UK National Screening Committee

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Prostate Cancer Screening Economic Model: Accompanying Narrative

FINAL (26 March 2026)

1. Purpose

This document provides a high-level summary of the purpose, methods and conclusions of the model used to generate a measure of the benefits, harms and costs (the 'economic' model) of various strategies for offering prostate cancer screening in the United Kingdom (UK). The economic model was developed by the Sheffield Centre for Health and Related Research (SCHARR). The aim of the work was to assess whether a national screening programme for prostate cancer (either for all men or for targeted groups) would do more good than harm and at reasonable cost, compared to current care.

2. Context

2.1. What is prostate cancer?

The prostate is a gland of the male reproductive system, located below the bladder, in which cancerous cells can develop. The gland normally produces a protein called prostate-specific antigen (PSA) that can be measured using a blood test. If the level of PSA in the blood is high this might indicate prostate cancer but if can be raised for other reasons too. Next investigations for prostate cancer would typically be scans and biopsies of the prostate.

In the UK, prostate cancer is the most common type of cancer in men, accounting for just over a quarter (28%) of all new male cancer diagnoses – about 55,000 new cases each year[1]. It is also the second most common cause of cancer death in UK males, after lung cancer. Despite this, survival from prostate cancer is high: nearly 8-in-10 people (78.9%[2]) diagnosed with prostate cancer survive for 10 or more years after their diagnosis and it is extremely rare for younger men (aged 45 and under) to die from prostate cancer. While the majority (76%) of prostate cancer deaths occur in older men (aged 75 and above[3]), many men will die with the disease rather than from it – meaning that their death was caused by a different health issue and not prostate cancer itself. One reason for this is that many diagnosed prostate cancers are very slow-growing and so do not significantly shorten someone's lifespan.

Some people are more likely to get prostate cancer than others. Prostate cancer typically affects older men: more than half of all prostate cancer cases are diagnosed in men aged 70 and older [4]. It is also more common in men of Black ethnicity compared to other ethnicities with some studies suggesting that Black men having a 1 in 4 lifetime risk of having prostate

[1] https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer
[2] Ibid
[3] Ibid
[4] https://cks.nice.org.uk/topics/prostate-cancer/background-information/prevalence/

cancer compared to 1 in 8 for White men [5]. People are also at higher risk of prostate cancer if they have a close relative who has had the disease due to shared familial risk factors. Genetic familial factors include variations in the BRCA genes.

In the absence of a national screening programme, investigations for prostate cancer happen either when a man presents to a clinician with symptoms that may indicate cancer or other suspected prostate issues, or when a man (mainly over the age of 50) without symptoms requests a PSA test from their GP. Information is available to guide men and their GPs when considering whether to have the test.

The number of men diagnosed with prostate cancer has increased over the past 10 years. This may be due to an ageing population and more people having PSA tests.

2.2. Why is there no screening programme for prostate cancer?

The UK National Screening Committee (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. Screening can do harm, as well as good (benefit), and someone can experience both the harms and benefits of screening at the same time. For example, a man might live because his prostate cancer is detected and treated, but also live with the serious side effects of treatment.

The aim of prostate cancer screening would be to detect prostate cancer early to prevent death and reduce suffering from the disease. For men with aggressive and/or advanced prostate cancer, early intervention and treatment can allow them to live longer by preventing prostate cancer death and reduces their chances of serious complications such as prostate cancer spreading to other parts of the body. Prostate cancer can spread to the area just outside the prostate (locally advanced or locally invasive cancer) and cause symptoms such as erectile dysfunction, difficulties emptying the bladder, and pain. It can also spread farther (metastatic cancer), most commonly to the bones and spine, where it can cause severe pain, fractures, or spinal cord compression. Just over 1-in-10 (12%) men in England have metastatic prostate cancer at the time of their diagnosis.[6] These are important, serious outcomes that screening would try to prevent.

There are also several harms associated with screening. These arise from the additional tests that men go through to get a prostate cancer diagnosis (including a biopsy of the prostate) and the treatment they may then receive. Harms can arise as early as 2 weeks

[5] https://www.gov.uk/government/publications/prostate-specific-antigen-testing-explanation-and-implementation/advising-well-men-about-the-psa-test-for-prostate-cancer-information-for-gps
[6] https://www.natcan.org.uk/reports/npca-state-of-the-nation-report-2025/

after beginning treatment [7], and can persist for a very long time (6 years or more, or possibly a lifetime)[8]. For example, after just 6 months:[9]

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

The majority of men (c.80%[10]) whose prostate cancers are identified through screening have cancers that would not be life-threatening and could be left alone without getting worse or affecting their lives. These men will therefore receive treatment they do not need and the harms of screening will quickly outweigh any benefit. For more information on how the benefits and harms of prostate cancer screening were considered within the prostate cancer screening model, see Sections 3.3, 4.4 and 4.7.

When the UK NSC last considered prostate cancer screening in 2020, based on the most up-to-date evidence available at that time, it determined that the potential benefits of prostate cancer screening did not outweigh the potential harms. Therefore, it did not recommend whole-population screening.

