UK National Screening Committee

UK National Screening Committee (UK NSC)

Screening for prostate cancer

Date: 26 March 2026

Contents

1. Aim

To ask the UK National Screening Committee (UK NSC) to make a recommendation, based on the findings from the Sheffield Centre for Health and Related Research (SCHARR) modelling study, the outcome of the public consultation exercise and the evidence presented in this document, whether or not screening for prostate cancer meets the UK NSC criteria for a screening programme.

2. Background

The UK NSC advises ministers and the NHS in the 4 UK countries about all aspects of screening and supports implementation of screening programmes. Conditions are reviewed against evidence review criteria according to the UK NSC's evidence review process. The ethical principles of health screening are encompassed within the criteria for assessing the viability, effectiveness and appropriateness of a screening programme. To further clarify and explain the overarching goals of screening, the UK NSC has developed an ethical framework.

The UK NSC does not currently recommend systematic population screening for prostate cancer. The committee based this recommendation on the evidence provided by the 2020 review carried out by Costello Medical.

The 2020 review found that prostate-specific antigen (PSA) as a screening test should not be offered within a national programme as it did not meet several of the

UK NSC criteria. In particular, there were concerns about high levels of overdiagnosis, overtreatment and false positive results as consequences of PSA screening.

2.1 PSA testing

Screening programmes can be beneficial by helping to detect treatable disease early, potentially improving morbidity and mortality. However, screening can also cause harm. The UK NSC's role requires it to balance the benefits and harms so that the health of all those offered screening is considered. The harms can be less obvious but must be carefully weighed when looking at whether a screening programme should be introduced.

The main screening test available for prostate cancer is the PSA blood test. This test measures the amount of the prostate specific antigen (PSA) in the blood. PSA is a protein produced by the prostate, so it is specific to the prostate, but not specific to prostate cancer because even normal, non-cancerous cells also produce PSA. This means that levels of PSA in the blood can rise for many reasons, including benign enlargement, inflammation, infection, recent ejaculation, or medical procedures. Therefore, an elevated PSA result does not necessarily indicate prostate cancer and a normal PSA level does not necessarily exclude it.

As a screening tool, PSA has both strengths and limitations. The test can detect prostate cancer earlier than symptoms would appear and, once a cancer has been diagnosed, it can help monitoring cancer progression or recurrence. However, because PSA is not specific to prostate cancer, this means that many men[1] with an elevated PSA result do not have cancer (false positives), and some men with prostate cancer have a PSA level within the normal range (false negatives). False negatives create a risk of false reassurance and false positives can lead to unnecessary investigations such as prostate biopsies, which carry a risk of bleeding, blood in urine, blood in semen, infection, urinary difficulty, pain and worry. PSA testing can also lead to overdiagnosis, that is identifying slow growing cancers that would never have caused harm in an individual's lifetime if undiagnosed. Most of these cancers are treated which means many men receive treatments for cancers that would not have affected them.

2.2 Prostate cancer treatments and associated harms

Prostate surgery

The most common lifelong harms associated with surgery include urinary incontinence such as leakage when coughing, exercising or lifting (where incontinence pads may need to be worn) and erectile dysfunction – the inability to have or hold an erection due to nerve damage. Other surgical complications that

[1] Prostate cancer affects men, trans women and non-binary people with a prostate. The term 'men' is used throughout in this document for ease, but any screening recommendation would include all eligible individuals with a prostate.

could arise include bleeding, infection, blood clots or damage to nearby organs (bladder, rectum). All of these can cause harm that significantly affects someone's quality of life: physically, emotionally and psychologically.

Radiotherapy

Radiotherapy can harm the bladder and urinary tract, and this can lead to multiple issues such as the frequency of passing urine, experiencing pain when passing urine, and incontinence. The treatment can also lead to bowel problems such as rectal bleeding and chronic rectal inflammation. Another common side effect is erectile dysfunction. All these physical effects can also lead to psychological harms that affect quality of life.

Chemotherapy

As chemotherapy suppresses the immune system, it can significantly increase the risk of infections and that can be detrimental to overall health. Other risks of this treatment include chronic fatigue, nausea, hair loss, bowel problems, and infertility. Chemotherapy is also known to cause numbness and pain in hands and feet (peripheral neuropathy). It can also cause someone to bruise or bleed easily. These physical harms can contribute to men experiencing psychological harms such as anxiety, worry and low mood.

Hormone treatment

Hormone treatment can help slow the disease progression but carries significant harms. The most commonly reported side effects include hot flushes, fatigue, and sexual dysfunction such as loss of libido and erectile problems. Long-term use of hormone treatment drugs can cause bone thinning and fractures, changes to weight, risk of diabetes, higher cardiovascular risk, and infertility. Some men can also experience difficulty remembering things (cognitive effects) and breast tenderness. All these physical side effects can further impact on quality of life.

Active surveillance

Active surveillance can lead to the avoidance of radical treatment induced side-effects provided patients remain on active surveillance. However, active surveillance by itself can cause harm either through switching to a radical treatment unnecessarily, or through anxiety from the diagnosis and during follow-up.

2.3 International screening

Currently, Lithuania is the only country with a national screening programme for prostate cancer, with PSA-based screening offered in a primary care setting for men aged 50-74 years. Croatia is set to introduce checks for men aged 55 to 69 from 2027. In 2018, the United States Preventative Services Task Force (USPSTF) recommended that men aged 55 to 69 years make an individual, informed decision about PSA-based screening in consultation with their clinician (USPSTF Grade C).

For men 70 years and older, the USPSTF recommends against routine PSA-based screening (USPSTF Grade D)[2]. The USPSTF is currently in the process of updating the topic of screening for prostate cancer. In the EU, the 2022 Council Recommendation advises member states to take a stepwise approach, including piloting and further research to evaluate the feasibility of implementation of risk-stratified organised programmes rather than universal PSA testing. Sweden offers a regional organised prostate cancer testing programme for men aged 50-74 years. Various countries offer opportunistic PSA testing or, as in the UK, provide guidance that supports individual decision making for men on PSA testing. Although there is variation in how prostate cancer testing is offered internationally, organised national programmes are rare.

2.4 Expansion of UK NSC remit and current work on prostate cancer

Following the publication of several large long-term studies on prostate cancer screening, the UK NSC noted their outcomes and welcomed that some are looking at targeted or risk stratified screening as well as large populations simply based on age.

Since the 2020 review, the UK NSC's remit has been formally expanded to include targeted and risk-stratified screening. Through the 2022 open call for topics, the UK NSC received 6 submissions requesting that several different screening strategies for prostate cancer be explored. The UK NSC was asked to look at: population screening for all men and targeted screening for black men, men with relevant family histories, and carriers of BReast CAncer susceptibility (*BRCA*) gene variants. It was also asked to add the findings of the Stockholm 3 trial but the data was not used as, due to commercial sensitivities, the company would not allow the UK NSC to publicise the results of the SCHARR analysis.

The open call proposals were considered by an evaluation group that included the UK NSC chair, the chairs of the UK NSC's Fetal, Maternal and Child Health (FMCH) group and Adult Reference Group (ARG), patient and public voice (PPV) members, and the UK NSC evidence team. After consideration, it was agreed that work should be undertaken to assess the proposals in the form of a disease, effectiveness and cost model. This approach would enable the UK NSC to compare the different screening strategies (for example, exploring testing different groups of men, at various frequencies and ages), in order to help identify pathways with robust evidence and understand the balance of benefits and harms.

3. Modelling project

The disease and cost effectiveness model was developed by SCHARR using a large body of published scientific evidence and official statistics, and received input from clinical experts, technical experts, and lay members. The model was then validated (checked) against 2 large long-term studies that used PSA to screen for prostate

[2] Grade Definitions | United States Preventive Services Taskforce

cancer. This collaborative process ensured the model incorporated high quality evidence, reflected real-world up to date clinical practice, and was informed by different perspectives.

The SCHARR model used the most modern screening pathway which has evidence to support it. The screening pathway consisted of PSA testing, followed by multiparametric MRI (MP-MRI), then local anaesthetic transperineal prostate (LATP) biopsy, and finally treatment/surveillance. The findings of the model have been shared with the ARG and the UK NSC, as well as with clinical experts, economists, and PPVs at dedicated workshops. The report on the SCHARR model and an accompanying narrative document (which provided a high-level summary of the purpose, methods and conclusions of the model) formed part of the consultation suite of documents which were made available during the public consultation exercise.

As a result of feedback received during the public consultation and expert stakeholder dialogue, the SCHARR model has undergone an additional round of updates which are described in section 5 below.

4. Modelling summary of strategies

Full, technical details of the model are available in the updated model report.

The key findings from the model are outlined below.

4.1 Whole population screening

Screening all men for prostate cancer in the UK, regardless of their risk, would only slightly reduce the number of deaths but would cause a very large number of men to be treated for a cancer that would never have caused them harm. It is estimated that around 40-50% of prostate cancer cases detected by PSA screening will be slow growing. Offering screening, further testing and treatment for these slow growing cancers would lead to high levels of overdiagnosis and overtreatment, causing men's lives to be turned upside down by receiving a diagnosis of cancer: unnecessary anxiety and lifelong side effects such as incontinence, erectile dysfunction, and bladder problems for a cancer that would never have caused harm.

The model reported that the risk of unnecessary treatment increases with age. For example, at age 60, the model predicted that half of the cases of screen-detected cases would be overdiagnosed. There is very little evidence from the model and existing literature that screening men over the age of 70 is beneficial. All scenarios explored, including one-off screening tests at different ages and repeat screening tests, resulted in substantial overdiagnosis. As a result, current evidence and modelling suggests that whole-population screening does more harm than good.

4.2 Targeted screening for black men

Screening black men for prostate cancer is likely to detect more cancers among those screened compared to screening the general population. However, it can also lead to high rates of overdiagnosis and overtreatment. For example, the consultation version of the model estimated that, for annual screening of black men aged 55-60, about 44% of prostate cancers detected would be overdiagnosed.

The biggest issue with this screening strategy is the uncertainty, as there is very little evidence about screening in black men.

4.3 Targeted screening for men with a relevant family history

Men with a family history of prostate, breast, or ovarian cancer make up about a third of all men. While they are considered to be at a higher risk of developing prostate cancer, the model indicated that all strategies for screening within this group were subject to high levels of uncertainty (similar to that reported in whole population screening). Similar to whole population screening, screening men with a relevant family history was predicted to result in many cancers being overdiagnosed and overtreated.

Based on expert stakeholder dialogue, updated modelling work has now examined screening in men with a family history of prostate cancer as a separate group. The findings from this analysis are described in section 11 of the updated model report and section 5 below.

4.4 Targeted screening for prostate cancer in men with a known pathogenic *BRCA1* or *BRCA2* gene variant

Screening men with a confirmed pathogenic *BRCA1* or *BRCA*2 gene variant is the strategy that the consultation version of the model estimated to be effective. There is some evidence about cancers in men with pathogenic *BRCA* variants which suggests that detecting and treating such cancers earlier is more likely to improve outcomes and outweigh the potential harm from overdiagnosis or unnecessary treatment, compared to men in the general population or from other risk groups. Based on the published evidence at the time, the UK NSC consulted on screening men with a confirmed pathogenic *BRCA1* or *BRCA2* gene variant every 2 years, from age 45 to age 61.

Based on expert stakeholder dialogue, updated modelling work has now examined screening in men with *BRCA1* variants and men with *BRCA2* variants separately. The findings from this analysis are described in section 11 of the updated model report and section 5 below. Cascade screening for men with *BRCA* variants was not evaluated in the analysis.

5. Updates to the model

The SCHARR model has undergone an additional round of changes as a result of expert stakeholder dialogue. The revisions include lower costs and higher uptake of MP-MRI, higher specificity of MRI, fewer men with pathogenic *BRCA* variants,

variations in the prostate cancer risk among *BRCA2* variant carriers, removal of increased cancer risk among *BRCA1* variant carriers, similar risk of high-grade cancer (high GGG) in black men compared with other population groups, lower sensitivity of LATP biopsy, and updated survival inputs. These changes reflect feedback received from stakeholders and are described in detail in section 11 of the updated model report.

The new data was added to the model and analyses were conducted for the general (all-risk) population, black men, family members of men with prostate cancer, family members of individuals with breast, ovarian, or prostate cancer, men with *BRCA1* variants, and men with *BRCA2* variants. Where results suggested potential cost-effectiveness, more detailed analyses were undertaken to assess decision uncertainty.

Under the updated assumptions and using a £20,000 per quality-adjusted life years (QALYs) threshold, screening did not do more good than harm at reasonable cost in the general population, *BRCA1* variant carriers, family members of men with prostate cancer, or family members of individuals with breast, ovarian, or prostate cancer. For black men, there was ongoing uncertainty on whether screening would cause more good than harm. The likelihood of repeat screening being cost effective in men with pathogenic *BRCA2* variants was sensitive to changes in key inputs, for example those related to prostate cancer risk. Discussion with geneticists emphasised that the original input data on prostate cancer risk was relevant to the population addressed in the UK Cancer Genetics Group (CGG) guidelines. In this population, repeat PSA testing in men with *BRCA2* variants is likely to be clinically and cost effective. The evidence of increased risk and aggression of cancer in these men is clear but the ideal approach to identifying people is not settled and there is work to do to understand how the tests and testing intervals can be optimised. Discussions with geneticists suggest that there are additional genetic factors which also confer added risk to men with *BRCA2* variants.

