therapy, could be done better. Until such time as all three are improved, it would do more harm than good to have generalised prostate cancer screening.

Although you are not recommending screening, it would be helpful to provide guidance on how often men should be tested should they choose to.

Targettted screening seems sensible and any targetting of black men to improve health may be beneficial

Please provide any additional optional comments on the UK NSC's draft recom...

The problem with family history is the public perception of what it means or where it stops. It is only relevant if that family member had prostate cancer at a relatively young age e.g. 50 or 60 years not 75 or 80 years, as some of my patients when asked, tell me

Considering there are no studies showing that surgery or radiotherapy increase overall survival, these recommendations are very reasonable

Prior to considering the introduction of screening to the whole population of men over 50 years of age we should await the results of the TRANSFORM trial - this will give us the best evidence as to which screening test is the most accurate (and economically viable) and also whether screening increases survival.

Access to BRCA 1 and 2 gene mutation testing is not evenly spread across the UK, which is why I believe screening should be offered to men with a family history of prostate and breast cancer.

flies in the face of common sense. How are we to reduce mortality from prostate cancer without screening

Targeted Screening has strong evidence base
Who on earth gets BRCA 1 and 2 tested before getting a PSA check!

I think the question of screening is the wrong one, the question is why do we not have a better screening test

Please provide any additional optional comments on the UK NSC's draft recom...

It is a well known fact that black men and men with family history of prostate cancer are relatively at a higher risk of getting prostate cancer. The NSC's current recommendations appear to be less practical by depriving targeted screening for these men.

None

There is no clear methodology for identifying the patients who are BRACA +ve.

S78	Kehinde Adeogun	Black Equity Organisation	The Black Equity Organisation (BEO) is a charity that was created to dismantle systemic racism, drive generational change and work to deliver better lived experience for members of Black communities across the United Kingdom. BEO's response speaks directly to the health inequality issues of the UK NCS recommendations. HEALTH INEQUALITY – THE EVIDENCE Health inequity is prevalent across the UK, and is seen in cancer testing, diagnoses, treatment and outcomes. Prostate cancer is the most commonly diagnosed cancer in the UK and is identified as a major public health issue. The disease however does not impact all communities equally, the facts are stark for Black men (Black African, Black Caribbean, those of Black mixed heritage) as – * 1 in 4 Black men will get prostate cancer. The stats generally are that 1 in 8 men get prostate cancer (Black men are therefore twice as likely to get this cancer) * Black men are twice as likely to die from the disease compared to other men. * Black men have higher rates of stage 3 and 4 prostate cancer diagnosis than any other ethnic group. * Black men are diagnosed with prostate cancer at all stages more often than white men. * Black men in their 60s who get a later diagnosis are 14 per cent less likely to receive life-saving NHS treatments that are proven to be their best chance of a cure. https://prostatecanceruk.org/about-us/news-and-views/2025/01/black-men-more-likely-to-be-diagnosed-at-later-stage The inequalities reflect that both biology and system failures are at play in the outcomes for Black men. CURRENT RECOMMENDATIONS- RISK EXACERBATING INEQUALITIES It is important that the UK National Screening Committee has undertaken a review and made recommendations of what screening should look like in the decades ahead. However, the current recommendations that form the basis of the consultation do not take proper account of the health inequalities of this disease. The recommendations are-

		* a targeted national prostate cancer screening programme to men with confirmed BRCA1 or BRCA2 gene variants every 2 years, from age 45 to age 61 * no general population screening * no targeted screening of Black men * no targeted screening of men with family history * collaborate with the Transform screening research trial team to: (1) answer outstanding questions on screening effectiveness for black men and men with a family history – as soon as trial data becomes available (2) await results of the study to develop and trial a more accurate test than PSA alone, to improve the balance of benefit and harm of screening Whatever screening process is adopted following this consultation BEO asserts that the final recommendations should be informed by and deal fundamentally with the health inequality that currently exists in prostate cancer prevalence and outcomes in the UK for Black men. The current recommendations do not deal with the equity gaps and will therefore continue to exacerbate health inequalities for Black men. There is likely to be no reduction in the disproportionate outcomes identified above. (i) By only recommending limited national screening to those men aged 45-61 who have the BRCA1 or BRCA2 gene variant, an assumption is made that men and Black men in particular are aware of the variant and have access to and the opportunity to test. This recommendation ignores the lack of access to or awareness about genetic testing that is rooted in existing barriers and mistrust. The ability to test for the variant will be most available to those who already have high health literacy and or better access to services that they trust. (ii) Not recommending targeted screening for Black men and/or those with a family history of the disease is problematic. These recommendations assume that members of those two subgroups have equal and trusted access to healthcare professionals that could lead them of their own volition to get tested. This recommendation ignores non genetic risk and the barriers that exist around access to and the lack of trust in health care services. (iii) The recommendation as to collaborating on the TRANSFORM screening research trial without putting in place mitigation measures to run before the outcome of the trial, holds the status