2.3. The reasons for reviewing prostate screening again

The UK NSC had previously only examined the evidence on prostate cancer screening across the whole eligible population: all men aged 50 to 74, regardless of their risk. The recommendation on whole-population screening requires reviewing as part of the UK NSC's regular update process. However, there are additional reasons why a review is needed now.

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[7] https://www.cancerresearchuk.org/about-cancer/prostate-cancer/treatment/radiotherapy/external-radiotherapy/side-effects-external-radiotherapy
[8] https://www.cancerresearchuk.org/about-cancer/prostate-cancer/treatment/surgery/problems-after-prostate-surgery
[9] https://www.nice.org.uk/guidance/ng131/chapter/Recommendations#assessment-and-diagnosis
[10] Expert-derived summary statistic, based on the Göteborg II Screening Study, CAP Screening Trial, and CAESAR studies.

In 2020, the UK NSC acknowledged that the evidence around this condition was rapidly evolving and that alternative approaches (such as targeted or risk-stratified screening) may be more beneficial than a whole-population approach. Since the 2020 review, there have been several changes – both to the remit of the UK NSC and the evidence base – which support a new review of prostate cancer screening.

The remit of the UK NSC was officially expanded to include targeted and risk-stratified screening in 2022. The committee has since received multiple submissions through its open call for screening topics asking the UK NSC to look again at prostate cancer screening, with a focus on targeted screening by age, ethnicity, family history and/or genetic risk. The open call for screening topics is an opportunity for stakeholders and members of the public to either suggest new screening programmes or highlight new evidence that might mean an existing recommendation should be reviewed earlier.

Updated data from 2 large, long-term studies were also published:

The UK Cluster Randomised Trial of PSA Testing for Prostate Cancer (CAP Trial)[11]:

- Initial findings reported that a one-off PSA test to men regardless of their risk was associated with a small reduction in mortality after 10 years: out of every 1,000 men invited for a PSA test, one less man died from prostate cancer than would have without a screening programme. But, even with only a one-off screen, men were still at a very high risk of being overdiagnosed and overtreated for prostate cancer.
- A second analysis of the CAP data was published in 2024[12]. This study reported that the risk of death 15 years after the PSA test was reduced by only 0.09% compared to men who were not invited to have a PSA test. This UK study highlighted that a one-off PSA test to screen for prostate cancer had a small effect on mortality from prostate cancer and no effect on overall survival. Yet, the harms from treatments (see above) were apparent in men at the 15-year follow-up.

The European Randomised Study of Screening for Prostate Cancer (ERSPC):

- In 2019, ERSPC published the results of its trial of prostate cancer screening offering PSA tests and following people up for 16 years[13] to look at their longer-term outcomes. This study found that repeat screening using PSA testing could reduce prostate cancer mortality and that the reduction in mortality increased over time, but this reduction in mortality was still small: screening reduced death by only 0.18%. There were also many cases of overdiagnosis (detecting and treating cancer that would not go on to cause harm) even over a longer follow-up period, meaning people were exposed to tests and treatment they did not need.
- In October 2025, the ERSPC published the results of follow-up at 23 years[14]. The study found that prostate cancer screening reduced deaths by 0.22% in absolute terms among men who were screened compared to those who were not. This means

[11] https://pubmed.ncbi.nlm.nih.gov/29509864/
[12] https://jamanetwork.com/journals/jama/fullarticle/2817322
[13] https://pubmed.ncbi.nlm.nih.gov/30824296/
[14] https://www.nejm.org/doi/full/10.1056/NEJMoa2503223

that prostate cancer screening using PSA testing can prevent about one prostate cancer death for every 456 men invited for screening over a period of 20-plus years, demonstrating a small benefit. Yet the harms associated with the screening offer would remain high as screening increased the number of men diagnosed with prostate cancer by about 30%, Of these, about half are likely to be overdiagnosis which would then lead to overtreatment. These updates were published after the SCHARR economic model was developed. The model predictions were compared with these 23 years of follow-up results and were almost identical in the number of overdiagnoses and the reduction in mortality.

Another factor prompting the need for an updated review is advancements in the tests and tools used in the pathway to diagnose prostate cancer which might be able to better identify which cancers need treatment. For example, more research has been published on whether MRI (magnetic resonance imaging) scans can better determine which men with an abnormal PSA test should be offered a targeted biopsy. Other studies investigated the best way to carry out biopsies using different approaches that are less invasive.

3. Using modelling for prostate cancer screening

3.1. Why we use modelling

The UK NSC makes its recommendations based on the best available evidence from high quality, peer-reviewed research. At times, however, a specific screening and treatment pathway relevant to the UK may not have been studied elsewhere or it is not practical to test such a scenario through research.

In such cases, economic modelling[15] can help to predict the impact a new screening programme may have on people being screened and assess the potential harms as well as benefits and costs.

Economic modelling brings together all the relevant evidence about a proposed screening pathway including:

- the uptake of the screening test
- how many people may screen positive or negative
- the additional tests and treatment they will have as a result of a positive screening result
- the longer-term health and wellbeing benefits and harms

These data points are then connected to estimate the overall balance of benefit and harm compared with costs in a standardised way. This allows for the screening pathway to be compared against what's being done now (the status quo – or usual care), or against different approaches to screening to identify which strategy the UK NSC should recommend.