6. Further research

On 21 November 2025, the TRANSFORM trial was launched. This is a large, randomised controlled trial that has been designed with UK NSC input to recruit hundreds of thousands of men to undergo screening using various testing strategies. The study aims to evaluate several modern screening strategies – including those using fast MRI scans and polygenic risk scores, as well as PSA testing – and compare them against each other to find the most accurate strategy. The idea is a better test will detect more life-threatening cancers and fewer cancers which are likely to be overdiagnosed. The study will then measure whether screening using the best new testing strategy does more good than harm. The trial has been designed to specifically address inequalities in age and ethnicity, with a commitment that at least 10% of the study invitations will be for black men. The committee will continue to work closely with the trial team and as research progresses. The TRANSFORM trial anticipates that it will be able to share data in the next three years.

Alongside TRANSFORM, other important research is ongoing, including the PROFILE study which aims to understand why some men, including those of Black African/Black-Caribbean ancestry, are at greater risk of prostate cancer overall, and the IMProVE clinical trial which aims to investigate whether a programme that combines PSA tests with MRI scans could save lives and if so, how it can be organised to reduce health inequalities. IMProVE will initially involve 4,500 people in Sheffield and Leeds and may be expanded to other parts of the region. In addition, the ongoing UK-specific IP7-PACIFIC trial aims to provide further evidence on whether biparametric MRI (BP-MRI) could be recommended as an alternative to multiparametric MRI (MP-MRI) for the detection of clinically significant prostate cancers.

Research in all these areas is extremely important and will help to build up the evidence base to address existing gaps and inform future screening decisions.

7. Consultation

A 12-week public consultation (28 November 2025 – 23 February 2026) was hosted on the UK NSC website. Direct emails were sent to 30 stakeholder organisations and 266 individuals who had subscribed personally to receive updates on work carried out by the UK NSC on prostate cancer (Annex A).

The screening recommendation that the UK NSC consulted on was:

- against whole population screening for men (at any age)
- against targeted screening for black men
- against targeted screening for men with a family history
- in favour of targeted screening for men with known pathogenic gene variants in *BRCA1* and *BRCA2* every 2 years, from age 45 to age 61

Stakeholders' views were sought on the above.

The total number of consultation comments received was 974. The consultation comments received are presented in separate documents. Comments were received from the following stakeholders:

- 895 members of the public
- 39 stakeholder organisations (plus 13 additional organisations who were co-signatories on one response)
- 40 individual stakeholders (mainly clinicians, public health professionals, and academics)

The 39 stakeholder organisations that submitted a response to the consultation are listed in Annex B.

41 respondents agreed with the UK NSC draft recommendation. These were:

- 23 members of the public
- Antegenes Ltd
- Beckman Coulter
- Cancer Research UK
- Jnetics
- Prostate Cancer UK
- Royal College of General Practitioners
- Royal College of Nursing
- Sutton Coldfield Group Practice
- 10 individual stakeholders

30 respondents gave mixed feedback on the UK NSC draft recommendation. These were:

- 23 members of the public
- Black Prostate Cancer Network
- Johnson & Johnson Innovative Medicine
- The Royal College of Pathologists
- UK Cancer Genetics Group
- United Against prostate Cancer led by University Hospitals of Leicester and East Genomics
- 2 individual stakeholders

834 respondents disagreed with the UK NSC draft recommendation. These were:

- 796 members of the public
- Association of Directors of Public Health

- Bayer PLC
- Black Equity Organisation
- British Association of Urological Surgeons
- Cancer Black Care
- Caribbean & African Health Network
- CHAPS
- Cotswolds Prostate Cancer Support Group
- Healthwatch Worcestershire
- Houston Kiltmakers
- Labour Men and Boys Steering Group
- NHS Race & Health Observatory
- Norfolk & Waveney Prostate cancer support group
- Pathaway Services Limited
- Prostate Cancer Research
- Prostate Cancer Victims
- Prostate Scotland
- Staffordshire Moorlands District Council
- One additional stakeholder organisation who asked not to be identified
- 19 individual stakeholders

69 respondents made no direct comment on the UK NSC draft recommendation. These were:

- 53 members of the public
- A3p Biomedical
- British Association of Black Surgeons
- CancerHelp (Preston) Ltd

- Friends & Bredrins Prostate Cancer Support Charity
- Furness Prostate Cancer Support Group
- Healthwatch England
- Yorkshire Cancer Research
- 9 individual stakeholders

Overall, many stakeholders, particularly members of the public, disagreed with the UK NSC draft recommendation, advocated for population screening for prostate cancer and were critical of the SCHARR model's findings. However, other stakeholders instead were supportive of the UK NSC's position and evidence-based approach, recognised that benefits must be weighed against ongoing substantial overdiagnosis and the risk of overtreatment, and considered the SCHARR model to have been undertaken to a high standard. Many stakeholders called for further research and highlighted the importance of ongoing trials, such as TRANSFORM, to provide robust data on the best approaches for safer and accurate prostate cancer diagnosis.

The key themes emerging from the public consultation exercise are presented in section 9, alongside UK NSC responses to each theme.

8. Recommendation

The UK NSC recognises the strong support for prostate cancer screening expressed by many stakeholders and the devastating effects of prostate cancer which they describe. The UK NSC supports screening where there is evidence that it will do more good than harm, and will continue to encourage research and examine evidence so that the benefits of an organised screening programme can be extended to more men as soon as the evidence supports this. The following recommendations are based on the UK NSC evidence review, modelling work, and consultation with stakeholders.

Repeat screening in men who have a pathogenic[3] *BRCA2* variant with a family history of breast, ovarian, pancreatic, or prostate cancer is likely to do more good than harm. Guidance from UK Cancer Genetics Group (UKCGG) provides a starting point for an implementation strategy in this high-risk population. The UK NSC recommends that:

[3] Includes 'pathogenic' and 'likely pathogenic' *BRCA2* variants, as defined by clinical guidelines.

- a nationally managed approach to biennial PSA testing in men aged 45 to 61 who have pathogenic germline[4] *BRCA2* variants with a family history of breast, ovarian, pancreatic, or prostate cancer should be implemented

- the best methods to ensure cascade screening for germline BRCA2 status in order to proactively identify and invite men for repeat PSA testing should be evaluated. Evaluation should include, for example, acceptability to the population and professionals, accessibility, and the resource impact associated with the strategy

- population screening of men for *BRCA2* variants is not currently recommended as the evidence suggests that the presence of a pathogenic *BRCA2* variant in the absence of a relevant family history of cancer confers a lower risk of clinically significant prostate cancer.

Beyond *BRCA1* and *BRCA2,* the current modelling exercise did not consider any other genetic variants that might confer an increased risk of prostate cancer. Other genetic variants may be considered as new evidence emerges. The intention is to learn as screening is rolled out and work with experts to optimise the pathways and agree evidence requirements that will allow the addition of other high-risk genetic variants to the screening offer.

The UK NSC does not currently recommend prostate cancer screening in the general population or targeted screening of men with a family history of breast, ovarian, pancreatic, or prostate cancer, without a pathogenic *BRCA2* variant, as screening in these groups is likely to cause more harm than good. The main harms of screening include causing incontinence and erectile dysfunction in men who did not need treatment.

The UK NSC does not currently recommend targeted screening of black men who do not have a pathogenic *BRCA2* variant for prostate cancer. This is due to a lack of available data, which means we do not know whether screening would cause more good than harm. The UK NSC will work closely with the UK TRANSFORM trial to resolve these uncertainties as soon as possible.

The UK NSC is in close contact with researchers and aware that new evidence is likely to be published over the next few years. The committee is hopeful that there will be new tests and a better understanding of prostate cancer that will support much wider screening. To ensure that the committee is able to review significant new evidence and update its position, the model will remain “open” so that new information can be fed in as it arrives.

[4] Germline variants are inherited genetic variants, which are present in every cell of the body; these are different to somatic variants, which are not inherited and are confined to specific cells or tissues.

9. Consultation themes and responses

Personal stories of diagnosis and treatment

Theme:
The UK NSC received several hundred consultation responses from people who have personal lived experience of prostate cancer or who have had a relative or friend with the condition. These responses came predominantly from people who disagree with the draft UK NSC recommendation and also from people who agree with it.

The majority of responses opposed the recommendation and said that the underlying rationale was flawed. Several argued that PSA testing is a simple first step that saves lives and that not offering it is unreasonable. Many shared personal experiences and considered that the diagnosis of early-stage cancer had saved their lives. Drawing on this experience, it was suggested that population screening should be recommended and that the unwanted effects of treatment were an acceptable price to pay for survival.

Those who agreed with the draft recommendation were fewer in number but praised the committee's evidence-based approach. They supported not recommending general population screening, citing the shortcomings of PSA testing, the high risks of overdiagnosis and overtreatment, and the harms and poor quality of life following treatment. Several individuals shared stories of the harms they or their loved ones experienced from PSA testing, biopsy, and/or treatment. Some respondents considered the pressured environment to be difficult for decision making and suggested that the scientific evidence from ongoing research, for example TRANSFORM, would significantly improve the basis for UK NSC recommendations, particularly for whole population screening.

Response:
The UK NSC is incredibly grateful to the many individuals who responded to this consultation by sharing their personal stories, perspectives and opinions. Prostate cancer is a significant health problem, and these personal accounts are a powerful reminder that a diagnosis of prostate cancer can have a profound impact on men, their families and friends.

Many of the stories highlighted in the media and elsewhere have focussed almost exclusively on individual men who had been diagnosed with prostate cancer after having a screening test, usually PSA. Understandably, these individuals support screening because that is how their cancer was found. However, any screening programme is aimed at a population, and the benefits and harms need to be examined for this population as a whole, in the same way as any other cancer screening test, and indeed cancer therapies. The UK NSC recommends screening

programmes that can save lives and improve a person's quality of life. This can only be done if high quality evidence demonstrates that the benefits would outweigh the harms overall for the people who would be invited. This means not only considering the lives that might be saved, but also the unintended and negative consequences of screening, such as false positive results, unnecessary investigations, and unnecessary treatments. The UK NSC must also determine whether delivering a national prostate cancer screening programme would be cost-effective, given that it would be paid for by the NHS. There is an obligation to ensure that NHS funds are used properly and effectively.

The committee recognises that a cancer diagnosis is very distressing and leads to a desire for rapid and complete treatment. Prostate cancer is often slow growing and older men can live with an undetected cancer like this for many years without it causing symptoms, spreading, or resulting in death. It is estimated that about 29% of men aged 60-69 years have undetected prostate cancer and this figure rises with age to approximately 36% of men aged 70-79 and almost 50% of men aged over 80 years[5]. Finding cancers through screening that would otherwise be undetected can cause distress to men, their families and their wider support networks. It leads to treatment that is not needed but that can result in life-altering side effects (incontinence and erectile dysfunction). Many respondents expressed that they felt the committee had focused disproportionately on harms. It is true that all screening programmes do some harm. But in the case of prostate cancer screening, the harms are significant and can last a long time. These facts combined with the very large number of men who have treatments when their cancer would not have spread or caused their death means that whole population screening based on age cannot be recommended at the current time. We take the comments on board and will aim to ensure that the benefits (for example, reduction in prostate cancer deaths) and harms are clearly outlined together to give a balanced evidence base.

The recent evidence review indicates that men with a pathogenic *BRCA2* gene variant are more likely to get cancer at a younger age and get cancer that is more aggressive. This means their cancer tends to grow more quickly than in men without *BRCA2* gene variants. If treated, these men will live with the likely side effects of treatments (incontinence and erectile dysfunction) just as other men treated would. However, the number of more aggressive cancers detected and treated earlier, and the more years these men will live as a result of their treatment, means that the

[5] Jahn JL, Giovannucci EL, Stampfer MJ. The high prevalence of undiagnosed prostate cancer at autopsy: implications for epidemiology and treatment of prostate cancer in the Prostate-specific Antigen-era. Int J Cancer. 2015 Dec 15;137(12):2795-802. doi: 10.1002/ijc.29408.

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estimated effect of regular PSA testing in this group was more favourable than for the whole population of men.

PSA as a screening test

Theme:
Some stakeholders agreed that evidence presented in the SCHARR model showed that the PSA test has limitations, that the harms are substantial, and that the evidence used in the model was appropriate. There was also scepticism from some stakeholders about the mortality benefits of PSA-based screening.

Others stated that the PSA test is adequate when combined with modern pathways and not used in isolation. Several stakeholders took the view that although the PSA test has limitations, it should be implemented in a screening programme because there is currently no better alternative and the technology and methods underpinning a screening programme would improve over time. Some stakeholders asked for more funds to be put into research for the development of new, more reliable tests.

Response:
The SCHARR model used a screening pathway starting with a PSA test, followed by a confirmatory MP-MRI scan and then a biopsy, if required. At the time of modelling this is the National Institute for Health and Care Excellence (NICE) guidance. This means that, in the SCHARR model, biopsy and treatment are not simply triggered by the results of a PSA test on its own. Therefore, the results of the model are not based on the use of PSA testing alone.

The PSA test measures the concentration of a protein produced by both normal and cancerous prostate cells. It is a blood test, widely available and inexpensive. PSA is specific to the prostate, but it is not specific to prostate cancer; non-cancerous cells also produce PSA. It is known that PSA levels can rise for many reasons, including benign enlargement, inflammation, infection, recent ejaculation, or medical procedures. This means that an elevated PSA result does not necessarily indicate cancer and a normal PSA result does not necessarily exclude it.