		quo in place and will not address the current inequality and disproportionate impact for Black men. TRUST, ENGAGEMENT, AND QUALITY DATA- ESSENTIAL (i) The Covid pandemic highlighted the lack of trust that exists between members of Black communities and health care settings and healthcare professionals. The lack of trust has to be factored into the recommendations. (ii) Trials historically predominantly cater to white populations with underrepresentation of Black participants, leading to relevant missed subgroup information. (iii) Black men are not routinely included in research studies, many reasons apply, but lack of trust and understanding are factors. There should be acknowledgement that there is well founded mistrust in taking part in trials.https://www.sciencedirect.com/science/article/pii/S2451865425000493#abs0010 It is noted that in the TRANSFORM trial 1 in 10 men invited to the trial will be Black men. Ensuring adequate take up of Black research participants will be crucial in guaranteeing that data outcomes accurately reflect different demographics. That uptake will be dependent on co-designed engagement from the outset and a recognition of the barriers that exist in participating e.g. language, cultural sensitivity and cultural competence. LEGAL DUTY- COMPLIANCE The eradication of health inequalities in prostate cancer trials, screening, and treatment can only be effectively implemented if the recommendations have been through a process that ensures that due regard to the public sector equality duty sec 149 Equality Act 2010 has been undertaken. Without a commitment to principles of equality and adherence to Equality Act obligations there can be no confidence that there is understanding or acknowledgment of the disparity that will exist when recommendations are made. (i) A thorough Equality Impact Assessment should be undertaken that indicates how the recommendations will eliminate discrimination and advance equality of opportunity. (ii) There needs to be clear disaggregated data that shows how Black men were engaged, how evidence on higher risk and poorer outcomes for Black men influenced the recommendations and what mitigation measures are to be put in place if the targeted screening of Black men is not to take place. CONCLUSION-

			BEO does not support the current recommendations, they lack a comprehensive view as to the clear health inequity experienced by Black men and as a result will widen the existing gap in incidence, late diagnoses and mortality for Black men. In order for health inequalities not to be perpetuated in prostate cancer care the UK NSC's final recommendations should include- (i) Targeted screening for Black men and those with a family history in recognition of higher lifetime risk, early onset and mortality outcomes. (ii) Funded and supported access to BRCA genetic testing in recognition of the disparity in health literacy and access to testing. (iii) Ensure drive for engagement in trials or service pilots is co designed and co-produced from the outset. With Black clinicians and trusted Black advocacy groups visibly involved. (iv) Collate data in trials and service pilots that is disaggregated and transparent and publish to show demographic outcomes. (v) Conduct and publish a full and extensive EqIA of the recommendations. (vi) Include equity input reviews in all stages of decision making /recommendations on service delivery, with remedial steps triggered if disparities persist.
S79	Chidi Anyaeche	Pathaway Services Limited	The Case for Risk-Stratified Prostate Cancer Screening in Black Men and Men with a Family History. I am writing to set out the evidence-based rationale for implementing a targeted, risk-stratified approach to prostate cancer screening, specifically for Black men and men with a significant family history of prostate cancer. 1. Disproportionate Risk in Black Men Prostate cancer incidence and mortality are substantially higher in Black men compared with White men. UK data consistently demonstrate that Black men are approximately twice as likely to be diagnosed with prostate cancer and experience higher mortality rates. In addition, they are more likely to be diagnosed at a younger age and with more aggressive disease. Given this elevated baseline risk, the balance of benefits and harms associated with screening differs from that of the general population. Earlier, risk-based PSA testing in Black men may increase the likelihood of detecting clinically significant disease at a stage amenable to curative treatment, thereby reducing advanced presentation and mortality. 2. Increased Risk in Men with a Family History

		A family history of prostate cancer, particularly in a first-degree relative (father or brother), significantly increases a man's lifetime risk. The risk is higher still where multiple relatives are affected or where diagnosis occurred at a younger age. Family history is one of the strongest non-modifiable risk factors for prostate cancer. A screening policy that does not account for this risks under-identifying men at materially higher probability of clinically significant disease. 1. Rationale for Risk-Stratified Screening The UK does not currently operate a population-wide prostate cancer screening programme, largely due to concerns regarding overdiagnosis and overtreatment associated with PSA testing. These concerns are valid in average-risk populations. However, in higher-risk groups, the potential absolute benefit of screening increases because: 2. The underlying incidence of clinically significant cancer is higher. 3. The probability of aggressive disease is greater. 4. The consequences of late diagnosis are more severe. A risk-stratified approach would better align with modern screening principles: targeting those most likely to benefit while limiting unnecessary intervention in lower-risk men. Advances in multiparametric MRI and more selective biopsy pathways further mitigate historic harms associated with PSA-led screening. 1. Equity and Health Inequalities Failing to incorporate ethnicity and family history into screening policy risks perpetuating health inequalities. Black men in the UK face a clearly documented excess burden of prostate cancer. A uniform screening approach may inadvertently disadvantage those at greatest risk. A targeted strategy – for example, proactive invitation or facilitated access to PSA testing from age 45 for Black men and men with significant family history would represent a proportionate and evidence-aligned response to demonstrable risk differentials. Conclusion The current evidence supports the view that prostate cancer risk is not evenly distributed across the population. Black men and men with a strong family history face significantly higher incidence and mortality. In these groups, the potential benefits of earlier detection are likely to outweigh the harms that have historically limited population-wide screening.

			I respectfully urge the Committee to consider a formal risk-stratified screening framework that incorporates ethnicity and family history as core eligibility criteria, in line with contemporary evidence and principles of equitable healthcare delivery. A 2026 peer-reviewed analysis using National Prostate Cancer Audit (NPCA) 2024 data models the budget impact of a risk-stratified screening pathway tailored to clinical risk of which I am a co-author: Fitzjohn, J.-P., Bolodeoku, J., Chinegwundoh, F., Rogers, J., Chambers, K., Anyaeche, C., & Odeyemi, I. (2026). Budget Impact Analysis of Risk-Stratified Prostate Cancer Screening in the UK using National Audit Data. <i>British Journal of Healthcare and Medical Research</i>, 13(01), 63–90. https://doi.org/10.14738/bjhr.1301.19846 The findings from the above peer-reviewed article established a compelling case for policy reassessment. In a nutshell, it makes a compelling argument for the benefits of risk stratified prostate cancer screening.