[15] https://www.gov.uk/government/publications/uk-nsc-disease-clinical-effectiveness-and-cost-effectiveness-modelling

3.2. Building the economic model for prostate cancer screening

The economic model for prostate cancer screening was developed by specialist modellers, who drew on input from clinicians, technical experts, patient and public voice representatives, and a large body of published scientific evidence and official data. This collaborative process ensured the model reflected real-world clinical practice, was informed by different perspectives, and that the assumptions made were reasonable and practical. The economic model was also checked against data from the CAP Trial and ERSPC.

The final model centred around the natural history of prostate cancer – meaning how the disease develops over time – and the expectation that certain risk factors influence prostate cancer onset. The modellers simulated dozens of different prostate cancer screening pathways, involving different groups of people invited at different ages and at different frequencies, to see what the benefits and harms would be.

For example, the model simulated all men being invited for a one-off PSA test at age 50 years and then estimated:

- how many would take up the test and end up with a positive result
- how many would go on to have an MRI scan and then a biopsy
- how many would be reassured by the results of that biopsy that they do not have cancer
- how many would have to undergo additional PSA tests or require follow-up (such as surgery or radiotherapy)

Data were added to each step of the pathway, from published, peer-reviewed research or from national databases. This included data on personal characteristics such as age, ethnicity, family history; and data on prostate cancer such as how many cancers are diagnosed each year and at what stage, how many people typically require a biopsy after a PSA test and how many of these people go on to have prostate cancer, among others. Where data were not certain, the modellers evaluated conclusions with different modelling assumptions when opinions of experts varied. The model then estimated how many men may be helped by screening, for example through the earlier detection of prostate cancer and prevention of prostate cancer death. The model also estimated how many men may be harmed by the tests and treatment they receive.

All these possible screening pathways were then compared against what happens now in practice (usual care) to see what difference screening would make.

The SCHARR economic model looked at screening in all men (regardless of their risk level) and targeted screening in Black men, men with a known *BRCA1* and/or *BRCA2* (*BRCA1/2*) pathogenic variant, and men with a family history of prostate, breast or ovarian cancer as was requested by submissions to the UK NSC via its open call.

3.3. How the economic model helps us understand whether or not to offer prostate cancer screening

All screening programmes cause both good and harm. The UK NSC will only recommend a screening programme when it is confident that screening will do more good than harm, at reasonable cost. The prostate cancer screening model can help to understand if this is the case, for whole-population screening and screening in specific target groups at higher risk.

Some of the key concerns with screening include the impact of when:

- the disease is present, but the screening test misses it (false negatives)
- the screening test incorrectly identifies the person as having the disease (false positives)
- true disease is identified by screening, but it would not have gone on to cause the person any harm (overdiagnosis)

Men in the second and third of these scenarios will receive further tests and possibly treatment that they do not need. We know from large studies that a large number of men will have cancer diagnosed, follow-up, and treatment for disease that would never have affected them in their lifetime (overdiagnosis).

It is helpful to understand their experience and likely outcomes, to determine whether the benefit they get from screening outweighs any potential harms. For example:

1. A man is screened for prostate cancer and this detects a severe disease earlier than if screening had not been available. He goes on to receive radical (surgery or radiotherapy) treatment that cures his cancer. He experiences some side effects from this treatment (see Sections 4.4 and 4.7 below) but his death from prostate cancer is prevented and, as a result, he lives a longer life. In this scenario, the benefits of screening outweigh the harms.
2. A man is screened for prostate cancer and this detects less severe disease, which may never have caused him harm. He is moved onto a pathway of ‘active surveillance’, meaning he receives regular PSA tests and feels anxious about having cancer but not receiving any treatment. Eventually he may opt for radical treatment like surgery or radiotherapy and experience the side effects of these treatments. His life may have been extended by curing his prostate cancer, but he died of a heart attack in his later years. In this scenario, the balance between benefit and harm is less clear.
3. A man is screened for prostate cancer and he is found to have a high PSA level. He undergoes further tests (an MRI and a biopsy) and is later found not to have prostate cancer – his elevated PSA had been due to something else (a false positive result). He also experiences the side effects of his biopsy and was very anxious while waiting for further tests, but his life is not extended due to screening. In this scenario, he did

not experience any benefit from screening but did experience harms. An estimated 72% of people with a raised PSA level will experience this false positive scenario[16].

The prostate model helps to predict the number of men who will fall into these different scenarios, based on who is invited for screening, to understand the balance of benefit and harm of a prostate cancer screening programme.

4. Key inputs (data) into the model

It is important to understand what data went into building a model when interpreting the predictions a model makes. Limitations and uncertainties in the model inputs and assumptions can affect how confident we can be of its outputs.

4.1. Ages screened

In considering at what ages men should be invited for screening, the model drew data from a large representative population survey – the Health Survey England (HSE) – and created a population of men who were evaluated starting from an age when the model assumed that no men had cancer (20 years) until maximum life expectancy (age 100 years).

The model looked at several ages to start screening (age 50 and up for the general population and age 45 and up for target groups) to understand at which age it would be most cost-effective to screen for prostate cancer. It modelled both one-off PSA screening and repeat screening (that is, screening several times). It also modelled a third approach where the time between screening tests (the screening interval) was determined by the initial PSA level.