As the first step in the screening pathway, PSA has both strengths and limitations. The test can detect prostate cancer before symptoms appear. A single large randomised trial in a few European countries has shown a reduction in prostate cancer deaths from PSA screening. However, PSA has relatively high false-positive rate (approximately between 67-91%, depending on age and the PSA cut-off values), which means most men with an elevated PSA result do not have cancer at the time, and so would have unnecessary cancer investigations (scans, blood tests, and occasionally invasive biopsies). As noted by NICE, it is estimated that around 75% of people with a raised PSA do not have prostate cancer. Although the PSA test has a relatively high sensitivity (approximately between 75-90%, though this depends on age and the PSA cut-off values and therefore, it can be lower), this still means that a significant minority of men (10-25%) with prostate cancer have a PSA

level within the normal range and would not be found by screening[6]. This creates false reassurance and could lead to men not seeking or receiving further investigations when they need them. PSA testing can also lead to overdiagnosis, identifying slow growing cancers that would never have caused harm in an individual's lifetime. This, in turn, exposes men to avoidable treatments and their associated side effects. These clinical and psychological consequences contribute to ongoing debate about the value of PSA as a population-level screening tool, beyond the personal experience of benefit by individuals.

The controversy reflects differing interpretations of the balance between benefit and harm. Some stakeholders emphasise the potential life-saving value of early detection, particularly when PSA is used within modern diagnostic pathways that incorporate MRI and targeted biopsy, which can reduce unnecessary invasive procedures. Others highlight the risks of overdiagnosis, the uncertain impact on reduction of prostate cancer mortality, and the variability of PSA as a biomarker. The current SCHARR model supports the conclusion that although PSA remains a useful component of prostate cancer assessment, it is not considered robust enough to support general population screening on its own. The model confirmed that the test performance improves when combined with contemporary imaging and risk-stratification approaches but, even then, the harms of screening with PSA remain high. Continued research, an improved balance between benefits and harms, and careful evaluation of possible screening pathways will be essential to inform future decisions on this.

The UK NSC makes recommendations to ministers and the NHS across the 4 nations of the UK, based on an assessment of high-quality, peer-reviewed evidence on whether screening for a certain condition would do more good than harm at reasonable cost. A UK NSC recommendation is made at a single point in time, based on the high-quality, peer-reviewed evidence available at that time. The absence of a better alternative is disappointing, but it does not provide an evidence-based justification for the implementation of a national screening programme. It is worth noting that no other cancer screening test and very few cancer therapies have been introduced into routine clinical practice on this basis.

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[6] David MK, Leslie SW. Prostate-Specific Antigen. [Updated 2024 Sep 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available at: https://www.ncbi.nlm.nih.gov/books/NBK557495/

Hoffman RM, Gilliland FD, Adams-Cameron M, Hunt WC, Key CR. Prostate-specific antigen testing accuracy in community practice. BMC Fam Pract. 2002 Oct 24;3:19. doi: 10.1186/1471-2296-3-19

Leal J, Welton NJ, Martin RM, Donovan J, Hamdy F, Neal D, Noble S, Lane A, Wolstenholme J. Estimating the sensitivity of a prostate cancer screening programme for different PSA cut-off levels: A UK case study. Cancer Epidemiol. 2018 Feb;52:99-105. doi: 10.1016/j.canep.2017.12.002. Epub 2018 Jan 4. PMID: 29278842.

NICE. How should I assess a person with suspected prostate cancer. Available at: https://cks.nice.org.uk/topics/prostate-cancer/diagnosis/assessment/ Accessed 03 March 2026

For prostate cancer screening, the currently available evidence does not support screening in the general population, black men, men with a relevant family history, and men with *BRCA1* gene variants. However, it is entirely reasonable to expect recommendations to change over time if methods and technologies improve and new evidence is published which updates the benefits, harms, and costs of screening. This is why the UK NSC regularly reviews its recommendations. If new evidence shifts the balance of benefits and harms in favour of screening, either in the general population, black men, men with a family history, or men with *BRCA1* gene variants, then the recommendation can be revisited before 3 years if necessary. If significant evidence is published in between regular reviews, the UK NSC can consider proposals for an early topic update. Individuals or organisations can submit proposals for an early update via the open call for topics.

Screening pathway — use of MRI, modern biopsy techniques, and modern treatments

Theme:
There was a common misconception among many responses that the modelled screening pathway did not include the use of MRI and modern biopsy techniques. Stakeholders wrote that the model did not take account of recent advances in treatment, particularly advances in robotic surgery and focal therapies, and therefore the estimates of harm used in the model were based on historical data. Some stakeholders highlighted that high-quality, peer-reviewed evidence can lag behind the most recent technological developments and claimed that the UK NSC was basing its assessment on outdated evidence about benefits and harms.

Response:
The SCHARR model simulated the most modern screening pathway which has evidence to support it. As outlined in the model report (section 6.8), the modelled screening pathway was PSA, followed by multiparametric MRI (MP-MRI), then local anaesthetic transperineal prostate (LATP) biopsy, and finally treatment/surveillance. As stakeholders highlighted, the use of MP-MRI as a triage test following a positive PSA is likely to result in fewer harms than a pathway that proceeds straight to biopsy. Hence, the pathway modelled included MP-MRI as a triage test. Therefore, the results of the model are **not** based on a “direct PSA to biopsy” pathway.

Screening is a form of public health intervention which has an impact on very large numbers of people; millions of individuals per year for population-wide cancer screening programmes. While it is true that high-quality, robust evidence takes time to generate, the largely asymptomatic nature of the population, the wide reach of screening, and the potential for significant harms means it is essential that new programmes have a solid evidence base supporting them. At present, there is a lack of evidence to support the accuracy and effectiveness of the alternative testing and treatment strategies proposed by some stakeholders. For example, NICE guidance recommends that focal therapies using High-Intensity Focused Ultrasound (HIFU) and cryotherapy are not offered to people with locally advanced prostate cancer or people with localised prostate cancer other than in the context of controlled clinical

trials comparing their use with established interventions due to uncertainty about their efficacy. While some NHS centres do offer focal therapy (following NICE HealthTech guidance HTG667, HTG284, and HTG668, under NICE special arrangements) they are not currently widely used in the UK. We note that the TRANSFORM study will require eligible participants to have access to the full range of treatment options including focal therapy.

The estimates of harm in the model were based on the recent experience of prostate cancer patients, with the data coming from NHS Digital, the Office for National Statistics (ONS), Public Health England (PHE), and the most recent published National Prostate Cancer Audit (NPCA) report available at the time of model development, with the data validated by clinical stakeholders. The model does not simulate each different type of treatment that patients receive but instead uses the average outcomes across all patients diagnosed with each stage of prostate cancer. Robotic prostatectomy surgery has been routinely in place for the last decade, so these outcome data reflect clinical practice for prostatectomy using robotic surgery. By using real patient outcome data, the model reflects current practice rather than an idealised situation.

Input of good quality data into a model is very important. Incorporation of new screening tests or improvements in treatments would require relevant and reliable data that demonstrates uptake with this intervention and improved outcomes for patients. The impact of new interventions on the cost-effectiveness of screening has been explored in scenario analyses (see the "fitted mortality" scenario as shown, for example, in Figure 27) — as expected, if the treatment of late-stage cancer improves then screening becomes less cost-effective).

Screening pathway — different screening tests and alternative delivery strategies

Theme:
Stakeholders highlighted that there are alternatives to the PSA test which were not considered in the model, including polygenic risk scores and the Prostate EpiSwitch (PSE) test. Some stakeholders felt that not enough consideration was given to alternative test delivery strategies, particularly PSA home-testing kits, which do not rely on the individual having to attend an appointment with a healthcare professional.

Response:
The UK NSC commissioned the SCHARR modelling exercise to respond to a number of proposals received through the open call for topics. The model explored the strategies which were suggested through this route and updated the committee's recommendation on whole population screening. Other strategies would have been considered for inclusion if they had been received. One of the proposals came from the Stockholm 3 group which has developed a screening algorithm that incorporates polygenic risk. Eventually, the Stockholm 3 strategy was not included in the modelling exercise because, due to commercial sensitivities, the company would not allow the UK NSC to publicise the results of the SCHARR analysis. No other

proposals to explore the use of polygenic risk were received. The committee acknowledges that the modelling exercise is not exhaustive and would welcome proposals in future open calls for topics.

Incorporation of new screening tests into the model, such as polygenic risk scores or the PSE test, require relevant and reliable data that demonstrate uptake with the intervention and improved outcomes for individuals. The global screening trial evidence shows that reductions in deaths take more than 10 years to show. This is because most prostate cancers are slow growing. As there is no way to determine whether deaths or cancer spread will be reduced after a couple of years this means waiting for long-term outcomes. To date, the only real-world data on polygenic risk scores in prostate cancer screening comes from the BARCODE1 study. Further studies and longer-term outcome data are needed to evaluate the implementation of polygenic risk scores as part of a national prostate cancer screening programme. The UK NSC awaits the findings of the TRANSFORM trial, which will examine the use of polygenic risk scores and report on outcomes which are important for UK NSC decision-making.

There is a lack of evidence to support the evaluation of the PSE test in prostate cancer screening. To date, the largest published study on the PSE test was a single-centre manufacturer-funded observational study of 187 individuals in the USA which did not report long-term patient outcomes.

In order to recommend a screening programme that includes PSA home-testing, the UK NSC needs to see high-quality evidence which shows that such a screening programme is safe and effective. Evidence on PSA home-testing is currently limited to small proof-of-concept studies, and substantial further work is needed to validate the accuracy and acceptability of PSA home-testing in a screening population. The potential benefits of a PSA home-testing delivery strategy are a reduction in the costs of, and barriers to, screening. However, PSA home-testing would not mitigate the harms of overdiagnosis and overtreatment, which remain a significant concern.

The UK NSC welcomes further research into alternative testing strategies that can provide additional benefits and further reduce the harms and costs of screening.

Benefits and harms of screening

Theme:
Many stakeholders discussed the benefits and harms of screening. Some stakeholders considered that the UK NSC had overestimated the harms of overdiagnosis and overtreatment, and underestimated the benefits associated with earlier detection and treatment. They highlighted that treatments for prostate cancer detected at early stages are more effective and have fewer side-effects.

Other stakeholders considered that there is significant uncertainty around the benefits of treatment for prostate cancer and that overdiagnosis and overtreatment are real and common harms associated with prostate cancer screening. They

highlighted that large scale clinical trials show that screening only leads to a small reduction in deaths from prostate cancer.

There was also a call for more research to better understand men's values around prostate cancer screening, particularly whether most men would accept the risk of harm to reduce cases of late diagnosis.

Response:
In the context of prostate cancer screening, overdiagnosis means identifying slow growing cancers that would never have caused harm in an individual's lifetime, while overtreatment means providing unnecessary, potentially harmful treatment for a cancer that would not have gone on to cause harm in a person's lifetime. Overtreatment often stems from overdiagnosis.

Prostate cancer screening can have positive (benefits) or negative (harms) impacts on the health of individuals. A person can experience both the positive and negative impacts of screening (benefits and harms) at the same time. For example, someone may have prostate cancer detected and they may live longer as a result (where the benefit is captured as additional years of life), but they may also develop life-long side effects from biopsy and treatment (this is a harm that is captured as a reduction in their overall health). In some cases, an individual may live longer, but their overall health is worse than it would have been without screening because of the associated harms. At an individual level, it is impossible for any man with asymptomatic prostate cancer to know if he has benefited from PSA testing or if his cancer has been overdiagnosed. This is because it is impossible to know if an individual cancer would have developed to the point of causing harm had it not been detected. However, by examining overdiagnosis at the population level the model can determine the proportion of prostate cancers which would be overdiagnosed under different screening strategies.

In the model, the harms associated with prostate cancer diagnosis — decrements in quality of life — were based on real data from the 2024 NHS Cancer Quality of Life Survey[7]. This survey asked people who were diagnosed with different stages of prostate cancer about their health-related quality of life 18 months after they were diagnosed. This survey, combined with data on clinical outcomes and survival, captures the harms associated with late diagnosis of prostate cancer, and this information was incorporated into the model. For example, a patient diagnosed at later stage will on average have lower quality of life and lower survival than if he was diagnosed at an earlier stage. The survey also captures the harms associated with the diagnosis and treatment of prostate cancer, such as those from radiotherapy and surgery. One additional harm included in the model was the harm of having a LATP biopsy; this harm was considered to be short-term and minor.

Stakeholders are right that treatment at early stages is often more effective than in later stages, and the approach used in the model reflects this. However, the high

[7] https://digital.nhs.uk/ndrs/data/data-outputs/cancer-data-hub/cancer-quality-of-life-survey

survival rates in early detected cancers are also partially due to overdiagnosis. That is the detection of cancers that would not otherwise be diagnosed during a lifetime if the man did not attend an organised screening programme. The rate of overdiagnosis predicted by this model is similar to some other well-validated models, such as the Cancer Intervention and Surveillance Modeling Network (CISNET) model.

The intention of screening for prostate cancer would be to detect cancers earlier, for those who would benefit from screening this would be achieved through avoiding harms associated with late-stage prostate cancer. Based on the results of large prostate cancer screening trials, we know how many cancers are likely to be detected earlier by screening. We also know how patients diagnosed with cancers of different stages fare in terms of survival, clinical outcomes, and quality of life. Therefore, we can estimate the reduction in harms (i.e. the benefits) that would arise from screening. In simple terms, this is what the model has done. Therefore, in the SCHARR model, the estimates of benefits and harms are based on large-scale clinical trials and the most up-to-date lived experience of recently diagnosed prostate cancer patients in England.

As new high-quality, peer-reviewed evidence becomes available, this will be incorporated into the model to provide an updated overview of the balance between benefits and harms when screening for prostate cancer. Ensuring that a screening programme provides more benefits than harm at a reasonable cost is a key aspect of the UK NSC's role.

Evidence from other countries

Theme:
Some stakeholders noted that only a few countries recommend some form of screening for prostate cancer. In general, there are very few examples of prostate cancer screening programmes internationally.

However, other stakeholders believed that the UK sets the evidence bar too high for its screening recommendations. They suggest the UK should follow the example of other countries which have implemented risk-stratified screening, such as Sweden, and that relevant international evidence has been overlooked by the UK NSC's evidence review. Some stakeholders highlighted that Sweden has fewer men of black ethnicity than the UK, which could, in theory, make the case for whole population screening stronger in the UK than in Sweden.

Response:
Currently, only Lithuania has implemented a long-standing, national, population-based PSA-based screening programme for prostate cancer. Croatia is set to introduce checks for men aged 55 to 69 from 2027. Most other high-income countries and international guideline bodies do not recommend population-wide PSA screening. Instead, they advocate individualised decision making or risk-adapted early detection models. In the EU, the 2022 Council Recommendation advises

member states to take a stepwise approach, including piloting and further research to evaluate the feasibility of implementation of risk-stratified organised programmes rather than universal PSA testing.

The UK NSC considers high-quality studies from across the world including those conducted in other countries or healthcare systems where the findings are judged to be sufficiently generalisable to the UK context. Differences in eligibility criteria, participation rates, diagnostic infrastructure, and access to services mean that perfect equivalence cannot be achieved when data from other systems is used. Models designed to reflect a US or Swedish context will use different parameters compared to models based on the UK context, and will, for example, estimate different figures for overdiagnosis rates. The parameters and assumptions in the current SCHARR model were based on the latest published data and expert input, and designed specifically for the UK context. The current SCHARR model has higher overdiagnosis rates than other models at older ages, but comparable overdiagnosis rates at younger ages to the SCANS (Michigan) model and lower average overdiagnosis rates than the MISCAN - PRO (Rotterdam) model.

With respect to the demographic differences between the UK and Sweden, it is important to note that every country has its own unique demographic profile, and the UK and Swedish populations are different in many ways. Thus, directly comparing the UK to Sweden when making the case for whole population screening is challenging. Beyond demographic considerations, it is also important to recognise that screening policies in different countries are shaped by broader factors, including cultural differences, variation in how health services are delivered and funded, how screening is described, and how screening policy is made.

Ideally, assessment of prostate cancer screening should draw principally on UK-based evidence, supplemented where appropriate by international studies from health systems with comparable structures, population risk profiles, and care pathways. This approach ensures that conclusions are grounded in evidence that is both robust and relevant to the NHS, while allowing the committee to consider the broader international evidence base where it can meaningfully inform its decision making.

Health economics

Theme:
Some stakeholders wrote that the UK NSC recommendation is based solely on financial costs, and that the potential improvement in outcomes for men with prostate cancer was not appropriately considered. Some stakeholders believed that the model only considered the short-term costs and benefits of screening and that, over the longer term, screening would be cost saving. Stakeholders highlighted that the cost to treat stage 4 prostate cancer is much higher than for cancer detected at earlier stages and questioned whether the model had fully considered the costs of treating late-stage prostate cancer. Some stakeholders also criticised the model for not considering the knock-on impact on the healthcare service of unnecessary

biopsies, which would delay treatment for those who need it. Other stakeholders supported the recommendation as a way of helping to ensure the effective use of scarce NHS resources.

Response:
The UK NSC is an independent scientific advisory committee which advises ministers and the NHS in the 4 UK countries about all aspects of screening and supports implementation of screening programmes. The UK NSC considers a number of criteria when making recommendations about potential population and targeted screening programmes. The purpose of screening is to improve health outcomes, and this is central to the committee's decision-making. As described above, screening for prostate cancer can cause harms as well as benefits, and the committee carefully weighed the potential benefits and harms described in the SCHARR model when producing its draft recommendation.

The costs of a potential screening programme must also be considered in any recommendation. The NHS, like all healthcare systems worldwide, operates with a finite amount of resources, and it is essential that these resources are used in a way that maximises the health benefits for the UK population. Screening for prostate cancer was not cost saving under any scenario examined.

The model considered both the short- and long-term costs and benefits of screening. The model uses a lifetime horizon, which means that costs and benefits were considered from the time of first screening until the end of an individual's life. This approach ensures that the potential long-term health benefits of screening are captured in the model. Several stakeholders assumed that screening was not cost-effective due to high initial costs of setting up a screening programme. However, the model did not include these set-up costs. If such costs were included, it would lead to screening being considered less cost-effective.

Stakeholders are correct that treatment costs for late-stage prostate cancer are much higher than for early-stage cancer. The UK NSC acknowledges that prostate cancer treatment is changing rapidly as new therapies become available; this inevitably leads to estimates of the costs of treatment becoming quickly out of date. The model incorporated the most up-to-date treatment costs available at the time for cancer diagnosed at each stage, including stages 3 and 4. Treatment costs are described in full in section 6.11.6 of the model report. The modelling work estimates prostate cancer treatment costs by combining published cost data with updated prices and newer information about how treatment has changed over time. First year costs come from a published study[8] and were adjusted to current NHS prices. Longer-term costs were based on trial data showing how spending typically changes over the first 10 years after diagnosis. Expert clinicians advised SCHARR that treatments for advanced cancer have shifted toward newer, more expensive drugs, so SCHARR recalculated costs for later-stage disease using up-to-date drug prices

[8] Wills, L., et al., Estimating surgery, radiotherapy and systemic anti-cancer therapy treatment costs for cancer patients by stage at diagnosis. Eur J Health Econ, 2024. 25(5): p. 763–774.

and clinical practice. It is important to note that the expensive drugs used to treat late-stage prostate cancer are subject to patient access schemes, confidential discounts which the NHS receives off the list price; hence, calculations using the list price alone are likely to overestimate treatment costs. The new drug costs were adjusted to reflect how many people receive them and were used to replace older figures so that costs were not counted twice. Finally, these updated treatment costs were combined with ongoing monitoring costs to build a complete picture of long-term spending across all stages of prostate cancer. Palliative care costs were also considered in the model.

There is debate around the average duration for which men with late-stage prostate cancer receive Systemic Anti-Cancer Therapies (SACTs). The estimates in the model relied on the treatment duration observed in clinical trials, which accounts for treatment discontinuation but is limited by the trial duration. However, some experts suggest that the treatment duration used in the model was an underestimate, and that SACTs are usually taken for life unless the patient stops responding or decides to discontinue treatment. Data on SACT discontinuation is not currently available, and without it SCHARR cannot accurately estimate treatment duration. The UK NSC would welcome data on SACT discontinuation to address this.

The model relies on the availability of good-quality data. At present, there is no reliable data on the impact of unnecessary biopsies on diagnostic delays for prostate cancer cases. Introducing arbitrary assumptions to the model would not improve modelling outcomes but would increase modelling uncertainty.

The UK NSC acknowledges that the evidence around prostate cancer screening is changing rapidly. The UK NSC shares the desire of many stakeholders for the model to remain open so that new, high-quality, peer-reviewed evidence can be included as soon as it becomes available.

Populations for targeted screening

Theme:
There were conflicting views in relation to the draft recommendation for a targeted screening approach only in men with pathogenic variants in *BRCA1* or *BRCA*2. Some stakeholders supported the draft recommendation as an evidence-based, lower-harm approach; others argued that the draft recommendation was not broad enough and should include other at-risk groups, particularly black men and men with a relevant family history. Some stakeholders asked for carriers of other gene variants which increase prostate cancer risk, besides *BRCA1* and *BRCA2*, to also be considered for targeted screening. Other responses suggested that targeted screening is insufficient and would exacerbate inequalities, and that population-wide screening is required.

Response:
Since the 2020 UK NSC review on screening for prostate cancer, which focused on population screening, the UK NSC's remit has been formally expanded to include

targeted and risk-stratified screening. Through the 2022 open call for topics, the UK NSC received 6 submissions requesting that several different screening strategies for prostate cancer be explored. The UK NSC was asked to consider: population-wide screening, as well as targeted screening in black men, men with relevant family histories, and carriers of *BRCA* gene variants.

Cancer screening has traditionally been based on age and sex alone and determining additional factors for more targeted screening requires substantial supporting evidence. Targeted screening involves being able to reliably identify a particular group of high-risk individuals who would benefit from screening, whilst at the same time minimising the number of people without cancer who are test-positive and therefore referred to cancer clinics for unnecessary investigations including invasive biopsies.

The model developed by SCHARR has enabled the UK NSC to compare the different screening strategies outlined above to help identify pathways with robust evidence and estimate the balance of benefits and harms within the same analytical framework. Based on the modelling work undertaken, screening the general population for prostate cancer would lead to substantial overdiagnosis (detecting cancers that would not have caused harm), meaning that the balance of benefits and harms is not in favour of screening in this broad group. The same conclusion applies to screening men with familial risk.

The model suggested that screening men of black ethnicity is likely to identify more cancers among people who are screened, compared to screening the whole population. However, the model outlined a great deal of uncertainty about the findings in relation to screening black men. This is largely because of the lack of clarity on if and how prostate cancer progresses differently in black men compared to men of other ethnicities, and because of the absence of evidence from the large trials about the benefits and harms of screening in this group. The UK NSC cannot recommend screening, either a whole population or targeted programme, unless there is strong evidence that it would do more good than harm. Black men are more likely to get prostate cancer, to experience delays in diagnosis and treatment and to die from the disease. Yet historically too few black men have been recruited into trials to generate reliable evidence of how effective screening would be for them. This failure to properly include black men in scientific research entrenches existing inequalities in prostate cancer testing and hence it is of paramount importance that black men are included in research to address existing evidence gaps. The TRANSFORM research trial has been specifically designed to help tackle inequalities in prostate cancer research and at least one in ten men invited to the trial will be black. The UK NSC will collaborate with the TRANSFORM trial team to answer outstanding questions on screening effectiveness for black men as soon as good data becomes available.

The model was more conclusive about the balance of benefits and harms in relation to screening men with a known pathogenic *BRCA2* gene variant who have a relevant family history. Screening this group results in a favourable balance of benefit and

harm overall. This is because men with a pathogenic variant in *BRCA2* are more likely to develop more aggressive cancers, so the benefits to screen would outweigh the harms.

On this basis, the UK NSC recommends that a nationally managed approach to biennial PSA testing in men aged 45 to 61 who have pathogenic germline *BRCA2* variants with a family history of breast, ovarian, pancreatic, or prostate cancer should be implemented.

Currently, the model focuses on screening in the groups highlighted in the 2022 open call submissions. Future work could address screening for other at-risk populations, such as carriers of other mutations (for example, *MSH2*, *ATM*, *CHEK2*).

Screening interval and age range in *BRCA*

Theme:
A point was made that targeted screening should be offered to men with a pathogenic *BRCA1* or *BRCA2* gene variant annually, rather than every 2 years as in the draft UK NSC recommendation. Some stakeholders also advocated for a wider range of ages of men with *BRCA1* and *BRCA2* variants to be included in screening and there were also calls to screen only men with a confirmed *BRCA2* gene variant.

Response:
The draft UK NSC recommendation on prostate cancer screening was underpinned by health economic modelling conducted by SCHARR. The SCHARR model examined a number of screening scenarios for men with *BRCA1* and *BRCA2* variants, including different ages, one-time screening, and repeat screening with different screening intervals.

In the consultation version of the model, 22 different repeat screening scenarios were examined for men with *BRCA1* and *BRCA2* variants. Of these 22 scenarios, biennial screening of men with *BRCA1* and *BRCA2* variants aged 45 to 61 had the second lowest rate of overdiagnosis. The scenario with the lowest rate of overdiagnosis was screening every 5 years from ages 50 to 60; however, this strategy also detected fewer cancers overall. These findings underpinned the draft recommendation which the UK NSC consulted on.

The committee recognises that variants in *BRCA1* and *BRCA2* confer different levels of prostate cancer risk, with increased risk and aggression of cancer in the *BRCA2* group. On the advice of stakeholders, SCHARR has now modelled prostate cancer screening for men with *BRCA1* and *BRCA2* variants separately.

From this updated modelling work, screening appears cost-effective for men with pathogenic *BRCA2* variants, but not for men with *BRCA1* variants. Section 11 of the updated SCHARR model report provides an overview of the new scenarios. Specifically, for men with pathogenic *BRCA2* variants, one-off screening strategies in men aged 45–60 and also several repeat screening strategies, generated positive incremental net monetary benefit (NMB) and had probabilities of being cost-effective

exceeding 70%. Among the repeat screening strategies, biennial screening in men aged 45 to 61 was associated with higher probability of cost-effectiveness and higher incremental quality-adjusted life-years (QALYs) compared to annual screening strategies (see table 47). In contrast, across all annual screening scenarios, the mean NMB was negative and the probability of cost-effectiveness was low.