4.2. The screening test

4.2.1. Prostate specific antigen (PSA) tests

A screening programme starts with an invitation to screen and the offer of a screening test. In this model, the screening test used was the PSA test. This test measures the amount of PSA in someone's blood. It is normal to have some PSA in the blood, and levels tend to rise naturally with age, but a higher-than-expected level for someone's age may suggest prostate cancer. However, PSA can also be raised for other reasons, including benign (harmless) enlargement of the prostate, recent ejaculation, or a urine infection.

As a screening tool, PSA can detect prostate cancer earlier than symptoms would appear and, once a cancer has been diagnosed, it can help monitor cancer progression or recurrence. However, PSA is more commonly raised by benign enlargement of the gland.

Around three quarters (72%) of people with a raised PSA do not have prostate cancer (false positive results)[17]. Current guidelines suggest they should have further

[16] Expert-derived summary statistic, based on the Göteborg II Screening Study, CAP Screening Trial, and CAESAR studies.
[17] https://cks.nice.org.uk/topics/prostate-cancer/diagnosis/assessment/

investigations such as MRI scans or invasive prostate biopsy. In the men with benign causes for raised PSA these further investigations do not benefit them.

As many as 1-in-7 men (15%)[18] with prostate cancer may have a PSA test result that is considered 'normal' (false negative results) – so screening using a PSA test would miss these men entirely.

PSA tests are also not very good at telling the difference between harmless, low risk prostate cancers and aggressive cancers that need treatment. This means that some men who are found to have prostate cancer will undergo further tests and treatment that they do not need (overdiagnosis and overtreatment) and may develop severe, life-long side effects such as incontinence or erectile dysfunction.

Despite the PSA test having limitations, it remains the only screening test for which significant evidence has been collected.

In the model, the amount of PSA in the blood across the population was drawn from data from a UK screening trial (the PCPT Trial). Though these data are more than ten years old, it is one of the few UK trials that reported how accurate the PSA test is based on data from asymptomatic and otherwise healthy populations.

PSA values were modelled to increase by age in both non-cancer and cancer populations.

4.2.2. Uptake of the PSA test

Not everyone who is eligible for prostate cancer screening will accept their invitation to have a screening test. The model assumed the base case – or benchmark – uptake of prostate cancer screening to be 36%, based on data from the UK CAP Trial.

4.3. The usual care scenario

The modelled screening strategies were compared against 'usual care' – in other words, what testing and treatment is happening now in practice, without a national screening programme. Each of the screening strategies was compared to the usual care scenario to help estimate the possible benefits, harms, and costs of offering prostate cancer screening to these groups.

In the model, usual care was assumed to include a mix of:

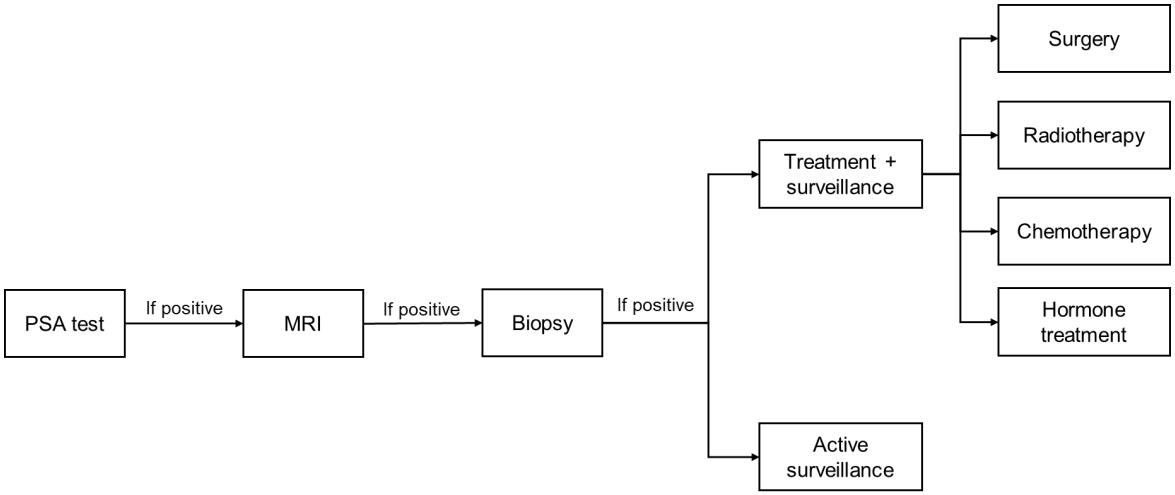
- symptomatic presentation: where men present at their GP with symptoms of prostate cancer or other diseases and are then offered a PSA test
- PSA testing via request to their GP: where some men may have a PSA test carried out as part of their routine care or where testing is offered based on individual concern but is not systematically offered to all men

[18] Ibid

Current PSA testing practice is an area of high uncertainty within the model. There was no simple way of knowing from the data whether a PSA test had been done because of a patient's request for one, a GP's concern about a patient's symptoms, as part of post-cancer treatment follow-up, or active surveillance of people with known (low risk) prostate cancer. Because of this, the model could only create one "current care" scenario. This means that the model cannot distinguish between those men who were diagnosed through a request to their GP and those who had symptoms, modelling them as one group. Due to the uncertainty around how much PSA testing of asymptomatic men is happening in current practice, it is difficult to clearly understand what and how much change to PSA testing practice the different screening pathways would have, and therefore the impacts on health and cost.