Therefore, the UK NSC proposes that identifying and screening men with *BRCA2* variants is regarded as the vanguard. The intention is to learn as screening is rolled out and work with experts to optimise the pathways and agree evidence requirements that will allow additions to the routine screening offer.

Identifying *BRCA* patients

Theme:
Many stakeholders raised concerns around the difficulty and cost of identifying men with *BRCA* gene variants. Stakeholders highlighted that more capacity is needed in genetic testing and counselling services, and that men need to be made aware of the eligibility criteria for genetic testing. Some stakeholders highlighted that the cost of genetic testing is decreasing and that some men with *BRCA* gene variants are already engaged with genetic services.

Response:
The committee acknowledges the challenges associated with identifying men with *BRCA* variants. These challenges reflect the complexity of designing appropriate pathways to identify individuals who may be eligible for targeted screening. The committee is aware that a screening programme for men with pathogenic *BRCA2* variants would rely heavily on the availability and accessibility of high-quality genetic testing and counselling services, which are currently subject to capacity constraints across multiple parts of the healthcare system. As some stakeholders noted, a subset of men with *BRCA* variants are already known to specialist services, either through previous clinical presentations or through participation in family-based testing. This existing engagement provides a useful foundation on which to implement a targeted screening strategy for this cohort of individuals. In addition, a threshold analysis is being undertaken to identify the point at which screening would no longer be cost effective. DHSC analysts are undertaking an exercise to estimate the cost of identifying new *BRCA* variant carriers. This will enable the UK NSC to consider the practical options for targeted screening in men with *BRCA2* variants.

The UK NSC's role is to advise ministers on matters related to screening policy. Detailed clinical pathways and service specifications are led by guideline and commissioning bodies (for example, NICE and NHS England), and the UK NSC will continue to work closely with these organisations and specialist clinical genomics services across the 4 UK nations to ensure a clear and consistent national approach to identifying eligible men. To enable this, improved registry systems, data linkage between genetic services and cancer registries, and routine monitoring of access and outcomes across demographic groups will be necessary to ensure that the

targeted screening programme reaches those it intends to benefit and does not exacerbate existing inequalities.

Definition of family history

Theme:
Some stakeholders suggested that the definition of family history used in the model was too broad. Stakeholders also highlighted that men may not know their family history.

Response:
The point regarding the broad definition of family history is valid. Family history can indeed be defined in several ways, and there is uncertainty around the best definition to use when evaluating a potential targeted prostate cancer screening programme. Since the underlying causes of family histories of prostate cancer may be varied, and no prior studies have evaluated the cost-effectiveness of screening in men with familial risk considered as a single group, in the SCHARR model, familial risk was defined broadly as having a first-degree relative diagnosed with breast, ovarian, or prostate cancer at any age or stage. Since family history is also correlated with pathogenic *BRCA* variants, the SCHARR model uses lifetime cancer risks among *BRCA* variant carriers and non-carriers to allocate family history in a realistic manner. The SCHARR model assumed that by the age of 70 years, all men with familial risk were aware of their risk status. This was a pragmatic assumption made in the absence of data on this subject. However, the UK NSC acknowledges that for many men this might not be the case.

Based on expert stakeholder dialogue, the SCHARR modellers have also run additional analyses in men with a family history of prostate cancer as a separate group. The findings of these updated analyses are that screening is not cost-effective in men with a family history of prostate cancer.

The UK NSC welcomes further research to establish a narrower, evidence-based definition of family history that could identify men with a higher risk of aggressive prostate cancer, who would benefit more from prostate cancer screening and also to better understand how different types of family history impact the diagnosis of aggressive prostate cancer, late-stage diagnosis and death.

Infographic

Theme:
Some stakeholders criticised the infographic, citing issues with the quality of the data and how it was presented. The main issues raised included:

- the infographic combines incompatible studies: Göteborg-2, CAP, ERSPC, ProtecT
- there is a temporal mismatch: mortality 15-23 years; overdiagnosis 4 years; harms 12 years

- modern MRI pathway (fewer harms/reduced biopsies) is not mentioned and old non-MRI mortality data (smaller benefit) is used
- Göteborg-2 has been used for the pathway but CAP/ERSPC have been used for mortality despite these using different populations/protocols with different age ranges
- there is a “visual hierarchy” and harms feature more prominently than benefits
- high-risk group context is missing and the focus is on general population figures only
- the link between overtreatment and switching from active surveillance to treatment is unclear
- overdiagnosed men are portrayed as harmed without explaining that the active surveillance pathway minimises treatment
- quality of life for men on active surveillance vs treatment is not distinguished

Response:
It is important to outline that the model report and the infographic presented during the public consultation have two distinct roles. The model compares screening with current ‘standard of care’, which includes opportunistic screening. Therefore, all the extra diagnoses in the screening pathway are over and above what are already found through opportunistic testing. The infographic does not do that. It is simply a visual tool to show what is likely to happen to a group of men who are not showing symptoms, have no particular risk factors and who get a PSA test. In addition, it is not the intention of the infographic to provide comparisons with other screening programmes, as these are complex diseases with different sets of benefits and harms.

In relation to the specific points raised:

Göteborg-2, CAP, ERSPC, and ProtecT are the most informative published studies available to date, and the information on screening issues were extracted carefully for the purpose of developing the infographic. Göteborg-2 has numbers diagnosed following PSA testing and MRI. It only has 4 years of follow-up, which is too short a period for long-term mortality data. ERSPC (23 years of follow-up), ProtecT and CAP (both 15 years of follow-up) were used for mortality. The Göteborg study investigated PSA testing with the contemporary MRI pathway, so the infographic does include the reduced number of men biopsied compared with the older diagnostic pathway. The differences in age ranges are those in the studies and are acknowledged in the footnote of the infographic.

Overdiagnosis was estimated over 15 years and treatment side-effects at 5 years follow-up. The numbers that relate to the overdiagnosed cases (20) and the lives

saved (2) are on the same line and in the same font. They are therefore given equivalent prominence within the infographic. Both boxes also contain qualifying asterisks to provide additional explanation.

Five men out of the 28 diagnosed with cancer were estimated to have high-risk (GG3-5) cancer and/or more advanced disease, and are included in the infographic. When it comes to the link between overtreatment and switching from active surveillance to treatment, it is important to note that in ProtecT, 61% of men switched from active surveillance to radical treatment over 15 years. Reasons for switching were not always related to cancer progression, but included, for example, patient choice or clinician recommendation for other reasons.

In relation to the active surveillance pathway, it is important to note that this can lead to the avoidance of radical treatment induced side-effects provided patients remain on active surveillance. Active surveillance by itself can cause harm either through switching to a radical treatment unnecessarily, or through anxiety from the diagnosis and during follow-up.

As for the quality of life of men on active surveillance, this is complicated to assess, because of the possible switch of these men to a radical treatment, and because of symptoms related to ageing. However, the risks of side effects from radical treatments are only avoided if men remain on active surveillance. An explanatory comment will be added to the infographic to clarify this point.

Implementation versus further research

Theme:
There was support for piloting a targeted screening programme and calls for further research, for example in black men. But there was disagreement about whether to wait for evidence from the upcoming TRANSFORM trial or to implement changes immediately. Some stakeholders stated that screening should happen without waiting for TRANSFORM and others advocated for the need for more UK data and encouraging recruitment to the TRANSFORM trial. Stakeholders highlighted that it would be possible to gather additional UK data through analysis of NHS electronic health records.

Response:
For black men, the balance of benefits and harms from screening is not known. This is because there has been historic underrepresentation of black men in prostate cancer screening trials, leading to uncertainty around the prevalence of prostate cancer in black men, whether black men present with more aggressive disease at diagnosis, and the potential uptake of a targeted screening programme for black men. Therefore, the UK NSC cannot confidently recommend a screening programme for this group straight away.

The TRANSFORM trial will compare multiple screening options and testing pathways – including fast MRI scans and genetic testing to identify high-risk men – to find the most accurate and cost-efficient way to screen men for prostate cancer. It will also

provide data on the experience of harms of screening (such as the side effects of treatment) and how prostate cancer affects men over at least a decade. Importantly, TRANSFORM has been specifically designed to help tackle inequalities in prostate cancer research. The TRANSFORM team is working to recruit a significant proportion of black men to provide evidence and data that is currently lacking and allow a better understanding of prostate cancer in this group of men, specific to a UK context.

The committee is hopeful that TRANSFORM will provide additional data and crucially, more robust evidence on whether screening black men leads to more benefits than harm for this population. We note that stakeholder organisations are working on generating additional real-world evidence, which may also help to address evidential uncertainties around prostate cancer screening in black men. The UK NSC will continue to engage with stakeholder organisations to incorporate the most recent evidence into its recommendations.

Communication and providing information

Theme:
Some stakeholders advocated the need for clearer communication on the pathways, harms, and benefits of screening and testing, showing the desire for information tools and infographics. Others felt that providing information on the adverse effects of treatment and lack of accuracy of the screening test could discourage men from getting tested.

Response:
The UK runs screening programmes that help millions of people every year to live longer, healthier lives and make informed decisions about their health. The UK NSC recommends a screening programme when it is confident that, overall, the benefits will outweigh the harms for those people invited. No screening test is perfect and there will always be some incorrect results, which mean that someone may either be falsely reassured or be unnecessarily worried and perhaps have invasive or harmful tests or treatments which they do not need.

The UK NSC supports the principle of personal informed choice through the provision of information that helps people to weigh the potential benefits and harms of participating in any screening programme. This applies to the recommended evaluative roll out of a national targeted screening programme for prostate cancer in men with a known pathogenic *BRCA2* variant, where harms could arise from false positive and false negative test results and the adverse effects of treatment.

The documents and infographic published alongside the technical model report were developed with the intent to provide a balanced summary of the modelling work that has informed the UK NSC recommendation. As work gets under way on the implementation of any screening programme recommended by the UK NSC, additional resources, including information for health professionals and the public, would be developed in collaboration with all relevant stakeholders.

Ethical and equality considerations

Theme:
Some stakeholders raised ethical concerns citing that consideration of harms and benefits should be a matter of individual choice and that the UK NSC recommendation undermines autonomy. Some stakeholders expressed concern that targeted screening only for men with *BRCA* variants would exacerbate existing inequalities in access to genetic testing for people from minority ethnic and socioeconomically disadvantaged groups. Some stakeholders also expressed concern that not screening men for prostate cancer would exacerbate health inequalities between men and women, citing the existence of screening programmes for female-specific cancers. An additional point expressed by some stakeholders was that black men are currently disadvantaged in accessing PSA testing within the current system of opportunistic/symptomatic PSA testing and that this inequity could be reduced by proactively offering screening to this group. In addition, some stakeholders criticised the lack of a published equality impact assessment.

Response:
When a screening test is already available (as it is with PSA), we agree that it involves individual choice whether to have the test or not. Some men will accept the risk of overdiagnosis and overtreatment in order to be diagnosed with prostate cancer if they have it, because their focus is on the harms of disease progression and the risk of dying from the cancer (even if it were a slow growing/latent cancer). But other men will find the benefit-harm balance difficult to manage and so opt to not have screening. Both scenarios are acceptable to individuals. However, a national screening programme will actively invite many thousands of men for testing and in order to justify this, the benefit-harm balance on a population scale (not for an individual) needs to be known with sufficient reliability. Because screening is offered to a large proportion of apparently healthy people who may have an increased chance of a condition, there is always the potential for harm; hence, the UK NSC uses a rigorous evidence-based approach, and this applies equally across all the groups considered for targeted screening.

Comparisons with other screening programmes are difficult because these are complex diseases with different sets of benefits and harms. There is good evidence that screening is effective in reducing cervical and breast cancer. In addition, if there was evidence that screening was effective in reducing male breast cancer the UK NSC would consider this. The bowel and lung cancer screening programmes are offered to both men and women whereas the abdominal aortic aneurysm screening programme applies only to men over the age of 64.

We know that inequalities in health and healthcare are longstanding and important issues. The ethical principles of health screening are encompassed within the UK NSC criteria for assessing the viability, effectiveness and appropriateness of a screening programme. To further clarify and explain the overarching goals of screening, the UK NSC has developed an ethical framework for screening. The framework is comprised of 4 broad ethical principles, which are: 1. improve health

and wellbeing, 2. treat people with respect, 3. promote equality and inclusion, and 4. use public resources fairly and proportionately. The principles are all equally as important as each other.

On the basis of the evidence review and modelling work conducted by SCHARR, screening the general population or those with familial risk is associated with high uncertainty and substantial overdiagnosis. Similarly, there are many uncertainties in the data related to screening black men for prostate cancer. This means that prostate cancer screening may not meet key elements of the UK NSC ethical framework, particularly the goals of improving the health and wellbeing of the population and ensuring that resources are distributed fairly and proportionately.

As described in principle 3 of the UK NSC ethical framework, screening programmes should not act to increase health inequalities and should aim to reduce them. The UK NSC is aware of existing inequalities in access to genetic testing; this is why it is essential that screening for men with pathogenic *BRCA2* variants is implemented and monitored carefully. The evaluative nature of the proposed screening programme for *BRCA2* variant carriers will help to ensure that strategies are put in place to monitor and mitigate any potential exacerbation of health inequalities.

The role of the UK NSC is to advise ministers and the NHS in the 4 UK countries on whether screening for prostate cancer should be implemented. The reason an equality impact assessment was not published with the rest of the documents made available online during public consultation is because the UK NSC recommendation was not yet final. It is only when the UK NSC makes a final recommendation that this is put to ministers and several impact assessments are produced, including an equality impact assessment. Following a decision from the Secretary of State, impact assessments are made publicly available.

Considerations about screening implementation

Theme:
Some stakeholders commented on specific issues relating to the implementation of a screening programme for prostate cancer. They noted challenges relating to MRI capacity constraints, and the impact on GP workload and demand. They also stressed the need for a national operating model for identification, invitation, testing, and results, with clear service specifications, patient information, and decision aids in place.

Some stakeholders thought that a recommendation to screen men with a pathogenic *BRCA1* or *BRCA2* variant would enable the development of a quality-assured screening pathway which could, in future, be expanded to other high-risk groups, if supported by the evidence.

Response:
The points raised by some stakeholders in relation to screening implementation are well made and highlight the real-world complexity of implementing a prostate cancer screening programme. The points about MRI capacity constraints and the potential

impact on already stretched GP workloads reflect genuine operational pressures across the system. Similarly, the emphasis on establishing a clear national operating model with clear service specifications, covering the entire screening pathway from identification and invitation through to testing and treatment, outlines the need for consistency at a national level to avoid local variations, if such a programme were to be introduced. The UK NSC agrees that ensuring that high-quality patient information is in place is also crucial, so individuals can make informed choices about taking up the offer of screening with confidence. These considerations are important and valid, and recognising them helps to ensure that any future screening programme is grounded in practicality and a commitment to high-quality care.

The UK NSC's role as an independent scientific advisory committee and representation on the committee

Theme:
Several stakeholders were unclear that the UK NSC is an independent scientific advisory committee which provides independent evidence-based advice to ministers and the NHS. Some stakeholders raised concerns about appropriate representation on the UK NSC, referencing that there are more women than men on the UK NSC and that there are no black men sitting on the committee.

Response:
The UK NSC is an independent scientific advisory committee which advises ministers and the NHS in the 4 UK countries about all aspects of screening and supports implementation of screening programmes. More information on the role of the committee is available on the UK NSC website.

The UK NSC and its host organisation, the Department of Health and Social Care (DHSC), values and promotes diversity and encourages applications from all sections of the community. The UK NSC operates an open recruitment process and advertises its vacancies on GOV.UK and via UK NSC blog articles disseminated directly to all the UK NSC's subscribed stakeholders. In addition, the UK NSC contacts ethnic minority groups and professional bodies directly to alert them of such campaigns. Although current representation on the main committee does not fully reflect our aspirations at a committee level, there is wider representation across the UK NSC's expert sub-groups which also work on examining and reviewing the evidence and consultation comments.

UK NSC processes / governance / stakeholder engagement

Theme:
Some stakeholders raised points which broadly related to UK NSC processes, governance and stakeholder engagement. These included:

- not enough involvement of medical professionals and of patients/the public
- stakeholder feedback and UK NSC responses not published

- response mechanism unclear for detailed technical submissions
- expert group identities not published
- consultation period falling over the Christmas/New Year period

Response:
In line with the UK NSC evidence review process, the SCHARR model and associated documents were published on the UK NSC website on 28 November 2025 for a 12-week public consultation exercise, which concluded on 23 February 2026. A blog article was published on 28 November 2025 to further highlight the opportunity for individuals and organisations to respond to the consultation. Registered prostate cancer screening stakeholders were also contacted directly and invited to respond to the consultation. For more information on how the UK NSC plans to review and build on its ongoing engagement with stakeholders, please see: UK NSC stakeholder engagement.

The UK NSC acknowledges that the consultation period between 28 November 2025 and 23 February 2026 fell over the Christmas/New Year period. However, the consultation timings had been carefully selected to ensure that the consultation comments could be promptly presented to the UK NSC meeting in March 2026. Had the consultation dates gone beyond 23 February 2026, this would have led to delays and shifted the timings of the UK NSC's deliberation on the topic.

The current SCHARR modelling report is a direct result of stakeholder involvement through the 2022 open call for topics, where the UK NSC received 6 submissions asking for several screening strategies for prostate cancer to be explored. These were: whole population screening, and targeted screening in black men, men with relevant family histories, and carriers of *BRCA* gene variants. These proposals directly informed and shaped the scope of the SCHARR model. In an initial phase of the modelling work (phase 1), SCHARR focused on evaluating the cost-effectiveness of one-time PSA screening in men at average risk, and separately, a one-time screening for high-risk men, analysed as single-age cohorts. The modelling report shared for consultation presents the full modelling methodology and describes the updates and enhancements made following the completion of phase 1, with key findings from phase 1 summarised in the report published for consultation. Expert clinicians, patient and public voice (PPV) representatives and organisations representing patients provided input into the model at several points in the model development process. Representatives from Prostate Cancer UK (PCUK) and several other stakeholders were involved in the conceptual model development process via a stakeholder meeting held in May 2024, as described in section 6.1.1 of the model report. A list of those who accepted the invitations and participated in the stakeholder meeting is available in Table 1 in the model report. The minutes from the stakeholders' meetings, along with the outputs and impacts (specifically detailing how stakeholder input was incorporated into the model), are provided in Supplementary I in the model report. Stakeholder input at an early conceptualisation stage was extremely valuable, and SCHARR made changes to the modelling plan

based on this input. As part of the model development process, the model was also reviewed by the UK NSC Adult Reference Group (ARG) and the UK NSC, both of which have PPV representatives as members.

Stakeholder feedback and UK NSC responses from the public consultation exercise can only be published after the consultation has taken place and after the UK NSC has made its recommendation. Though it is not possible to respond to each comment individually, themes are extracted from the consultation comments and responded to in as much detail as possible. The redacted consultation comments, together with the UK NSC responses, are published on the UK NSC website following the UK NSC final recommendation.

Considerations beyond screening

Theme:
Some stakeholders raised considerations beyond screening. These included:

- raising public awareness
- improving medical records to support risk recognition
- updating the current Prostate Cancer Risk Management Programme (PCRMP)
- the need to improve clinical management pathways for prostate cancer
- providing better psychological support following diagnosis
- better guidance and training for GPs
- the need for NICE to update its prostate cancer guidelines

Response:
The UK NSC acknowledges the challenges that individuals face before and after reaching a diagnosis. It agrees that increased awareness can help people recognise symptoms, understand personal risk, and know when to seek advice promptly. The UK NSC will continue to work with national partners and community organisations to promote plain-English information to ensure messages are accessible and trusted.

The UK NSC also recognises how difficult it can be to identify higher-risk individuals when key information such as ethnicity, family history, or *BRCA* gene status is incomplete or inconsistently coded, and the need to improve medical records so that risk factors are recorded consistently and visible to clinicians.

The UK NSC agrees that a streamlined clinical pathway, from presentation, through diagnosis, to treatment and follow-up, including psychological support after diagnosis, is essential. The UK NSC's role is to advise ministers on matters related to screening policy. Detailed clinical pathways and service specifications are led by

guideline and commissioning bodies (for example, NICE and NHS England), and the UK NSC will continue to support the work of these organisations.

The UK NSC also supports concise, practical guidance and training for GPs to aid informed conversations with men regarding prostate cancer. The UK NSC acknowledges the need to update the current guidance for men and their GPs including the Prostate Cancer Risk Management Programme (PCRMP).

In relation to the NICE guideline on the diagnosis and management of prostate cancer, it is worth noting that NICE has already taken steps through its formal surveillance process to update aspects of its prostate cancer guideline (NICE guideline NG131). This includes decisions in May 2025 and August 2025 to update sections on the treatment of high-risk hormone-sensitive non-metastatic prostate cancer (docetaxel/abiraterone) and the protocol for active surveillance in localised prostate cancer. Information on NICE's surveillance decision is available on NICE's website.

The following technical themes include responses from the SCHARR modellers

Model structure and assumptions

Theme:
Some stakeholders questioned the model structure and some of its assumptions. Criticisms included:

- an overreliance on CAP trial data
- the fact that different PSA thresholds (apart from ≥3 ng/mL) were not modelled
- the model did not consider using different PSA thresholds for different age groups (i.e. a lower threshold for younger men)
- the Markov cohort structure limits granularity for disease with variable progression
- the model was designed for population screening and is therefore not suitable for high-risk groups

Response:
The model did not rely on the CAP trial for data describing the natural history of disease or test accuracy. However, the model did construct a screening scenario similar to one evaluated in the CAP trial, as well as in the ERSPC trial. As demonstrated in section 7.2. of the model report, it is technically impossible for the model to predict screening outcomes that are similar to both the CAP and ERSPC trials, highlighting the heterogeneity that arises when trials evaluate different screening designs and populations. Models construct simplifications of a much more complex reality. The SCHARR model did not attempt to replicate identically the outcomes of either trial, but was designed to demonstrate general similarity between the model predictions and the observed evidence from multiple sources.

The choice of PSA thresholds was determined during the model conceptualisation phase, informed by input from both clinical and Patient and Public Involvement (PPI) stakeholders. Expert stakeholders recommended that a threshold of 3 ng/mL would be the most applicable for population-based screening, whereas the age-specific thresholds proposed by NICE were considered more likely to be used in symptomatic clinical settings (model report Supplementary I, p. 257). Feedback from stakeholders was broadly consistent in identifying a PSA threshold of 3 ng/mL as the most appropriate for screening purposes. Nevertheless, to reflect uncertainty and explore alternative approaches, the model also examined multiple PSA thresholds within each screening scenario (model report Section 9, p. 156). For all men, as well as men with a family history of prostate cancer, the model evaluated screening scenarios using either a flat PSA threshold of 3 ng/mL irrespective of age, or the

NICE-recommended age-specific PSA threshold (3.5 ng/mL). For black men and *BRCA* mutation carriers, the model assessed screening scenarios using either a flat PSA threshold of 3 ng/mL or a lower threshold of 2.5 ng/mL.

The PSA thresholds included in the model were selected because they align with thresholds used in previous prostate cancer screening trials and/or reflect current NICE guidance. While a wider range of screening options could be explored, the project scope necessarily required a focused and manageable set of scenarios to ensure feasibility of the modelling work.

The SCHARR model included high-risk populations from early conceptualisation stages. The structure of the model allows to model representative groups with different characteristics, including all high-risk groups together or each group separately. The SCHARR prostate cancer model uses a hybrid structure: the cancer onset is modelled within the Markov annual cycles, but the cancer progression has a time of progression component incorporated within it. This allows the model to simulate cancer progression at a granular level, outside the annual model cycles, with some modelled patients progressing across multiple stages within one year. The assumptions on sequential progression across stages is standard for cancer modelling and have been used in other known cancer models, including the Cancer Intervention and Surveillance Modeling Network (CISNET) models.

Time horizon and discounting

Theme:
Some stakeholders stated that the time horizon of 15 years truncates the mortality benefits and it should instead match the natural history of the disease (20-25 years or lifetime). They also raised concerns that the benefits of screening are discounted over decades, whereas the harms are captured immediately and hence the harms have a greater impact on the model conclusions. A point was also made that lead time was captured but mortality benefit was discounted asymmetrically.

Response:
The model uses a lifetime horizon and not a 15-year time horizon as some responses suggested. In the base case analysis, the model uses a 15-year extrapolation of survival data. This means the model assumes that unless someone has died from prostate cancer by 15 years after diagnosis, they will not die from prostate cancer after this time. This is not the same as a 15-year time horizon, and all benefits, harms, and costs of surveillance were modelled from first screening until death (that is a lifetime horizon). A survival of 15 years was chosen in the base case as the available data on prostate cancer survival only extends to 15 years post-diagnosis for early-stage cancer and 5 years post-diagnosis for late-stage cancer, and extrapolations of survival revealed high uncertainty (model report section 6.6.3, pp.43-48). SCHARR explored the impact of extrapolating the available survival data over lifetime in scenario 2, which demonstrated very little impact on the modelling outcomes.

The methodology of the model relies on the NICE reference case. Discounting is a well-accepted practice in health economics. It reflects the idea that people generally prefer to receive benefits sooner and to pay costs later, so future outcomes are "discounted" to make them comparable with present ones. A discount rate of 3.5% is recommended by NICE and was therefore used in the base case. However, SCHARR also explored the impact of different discount rates, including discount rates outlined in the UK government's Green Book, in scenarios 4-6.

Both benefits and harms are reflected and captured in the model. Because the model relies on the natural history, it eliminates the lead time bias observed in trials with short follow up. The lead time scenario in the model reflects something different: because it works at an individual level and uses probabilities (so outcomes can happen by chance), someone who may be diagnosed earlier might, by chance, still have a worse outcome (earlier death) than if their diagnosis had been later. While most of the people in the screening arm of the model would have either later time of death (those who benefit) or the same time of death (those who are overdiagnosed), simply by a random chance someone may have an earlier death. This concept is very common in microsimulation models of cancer. It is used to explore the clinically plausible possibility of someone dying earlier as a result of earlier diagnosis, for example because of treatment side effects. The choice of the baseline assumptions was validated by a group of clinical stakeholders and explored in scenario analysis (see the lead time scenario).