4.4. The diagnosis and treatment pathway

Screening is only the first stage of a screening programme and is followed by additional tests, scans and biopsies of the prostate and then either treatment for people who are found to have the disease or active surveillance, depending on the severity of the disease. The treatment pathway was modelled to be the same under usual care and in each screening strategy. The screening programme pathway deliberately included the current guidance. It did involve a PSA test, followed by an MRI scan and, if required, a biopsy before a diagnosis. More detail on the pathway is shown below:



After the PSA test, people who screen positive are offered multiparametric magnetic resonance imaging (mp-MRI) before their biopsy. The updated analysis included a proportion of the MRIs as bi parametric MRI. It was assumed that the uptake of the tests within the diagnosis pathway would be higher than the screening test, because people are more likely to take up further testing when they think it will directly benefit them. The uptake of the mp or bp-MRI was assumed to be 100% and 85% for biopsy, drawn from CAP trial data:

The type of biopsy modelled was a local anaesthetic transperineal prostate biopsy, or LATP biopsy, because this is now the more common technique. If the biopsy then identified someone as having prostate cancer, they will either:

- receive immediate treatment, and move onto a 'surveillance' pathway, with a follow-up PSA test every 6 months for the first 2 years after treatment, and then at least once a year after that; or
- not receive immediate treatment but instead fall under 'active surveillance,' (or watchful waiting) where they will receive:
    - in the first 12-18 months: a PSA test every 3 to 4 months in the first-year post-diagnosis, a digital rectal examination (DRE) at 12 months, and an mp/bp-MRI at 12 to 18 months; then
    - from 2 years on: a PSA every 6 months and DRE every 12 months.

The treatments for prostate cancer included in the model were surgery, radiotherapy, chemotherapy, and hormone treatment. Each of these treatments has some associated risks[19].

For example, hormone therapy is associated with lifelong physical and social harms such as erectile dysfunction, mood changes, osteoporosis, diabetes and heart disease. Surgery (radical prostatectomy) reports common side effects like blood clots, infection and a much higher risk of urinary incontinence following this treatment. Radiotherapy may lead to a higher risk of bowel incontinence as well as erectile problems particularly in the first 6 months, while chemotherapy can lead to hair loss, mouth sores, and possible nerve damage[20]. Those who do not receive treatment but who are under active surveillance may feel anxious about the presence of cancer that is not being treated.

For people with aggressive prostate cancer, these risks are more likely to be outweighed by the benefit of reducing the risk of death or cancer spreading. However, for people whose prostate cancer would not have progressed to severe disease, the treatments may have caused more harm than good.

It should be noted that the modelled screening pathway did not include the Stockholm3 test. Stockholm3 has been proposed as a second-line test, after PSA, to better identify patients who would benefit from an MRI. However, the data required to build use of Stockholm3 into the model was not publicly available at the time and there were concerns around the quality and suitability of the data. For these reasons, it was agreed that Stockholm3 data should be excluded.

4.5. Risk of cancer diagnosis and progression

One of the key concerns relating to prostate cancer screening is that there is limited evidence of how prostate cancer progresses over time, including which cancers will progress more quickly than others to cause serious disease.

The model on which the UK NSC consulted assumed that factors such as age, ethnicity, and *BRCA1 and BRCA 2* status influence not only the age at which someone is likely to get cancer (cancer onset), but also how quickly that cancer develops (cancer progression, or the

[19] https://www.cancerresearchuk.org/about-cancer/prostate-cancer/treatment
[20] https://nejm.org/doi/full/10.1056/NEJMoa2214122

stage of the cancer). During the consultation period, different published data was provided that suggested that men with *BRCA1* variants were *not* at higher risk of getting prostate cancer so this information was incorporated in updated analyses run by the model. Having a first-degree family member with either prostate, or breast, or ovarian cancers impacts one's chance of getting prostate cancer over lifetime. In addition, evidence was also provided that men with *BRCA2* variants ascertained through a strong family history of cancer have higher risks than men ascertained through a general population approach (for example biobanks).

The other measure considered was the aggressiveness of cancer. The level of aggressiveness of a cancer was defined in the model by grade. For prostate cancer, grades are categorised into groups called Gleason Grade Groups (GGG), where a higher grade (GGG 4-5) indicates a more aggressive and possibly faster growing cancer, while a lower grade (GGG 1-2) suggests the cancer may be slow growing. However, the GGG is not perfectly predictive: not all high GGG cancers will progress to severe disease and a number of men will receive radical treatments from which they will not benefit. Defining which cancers are clinically significant is challenging but important in order to balance the detection of harmful cancers against causing harm from overdiagnosis and overtreatment[21].

The GGG of prostate cancer when it is first diagnosed will vary between individuals and be influenced by certain factors such as age, ethnicity and genetic factors. This means that older men are likely to be diagnosed with a higher GGG. There is some limited evidence that men with a *BRCA1/2* variant have a higher GGG at diagnosis.

In the model, the distribution of GGG by age at diagnosis was based on national cancer registry data.

The model included a data point which suggested that people of Black ethnicity have a greater likelihood of being in a higher GGG (meaning a more aggressive cancer), based on data from the USA. There is, however, some evidence that socio-economic factors play an important role here rather than ethnicity per se. For example, Black men in the USA may present to healthcare later in their disease progression due to barriers to accessing privately-funded healthcare rather than any natural predisposition to more aggressive prostate cancer, and it is not known what difference a publicly funded healthcare system would make to the point of presentation in this context. This may mean that the model overestimates the aggressiveness of prostate cancer in Black men and therefore the benefit associated with screening in this group. As a result of expert stakeholder input the updated model assumed aggressiveness of prostate cancer in Black men was the same as other ethnicities.

People with *BRCA1 and BRCA2* variants were modelled to be more likely to have a higher GGG cancer at diagnosis based on published data, but it was assumed that this risk did not vary with age because there was no data to suggest the impact of age in these subgroups.

The model made a pragmatic assumption that cancers would progress sequentially from stage 1 through to stage 4. In reality, this may not always happen and cancers may regress and advance over time. It is also not known whether some cancers start as high grade.

[21] https://pubmed.ncbi.nlm.nih.gov/39288333

4.6. End point

The model takes data on all the inputs described above and uses these to predict the number of new prostate cancer cases that might arise and be detected (either through screening or by a clinician when symptoms develop), prostate cancer-related deaths, and non-cancer related deaths.

The end point within the model is death, either from prostate cancer or from any cause other than prostate cancer. An assumption was made that if someone was still alive 15 years after being diagnosed with prostate cancer, then they would not die from the disease. Using this assumption instead of extrapolating mortality over 70 years had only a small impact on cost-effectiveness. It is important to note that the assumption used does not mean that the model used a 15-year time horizon, as all benefits, harms, and costs of surveillance were modelled from first screening until death, which means that the model used a lifetime horizon.

4.7. Predicting the benefits and harms of screening

Prostate cancer screening can have a positive (benefit) or negative (harm) impact on the health of an individual. A person can experience both the positive and negative impacts of screening (or benefits and harms) at the same time.

For example, someone may have their 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 their 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.

For the men who are overdiagnosed, they do not live longer due to screening (because their prostate cancer would not have gone on to cause symptoms or harm) and they may still experience serious harms.

This nuance is why thinking about benefits and harms in relation to an overall measure of health is very important. The overall measure of health is made up of the number of years of life combined with the quality of health in those years.

4.7.1. Identifying screening benefits and harms

The benefits of screening captured by the model are detecting prostate cancer earlier (known as a ‘stage shift’) leading to a reduction in prostate cancer deaths. It does this by predicting the years of life saved through earlier cancer detection, diagnosis and treatment; improvements to health-related quality of life (especially if someone was living with severe disease); how many prostate cancers are diagnosed at early versus later stages; and the number of deaths from prostate cancer and other causes.

The harms of screening that the model captures are false positives (where a screening test incorrectly suggests cancer is present when it is not) and overdiagnosis (when a real cancer is found but it would never have caused harm over the person’s lifetime).

There are a whole range of harms, including the physical and emotional impact of cancer diagnosis and treatment-related side effects. Even if a man does live longer due to his

cancer being detected and treated, he may still experience lower health and a lower quality of life.

4.7.2. Measuring the benefits and harms

The positive and negative impacts – or the benefits and harms – of screening were linked to their impact on health by measuring the impact a harm or benefit has on the years and quality of life while living with the disease. This is called 'health-related quality of life'. These impacts were measured in the model using an indicator called EQ-5D. EQ-5D is a self-reported, standardised measure that describes impact of disease on health across five domains: mobility, self-care, usual activities, pain and anxiety.

A limitation to using EQ-5D is that the connection between these five domains and the benefits and harms we see in screening is not always obvious or explicit. But they are captured, for example:

- We know that advanced or metastatic prostate cancer can cause pain, fractures, or problems with the urinary tract and treating these can result in health benefits. The improvements to quality of life from the removal of the cancer will be included within EQ-5D.
- We know that a biopsy can cause an infection, be painful and make a man anxious. These effects will be included within EQ-5D.
- We know that more than half of men who initially start on an active surveillance pathway will move to having radical treatments (surgery or radiotherapy) over 15 years[22] – some of this is due to anxiety – and experience the associated benefits and harms. This will be included within EQ-5D.
- At six years after treatment, 36-50% men having radical treatments will have erectile problems, 5-13% will be incontinent of urine (unable to control their urine) and 2-4% will be incontinent of faeces (unable to control their bowels)[23]. These will be included within EQ-5D.

To describe the quality of life for people undergoing screening and treatment for prostate cancer, the model reduced the EQ-5D score (utility value) to reflect the negative impacts of testing and treatments.