Outdated screening pathway

Theme:
Some stakeholders assumed an outdated PSA-to-biopsy pathway was modelled and claimed that the more modern and less harmful PSA-MRI-biopsy pathway was not modelled. Or they thought the modern pathway was modelled but some parameters, including natural history, were based on a PSA-to-biopsy pathway. Stakeholders also claimed the MRI sensitivity and specificity data are incomplete. Some stakeholders claimed that newer, less harmful biopsy techniques, particularly transperineal biopsy, were not modelled or that even though transperineal biopsy was modelled, parameters relating to harms were from older transrectal biopsy data. Stakeholders suggested that biparametric MRI (BP-MRI) should be considered as a quicker and cheaper alternative to multiparametric MRI (MP-MRI).

Response:
As described in section 6.8 (pp.66-71) of the model report, the modelled screening pathway was PSA, then MP-MRI, then Local Anaesthetic Transperineal (LATP) biopsy, then treatment/surveillance. As stakeholders highlighted, the use of MP-MRI as a triage test following a positive PSA is likely to result in fewer harms than a pathway that proceeds straight to biopsy. Hence, the pathway modelled included MP-MRI as a triage test. SCHARR did not model a direct PSA-to-biopsy pathway.

Some stakeholders correctly noted that a number of model parameters are based on older data, before the wider adoption of MP-MRI. This is because for each

parameter, such as the accuracy of the PSA test or biopsy for detecting prostate cancer, the model used the most robust and relevant data available, ideally from large-scale randomised controlled trials conducted in screening populations representative of the UK population and providing data in a format that could be used in the model. For example, the accuracy of the PSA test was based on the PCPT trial, and the uptake of screening in the base case was based on the CAP trial. Large screening trials are rare and the model requires sensitivity values by cancer stage or grade, which is why many parameters are based on trials which did not include MP-MRI. It is important to note that because of lack of data on correlations between PSA outcomes and MP-MRI, each step of the pathway is independent of the other steps. This will be updated in the model when new data from ongoing trials (e.g. the IMPROVE trial) become available. For the accuracy of MP-MRI, consultation version of the model used the latest available published data which came from the 2017 PROMIS trial. Following feedback from stakeholders, SCHARR has now run an additional scenario which uses MP-MRI accuracy values from a 2021 systematic review by Bass et al; however, this use of this source comes with caveats as described in section 11.2 of the updated model report.

When the consultation version of the model was published, there was an absence of studies reporting sensitivity and specificity of LATP, so the model used a relative difference from transrectal ultrasound-guided (TRUS) biopsy, validating the assumptions with the clinical experts. The model has since been updated with the latest data on the accuracy of LATP biopsy from the TRANSLATE randomised controlled trial, as described in section 11.1.6 of the updated model report.

Current NICE guidelines on the diagnosis and management of prostate cancer recommend the use of MP-MRI as a diagnostic test. Most NHS trusts currently use MP-MRI for prostate cancer diagnosis, although the use of BP-MRI is increasing. In accordance with current NICE guidelines, the screening pathway in the consultation version of the model included MP-MRI, rather than BP-MRI; however, following feedback from the public consultation and expert stakeholders, SCHARR has updated the model to use a weighted average of BP-MRI and MP-MRI costs based on their reported usage in current clinical practice (see section 11.1.7 of the updated model report). The UK NSC is aware that limited MRI capacity represents a significant barrier to prostate cancer screening, and will consider alternative MRI protocols, such as BP-MRI, where these are shown by high-quality evidence to be non-inferior to MP-MRI for the detection of clinically significant prostate cancer. We note that results from the European PRIME paired cohort study showed similar performance characteristics between MP-MRI and BP-MRI. Level 1 evidence from the ongoing UK-specific IP7-PACIFIC randomised controlled trial will provide further evidence on whether BP-MRI should replace MP-MRI in the prostate cancer diagnostic pathway.

Treatment patterns and risk stratification

Theme:
Some stakeholders claimed that the treatment pathway was assumed to be identical regardless of stage at diagnosis, that the treatment parameters and utility values used in the model were based on early data from before active surveillance, and that active surveillance quality of life was not properly valued, with detection treated as an immediate harm. Some stakeholders also said treatment costs associated with advanced (stage 4) prostate cancer are substantially higher than those assumed in the SCHARR model. Some stakeholders also claimed that no subgroup analyses for black men were carried out and that combined risk factors (black + family history, multiple relatives) were not modelled.

Response:
In the model, treatment pathways differed by stage at diagnosis. As described in section 6.11.6 (pp.78-82) of the model report, the modelled treatment costs varied by stage at diagnosis and were based on published literature. Broadly, prostate cancers diagnosed at stage 1 are the least expensive to treat, and cancers diagnosed at stage 4 are the most expensive to treat. The estimated treatment costs for cancers diagnosed at different stages are outlined in table 27 of the model report. Survival also varied by stage and age at diagnosis, based on the data from ONS, PHE, and the ProtecT trial. Similarly, the utilities (quality of life) differed depending on cancer stage at diagnosis, with cancers diagnosed at later stages having a greater impact on quality of life.

Treatment utility values were based on the 2024 NHS Cancer Quality of Life Survey. This survey examined EQ-5D scores from prostate cancer patients collected at 18 months after diagnosis. The utilities by stage used reflect the average utilities of people diagnosed with prostate cancer of a specific stage, with a proportion of those men on active surveillance. This means that some of these men may not have had their quality of life impacted at all by screening, while others will have had their quality of life impacted significantly. The model averages the impact of cancer diagnosis on quality of life for each specific stage. There are indeed some limitations of EQ-5D from the perspective of its sensitivity. However, the methodology of the model relies on the NICE reference case, which enables compatibility with other UK models, and EQ-5D is a part of the NICE methodology.

Individuals whose cancer is identified through screening may experience benefits that outweigh potential harms, although this is not the case for everyone. If screening leads to an earlier stage of cancer being diagnosed, the individual could enjoy improved utility and quality of life, as those diagnosed at an earlier stage generally report higher quality of life compared to those diagnosed later. These benefits are acknowledged even if survival rates do not improve. Therefore, it is inaccurate to characterize detection as an immediate harm; such a scenario applies only to men diagnosed with non-aggressive cancers that would not have progressed to advanced stages. Furthermore, some treatments for early-stage prostate cancer (e.g. hormonal therapies) have major symptoms and side effects so quality of life can be

significantly impacted (e.g. fatigue, sexual function), and some men will find this unacceptable, particularly for overdiagnosed cancers.

In relation to the point about modelling combined risk factors, it is important to note that modelling relies on a provided scope. The model scope was informed by the proposals received during the 2022 open call for topics, which included the different screening strategies for prostate cancer to be explored. These were: population screening and targeted screening in black men, men with relevant family histories, and carriers of *BRCA* gene variants. There were no data identified that included three-factor correlations. When new data from ongoing large trials become available, the model could be updated with the correlations between the multiple parameters.

Calibration and validation

Theme:
Some stakeholders criticised the model calibration and validation, pointing out the acknowledged limitations, that the predicted prostate cancer deaths as a proportion of those diagnosed in the non-screening arm are higher than in the CAP data, and that calibration took place against a contaminated baseline (existing opportunistic testing). Other stakeholders believed the modelling methods provided a good demonstration of internal and external validity.

Response:
As acknowledged in Section 7.2.3, p.85, the modelling predictions are more similar to results from the ERSPC trial than the CAP trial. This signifies heterogeneity in predicted outcomes across the trials and that it would be impossible to predict the outcomes that would be comparable with both trials. The scenario analyses demonstrate that a better fit to mortality data from NHS digital (2020) would make screening less cost-effective than currently predicted. This means that additional calibration to mortality data would not change the conclusions of the report for population screening, screening in black men, and screening in men with relevant family histories, since a better fit to mortality data would lead to screening having a smaller impact on mortality, and thus being less cost-effective. The SCHARR team is planning to recalibrate the model using the latest trial data and updated assumptions on the natural history of disease and other parameters.

Information on the uptake of opportunistic PSA testing is not currently available, and so the model was calibrated to "current care" (which includes opportunistic PSA testing) and not to a "no screening" scenario. As a result, SCHARR could not incorporate assumptions about how an organised screening programme might affect ongoing opportunistic uptake. International experience, including Lithuania, suggests that the effects may differ significantly by age group and over time, with both increases and decreases in opportunistic PSA testing observed depending on programme maturity and invitation history. This complexity means that predictions of the impact of an organised screening programme on opportunistic testing are highly uncertain.

The limitations of the calibration are explored and discussed in the report. These limitations relate to correlations across multiple natural history disease parameters and age, as well as to the limited understanding of prostate cancer natural history. Options for addressing these limitations, specifically through the application of assumptions about disease progression (referred to as “priors” in Bayesian statistics), were discussed with clinical experts. While the use of priors could reduce uncertainty in the calibration process, clinical experts highlighted the substantial gaps in current knowledge of prostate cancer natural history and cautioned that imposing strong priors could artificially encourage certainty and lead to false confidence in the model outputs. Consequently, this component of the model was intentionally left unchanged.

Overdiagnosis

Theme:
Some stakeholders stated that the model’s overdiagnosis rates were at the upper end of the spectrum when compared with other models and that overdiagnosis was conflated with overtreatment, without distinguishing men on active surveillance. Some stakeholders also suggested that overdiagnosis is an assumption of the model rather than an outcome. One stakeholder raised that Grade Group 2 (GG2) cancers should not be considered overdiagnosed.

Response:
Section 12.3 (pp.222-224) of the model report describes the overdiagnosis estimates from other prostate cancer screening models. As noted in this section of the report, the overdiagnosis rate is not something which is chosen directly, but instead results from other model parameters and assumptions. Because different models use different underlying assumptions and parameters, comparing between them can be problematic. For example, models designed to reflect a US or Swedish context will use different parameters compared to models based on the UK context, and hence reach different figures for overdiagnosis rates. The parameters and assumptions in the current SCHARR model were based on the latest published data and expert input, and were designed specifically for the UK context. The current SCHARR model had higher overdiagnosis rates than other models at older ages, but comparable overdiagnosis rates at younger ages to the SCANS (Michigan) model and lower average overdiagnosis rates than the MISCAN - PRO (Rotterdam) model.

Overdiagnosis is not a model assumption but a model prediction. While the estimated rate of overdiagnosis depends on the model structure and the data used, overdiagnosis itself can only be quantified through modelling or by comparing screening and non-screening arms in clinical trials. For an individual person, it is not possible to determine whether they have been overdiagnosed; rather, the model can only estimate the probability that an individual would be overdiagnosed under a given screening strategy.

Importantly, because overdiagnosis is not an input or assumption in the model, but a prediction of the model, the model did not implicitly assume that men with GG2

cancers, or any other group, were overdiagnosed. Instead, the rate of overdiagnosis in each group was calculated based on the incidence in the screening arm versus the standard care arm (see section 4.2 of the model report). Cancers of any grade group can be overdiagnosed, and indeed every modelled group will have some degree of overdiagnosis, but the rates of overdiagnosis are higher for low-grade cancers. Therefore, it is an intended feature of the model that some men with GG2 cancers are modelled as benefiting from screening and others are modelled as being overdiagnosed, as this reflects the reality of screening.

Overdiagnosis estimates were based on all men diagnosed with prostate cancer which would not have caused them harm during their lifetime. Being diagnosed with prostate cancer and entering active surveillance can still cause harm (for example due to anxiety and psychological harms), and therefore the term overdiagnosed can also apply to these men. We use a separate term, overtreated, to describe men who undergo treatment for a prostate cancer which would not have caused them harm. A subset of overdiagnosed men will also be overtreated.

In the consultation version of the model, repeat screening of the general population led to substantial levels of overdiagnosis, with rates ranging between 44% and 58%. Similar rates of overdiagnosis were found also in the context of repeat screening in black men. Repeat screening in men with family history also led to substantial overdiagnosis, ranging between 46% and 63%.

Model perspective

Theme:
Some stakeholders argued that the model's economic framework is too narrowly confined to direct NHS costs and that the model should also take into account broader societal costs including, for example, productivity gains.

Response:
The UK NSC oversees the evaluation of evidence on the balance of benefits and harms associated with existing, new, or modified screening programmes, including their impact on healthcare costs and health outcomes. To date, the UK NSC has not defined a specific set of methods outlining how economic evidence to understand the impact of national screening programmes on healthcare costs and health consequences should be produced. Instead, over the years the committee has used the NICE Methods Guide for Health Technology Appraisal (HTA) framework as a broad reference point. The UK NSC has also recently commissioned a piece of work to develop a general methods guide for producing models for use in the economic evaluation of screening programmes.

The general purpose of all screening programmes should be to improve the health and wellbeing of the population, so the focus should be on the individuals who will be offered screening. Because the NHS bears the cost of any potential screening programme, it is essential that finite NHS resources are used in a way that maximises the health benefits for the UK population. Hence, the modelling choice of

using costs relating to resources that are under the control of the NHS and personal and social services (PSS) is considered appropriate. There is no formal agreement on what exactly constitute a 'broad societal perspective'. This often relates to many potential elements such as productivity, environmental, and family impacts which might not always be appropriate for health decision making. In addition, models rely on the availability of good-quality data and for many of these 'broad elements', the evidence with which to populate the model is often lacking. Therefore, introducing further assumptions to the SCHARR model (but more broadly, to any model) would not improve modelling outcomes but risks increasing modelling uncertainty.