The amount by which EQ-5D scores were reduced (known as utility decrements) following a diagnosis of prostate cancer was based on data from the 2024 NHS Cancer Quality of Life Survey. This survey asked people who were diagnosed with different stages of prostate cancer to complete EQ-5D surveys 18 months after they were diagnosed. For each disease stage at diagnosis, an average score was calculated and compared to the EQ-5D score of men of the same age but without cancer. This would include their experience of follow-up treatment and/or surveillance.

[22] https://www.nejm.org/doi/full/10.1056/NEJMoa2214122
[23] https://www.nice.org.uk/guidance/ng131/chapter/Recommendations

EQ-5D data were then used to calculate quality-adjusted life years (QALYs) in the economic model. QALYs are a common measure of someone's health. They are calculated by multiplying someone's health state (their EQ-5D score) by the length of time spent in that health state. A year spent in perfect health would be one QALY, a year spent in pain or with unpleasant physical or mental symptoms might be three quarters of a QALY. The amount of reduced quality of life is developed using information from actual people with these problems.

4.8. How did the model predict the cost of the screening programme?

The following elements of the screening programme were costed in the model:

- PSA test (including practice nurse consultation)
- Diagnostic costs
    - Mp/bpMRI
    - LATP biopsy (including histopathology)
- The cost of inviting people to have a PSA test, which was based on the invitation costs for bowel cancer screening and includes not only direct costs of invitations (for example, mail costs) but also costs of managing the programme (for example, someone sending the invitations, training, and indirect costs).
- Surveillance costs (including active surveillance) were calculated using the relevant diagnostic costs above, applied at the frequency of testing recommended by NICE (see Section 4.4) and based on the proportion of people who receive treatment at each cancer stage.
- Treatment costs were estimated based on the stage at diagnosis and four different treatment options: surgery, radiotherapy, chemotherapy, and hormone therapy.
- Palliative care costs were assigned in the year of death based on published data.

All costs were reported in pounds sterling for the year 2022/23. Costs were estimated based on published sources for specific items (unit costs). For example, unit costs for medicines came from the British National Formulary. Unit costs for other items such as diagnostic tests or surgical procedures came from sources such as NHS reference costs, NICE impact assessments, Prostate Cancer Audit Reports and from recent research studies.

4.9. How did the model measure cost-effectiveness?

The overall balance of benefits and harms (measured using QALYs to describe someone's overall health state) and costs to the healthcare system of each screening strategy in the model was calculated using a statistic called the incremental net monetary benefit (NMB). The incremental NMB is calculated by assigning a monetary value to the QALYs resulting from each screening strategy and subtracting the total health costs of that same screening

strategy. The QALYs gained from screening are valued using a willingness-to-pay (WTP) threshold: the maximum amount considered reasonable to pay for an improvement to health.

An incremental NMB of above £0 (so a positive NMB) means that the screening pathway would be considered to be comparable to current uses of health care money (cost-effective is a usual shorthand for this). An incremental NMB below £0 (a negative NMB) means that the pathway is more expensive than current accepted uses of health care budget.

The WTP threshold used in the model was £20,000. This is based on the typical threshold used for screening tests in the past. There is ongoing debate about what WTP threshold is most appropriate for screening programmes as they span public health and health care activities, which are not currently assessed against the same thresholds. In addition, because screening models make longer term predictions than treatment models, they are more uncertain, so traditionally lower decisions thresholds were used.

There are significant uncertainties in the data used to estimate the costs, harms and benefits (measured using EQ-5D and QALYs), and the incremental NMB for each screening strategy. For example, the evidence to support the model comes from large screening research studies carried out in the USA and in European countries which may not be applicable to the UK; and predicts a long way into the future. Some of the model inputs, such as how prostate cancer arises and progresses, were based on assumptions that were checked with experts but for which current data were not available. We need to understand if, and how, these uncertainties impact on the overall balance of benefits, harms, and costs. The NMB statistic makes it easier to observe the level of uncertainty – how confident we are in the results.

5. What did the model find for each of the screening strategies?

5.1. Whole population screening

Screening all men in the UK, regardless of their risk profile, may lead to a small reduction in the number of deaths from prostate cancer, but it would also result in substantial overdiagnosis, and this would increase with age. This means that many men would undergo treatment they do not need, due to screening identifying a cancer that would not have caused symptoms or death. For example, at age 60, the economic model predicted that half of the cases of screen-detected cases would be overdiagnosed. All the scenarios explored (one-off screening tests at different ages and repeat screening tests) resulted in substantial overdiagnosis. Other models conducted in other countries such as US and the Netherlands had similar predictions of overdiagnosis.

For whole-population screening for prostate cancer, regardless of age, this level of overdiagnosis means that screening may well do more harm than good. There was also significant uncertainty about the cost-effectiveness of screening.

5.2. Targeted screening for Black men

5.2.1. Definition of Black ethnicity

Ethnicity prevalence data were taken from the 2018 and 2019 Health Survey for England (HSE). Within the HSE, ethnic group is self-reported and recorded using categories from the 2011 Census, which have remained largely unchanged despite substantial demographic shifts and migration over the past two decades. In the model, “men of Black ethnicity” included men who identified as “African,” “Caribbean,” or “Any other Black, African or Caribbean background”. Epidemiological studies in the UK suggest that, on average, men in these Black ethnic groups have a higher incidence of prostate cancer than White men. Some published evidence suggests that certain South Asian and East Asian groups have lower rates of prostate cancer than White men, although findings are not uniform across all studies and groups.

In this report we refer to ethnic group rather than “race”, recognising that these categories are socially and historically constructed rather than biological, and that differences in prostate cancer outcomes are likely to be strongly shaped by structural and socioeconomic factors, access to care and other structural determinants as well as any underlying biological variation. A limitation of the HSE data is that all people reporting a mixed ethnic background are grouped into a single “any mixed” category. It is therefore not possible to identify which of these men are of mixed Black heritage, meaning they could not be included within the model’s Black target group. As a result, the model is unlikely to fully reflect the diversity or risk profile of people with more complex ethnic backgrounds. This, however, is not a limitation specific to HSE but to data in general with studies evaluating cancer risk in mixed ethnicity commonly grouping it as a single category. Additionally, the mixed ethnicity population in England is small. This means that the studies that would try to evaluate risk in these groups will struggle to have statistical power, unless they will purposefully try to engage people of a specific ethnic profile. Thus, not reflecting the diversity in ethnic profiles is a data and not a model limitation.

5.2.2. Modelling results

Screening men of Black ethnicity is likely to identify more cancers among people who are screened, compared to screening the whole population. It will likely also lead to a higher positive NMB, but there is a great deal of uncertainty about this. This means that, in some scenarios, the incremental NMB was positive and in others it was negative. This is largely because of the absence of evidence from the large trials about if and how prostate cancer progresses differently in Black men.

As with the other risk groups, many different screening strategies were explored, but because of lack of available data, there is a lot of uncertainty which means we do not know whether screening in black men would cause more good than harm.

5.3. Targeted screening for men with a known pathogenic *BRCA1 and BRCA 2* variants

This population includes any man with a known *BRCA*1 or 2 variant. The model, on which the UK NSC consulted, originally assessed the cost-effectiveness of screening in a combined group of men with a BRCA1 or BRCA2 variant. During the consultation, published

evidence became available that increased risk of cancer was limited to men with BRCA2 gene variants. However, these men in the general population are likely to have a lower risk than those with a family history, so the model used data on men who had been tested through family history clinics. The model suggested that these men would gain net benefit with regular PSA testing.

5.3.1. Definition of *BRCA2* gene carriers with a family history

This population includes any man with a known *BRCA2* variant ascertained through family history clinics and genetic services. The family history is usually of breast, ovarian and prostate cancer (sometimes also other cancers such as pancreatic cancer). "Cascade testing" usually follows initial identification in someone with cancer and a strong family history. The BRCA 2 genes are analysed in detail in this initial person and if one (of several thousand possible pathogenic variants) is found then testing is then offered for this particular variant in a cascade sequence within families. First degree relatives are tested first and then testing is offered to subsequent first degree relatives of anyone found to have the same variant.

The number of people with (prevalence) *BRCA2* gene mutations and a family history as above was taken from NHS England estimates.

5.4. Targeted screening for men with a relevant family history

5.4.1. Definition of a relevant family history

A family history was taken to mean any relative with breast, ovarian or prostate cancer. However, it is acknowledged that this term can include different levels of risk, for example men with more than one relative who has had cancer, or where these relatives had their cancer diagnosed at an early age.

This sub-group included about one-third of all men.

5.4.2. Modelling results

Similar to whole population screening, screening men with a relevant family history was predicted to result in many cancers being overdiagnosed and overtreated. The updated model examined screening in men with a family history of prostate cancer as a separate group from men with a family history of breast, ovarian and prostate cancer. Similarly to the original model results, screening did not do more good than harm at reasonable cost in men with a family history of prostate cancer, or in men with a family history of breast, ovarian and prostate cancer.

6. Next steps

6.1. The UK NSC will work with SCHARR to ensure that new evidence is reviewed for relevance, quality and, if sufficiently robust, added to the model.

The UK NSC is aware that there is more work to be done on:

- new tests that may be able to distinguish those cancers which will grow and spread from those which will grow slowly and not cause the man any symptoms. These so-called biomarkers hold out a hope that fewer men will need surgery and radiotherapy while preventing as many or more deaths
- risk of prostate cancer in men with high-risk familial history of prostate cancer (for example those who have two or more family member with cancer or those whose family member was diagnosed with cancer before age 60 years)
- the TRANSFORM trial which will be hugely important, particularly in understanding the effects of prostate cancer screening in Black men more clearly

6.2. The TRANSFORM Trial

The TRANSFORM Trial is a large, UK-based research study, jointly funded by the National Institute for Health and Care Research (NIHR) and Prostate Cancer UK. The study will compare multiple screening options – 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. The UK NSC has been in close communication with TRANSFORM to help ensure findings from the trial can address some of the uncertainties that remain in prostate cancer screening.

Importantly, TRANSFORM has been specifically designed to help tackle inequalities in prostate cancer research. It will ensure that at least 1-in-10 men invited to participate in the trial are of Black ethnicity, which will allow a better understanding of prostate cancer in this group of men, specific to a UK context.

The TRANSFORM trial began recruitment on 21 November and the UK NSC will continue to work closely with the trial team and as the research progresses.