However, it is worth noting that once a UK NSC recommendation is made, as it is common with other policies, DHSC officials produce impact assessments (IA) using the HMT Green Book methodology which covers any significant societal costs, benefits and risks impacting on the UK/England. Ministers then consider the IA together with advice from the NHS on operational considerations, such as equipment, workforce, and resourcing when reaching a decision on whether to implement a screening recommendation and the timescale required for doing this.

Decision threshold and probability of cost effectiveness

Theme:
Some stakeholders acknowledged the ongoing debate about what cost-effectiveness threshold is most appropriate for appraising screening programmes. Some stakeholders raised the additional point that no threshold for the acceptable probability of cost-effectiveness required for recommendation was stated.

Response:
Currently, there are no explicit guidelines on what probability of cost-effectiveness would be considered sufficient. For example, the modelling report concludes that there is substantial uncertainty around organised screening in black men, arising from uncertainty in the underlying data used in the model. In particular, data suggesting greater cost-effectiveness of screening in black populations are derived from the US and are not available for the UK context. As a result, the model may overestimate the benefits of screening in black men.

The goal of the UK NSC is to provide evidence-based recommendations about the use of health screening. Reviews of the best available international evidence are central to the evidence review process used in the development of recommendations. This includes evidence addressing internationally recognised screening criteria on the epidemiology and natural history of a condition, test accuracy, effectiveness of treatment, and the clinical and cost-effectiveness of the screening programme as a whole. Using this evidence, the UK NSC assesses whether the benefits of a screening programme would outweigh the harms at a reasonable cost to the NHS. Consequently, these decisions are not solely about cost, but they also involve assessing benefit, harm, and certainty of the evidence, which populations are benefited and harmed, and whether different sub-populations should be screened differently.

To date, the UK NSC has not yet published a methods guide to inform how to generate economic evidence and appraise economic models to support its recommendations. Instead, over the years the committee has used the NICE Methods Guide for Technology Appraisal as a reference guide. On 1 December 2025, NICE was instructed by government ministers to change the cost-effectiveness threshold it should use in its NICE Technology Appraisal programme. The ministers advised a new threshold range of £25,000 to £35,000 per QALY and this should apply to medicines. NICE was instructed to implement the new cost-effectiveness threshold for medicines in its Technology Appraisal programme on 1 April 2026. To date, it is not clear that NICE will change the cost-effectiveness threshold for the appraisal of interventions other than medicines. The UK NSC took the view that the appropriate cost-effectiveness threshold to use for this appraisal should be £20,000 per QALY. This view considers the cost-effectiveness threshold that has been historically used by the UK NSC and the substantial gaps in the current evidence base leading to considerable uncertainty in whether the benefits of prostate cancer screening outweigh the harms. The UK NSC has recently commissioned a piece of work to develop a methods guide for producing economic evidence and appraising economic models of screening programmes, and considerations on assessment of cost effectiveness, including aspects such as the appropriate cost-effectiveness threshold, will form part of this work. It is important to reiterate that the UK NSC makes its recommendations guided by the principle that screening should do more good than harm at a reasonable cost, with cost being one component among many others.

Uptake assumptions

Theme:
Some stakeholders highlighted that the model applies a flat uptake rate across years in the repeat screening scenarios, which is unrealistic. Stakeholders incorrectly interpreted the model report as assuming 100% uptake for *BRCA* scenarios, but 36% for other groups. Some stakeholders suggested that 36% is an unrealistically low uptake for a national screening programme, while others acknowledged that this is the best evidence-based indication of uptake.

Response:
In relation to the uptake rate, this is an acknowledged limitation of the model related to data constraints. For the general population and men with familial risk, this limitation will not have an impact on cost-effectiveness outcomes because repeat screening was not likely to be cost-effective in these groups even in scenarios assuming 100% uptake. For *BRCA* carriers and men with familial risk, new data that may be used to inform uptake in repeat screening has been published after the modelling report was completed. This will be incorporated into the model in the future.

The 100% uptake the stakeholders refer to has been used to calculate the net benefit of screening (that is, the potential benefit of screening that could be achieved under ideal conditions). This was calculated for all groups, including the general

population, men with a family history, and men of black ethnicity, not just *BRCA* mutation carriers. The uptake of PSA testing used to calculate the cost-effectiveness of screening was 36% for all groups; this figure was based on the uptake of PSA testing in the CAP trial. The potential for higher uptake of a national screening programme is highly uncertain since the uptake of repeat screening is commonly lower than for single screening, and other studies exploring the possibility of PSA screening in the UK have reported lower uptake; for example, 27% uptake in a GP-based PSA screening study by Langley at al. (2025)[reference 68 in the model report].

The TRANSFORM trial will provide additional data on the uptake of prostate cancer screening, albeit in a clinical trial setting, which will be used to inform future estimates of uptake.

Opportunistic testing assumptions

Theme:
There was a suggestion that the approach used by the SCHARR model is to assume that implementation of a population-based screening programme would make no difference to men's opportunistic screening behaviour and there would be zero other changes in NHS policy, when instead one would expect the NHS to end opportunistic testing once a PSA screening programme was in place.

One stakeholder disagreed that an organised screening programme would significantly reduce opportunistic PSA testing rates, citing data showing that existing PSA testing is predominantly driven by symptomatic PSA testing, with testing most common in the 70-89 age group. They believed that the model appropriately accounted for PSA testing interactions given the limited availability of data.

Response:
The SCHARR model does not assume that organised screening has zero interaction with opportunistic or symptomatic diagnosis. Rather, the impact is structural and limited, reflecting the constraints of the model specification. Specifically, organised screening affects outcomes for men who already have undiagnosed cancer at the time of screening by altering the timing and mode of diagnosis (earlier detection, different stage distribution, downstream survival and so overdiagnosis and quality-of-life effects). Men who would otherwise be diagnosed symptomatically or through opportunistic testing at a later point, are therefore partially reallocated within the model (that is, they may have different outcomes by attending organised screening). What the model does not currently capture is a behavioural change in PSA testing patterns among men without cancer (for example, substitution, displacement, or cessation of opportunistic testing following invitation to organised screening). So, the pre-existing opportunistic PSA tests are retained unchanged alongside organised screening, unless they result in cancer detection. Equally, it does not impose assumptions about large-scale behavioural shifts in PSA use in the absence of robust empirical evidence specific to the UK context and screening design being evaluated.

In the model, the SCHARR modellers were unable to separate opportunistically screened and symptomatically presenting cases. This limitation prevented them from adding assumptions about how an organised programme would affect those pathways. While including such assumptions might change point estimates, it would not eliminate uncertainty, nor would it necessarily make organised screening cost-effective. Most sensitivity and scenario analyses (i.e. scenarios with alternative assumptions run deterministically) suggest that screening would be less cost-effective than predicted in the base case. In addition, improved calibration would likely also further reduce cost-effectiveness. These considerations underpin the report's conclusion that current uncertainties are too substantial to conclude confidently that screening is cost-effective for the general population, familial risk groups, or black men, and motivate the modellers' plan to recalibrate the model using additional data, when these become available.

There is very little data available on the current landscape of opportunistic PSA testing in the UK. With respect to the Collins et al. (2025) study cited by stakeholders (doi: https://doi.org/10.1136/bmj-2024-083800), the modellers approached the authors and clarified with them that the focus of the paper is on PSA retesting and does not specifically examine or report opportunistic PSA screening. Moreover, the Collins et al publication does not estimate the probability of opportunistic testing, nor does it analyse factors associated with opportunistic testing. The probability of repeat PSA testing should therefore not be interpreted as an opportunistic screening uptake. The authors of the paper also noted that they are continuing to work with the data and may be able to derive or approximate estimates of opportunistic testing uptake that could be suitable for use in the model in the future.

Sensitivity analyses and additional scenarios

Theme:
A point was raised that multiple sensitivity analyses all confirm the base case findings rather than challenging them, suggesting some form of predetermined conclusion whereby the model confirms a hypothesis rather than testing it. Another criticism raised was that the deterministic sensitivity analysis shows greater benefit than the probabilistic analysis and this discrepancy is unexplained. Stakeholders identified a number of additional scenarios they suggested should be modelled to explore the impact of the model parameters and assumptions.

Response:
The SCHARR prostate cancer model estimates the long-term health outcomes and costs associated with different screening approaches. The model does this in two ways. In the deterministic analysis, the model uses a single "best estimate" for each input, such as the average value reported in published studies. For aspects of prostate cancer that cannot be directly observed (for example, how fast the disease progresses), the model uses the single set of values that best matches observed population data. In the probabilistic analysis, the model reflects uncertainty by allowing many of these inputs to vary. Instead of using just one value, the model repeatedly samples from a range of plausible values, giving more weight to values

that better match real-world data. This means the probabilistic analysis shows both the expected results and how uncertain those results are.

It is very common in health economic modelling that deterministic results demonstrate higher benefits than probabilistic results. It is even more common in natural history disease models, where high uncertainty exists about cancer onset and progression. Since deterministic models do not incorporate uncertainty, they are useful to explore the general trends and compare different scenarios. However, because uncertainty in prostate cancer progression and detection is substantial, the probabilistic results provide a more realistic picture and are therefore the main basis for the study's conclusions.

In relation to the point on the 'predetermined conclusion' of the sensitivity analyses, the fact that change in each parameter results in changing the net monetary benefit (NMB) in the same direction demonstrates that selecting alternative assumptions would not affect the conclusions of the study and not that there is a predetermined conclusion. Most scenarios selected to be tested were suggested as the most plausible alternatives to the base case. Based on basic modelling principles, one would expect that parameter change will result in a similar effect size though the magnitude of the impact may vary based on individual characteristics. This is exactly what is observed in the SCHARR model. This should not be confused with stress-testing – when the model is run with extreme or worst-case inputs to see how it behaves – in such cases one indeed would expect changes in cost-effectiveness outcomes. Health economic research does not require a null hypothesis to be tested and as such, the model cannot confirm or reject any hypothesis.

SCHARR analysed several scenarios in the model report. These scenarios were run for each modelled group across single and repeat screening strategies, leading to a high number of individual scenarios being modelled. During the public consultation, the UK NSC and SCHARR engaged with Prostate Cancer Research (PCR) and the York Health Economics Consortium (YHEC) to run 4 additional scenarios, based on parameters suggested by PCR and YHEC.

Many of the scenarios suggested by stakeholders were exploratory in nature and intended to model potential future practice, rather than current practice. In the absence of data, these scenarios would rely heavily on assumptions, resulting in significant uncertainty. While exploratory scenarios are valuable for testing the sensitivity of the model to changes in its underlying assumptions and investigating a wider range of screening options than current data allows, these scenarios are unlikely to influence a final recommendation on screening.

In the updated version of the model, SCHARR have run additional scenarios informed by expert stakeholder dialogue. These additional scenarios are described in detail in section 11 of the updated model report. The model will continue to be updated as new evidence emerges.

Reporting clarity

The modellers made a number of adjustments throughout the model report to improve reporting clarity.

Annex A: List of Organisations Contacted

1. Cancer Black Care
2. Cancer Research & Genetics UK
3. Cancer Research UK
4. CHAPS
5. Chestnut Appeal
6. Macmillan
7. Northern Ireland Cancer Network
8. Orchid
9. Primary Care Urology Society
10. Prostate Cancer Research
11. Prostate Cancer UK
12. Prostate Scotland
13. Royal College of General Practitioners
14. Royal College of Nursing
15. Royal College of Pathologists
16. Royal College of Physicians
17. Royal College of Physicians and Surgeons of Glasgow
18. Royal College of Physicians of Edinburgh
19. Royal College of Radiologists
20. Royal College of Surgeons
21. Royal College of Surgeons of Edinburgh
22. Society of Radiographers
23. Tackle Prostate Cancer
24. Tenovus

25. The British Association for Cancer Research
26. The British Association of Urological Surgeons
27. Yorkshire Cancer Research
28. Stakeholder organisation who asked not to be identified
29. Stakeholder organisation who asked not to be identified
30. Stakeholder organisation who asked not to be identified

Annex B: List of stakeholder organisations who responded to the consultation

Service providers/ professional bodies

1. Association of Director of Public Health
2. British Association of Black Surgeons
3. British Association of Urological Surgeons
4. NHS Race & Health Observatory
5. Royal College of General Practitioners
6. Royal College of Nursing
7. Staffordshire Moorlands District Council
8. Sutton Coldfield Group Practice
9. The Royal College of Pathologists
10. UK Cancer Genetics Group

Charities/ patient groups

1. Black Equity Organisation
2. Black Prostate Cancer Network
3. Cancer Black Care
4. Cancer Research UK
5. CancerHelp (Preston) Ltd
6. Caribbean & African Health Network
7. CHAPS
8. Cotswolds Prostate Cancer Support Group
9. Friends & Bredrins Prostate Cancer Support Charity
10. Furness Prostate Cancer Support Group
11. Healthwatch England

12. Healthwatch Worcestershire
13. Houston Kiltmakers
14. Labour Men and Boys Steering Group
15. Norfolk & Waveney Prostate cancer support group
16. Prostate Cancer Research
17. Prostate Cancer UK
18. Prostate Cancer Victims
19. Prostate Scotland
20. United Against prostate Cancer
21. Yorkshire Cancer Research
22. One additional stakeholder organisation who asked not to be identified

Industry

1. A3p Biomedical
2. Antegenes Ltd.
3. Bayer PLC
4. Beckman Coulter
5. Jnetics
6. Johnson & Johnson Innovative Medicine
7. Pathaway Services Limited