

## UK National Screening Committee

### Prostate Cancer Screening Economic Model: Accompanying Narrative

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## 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 to potentially 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 see whether a national screening programme for prostate cancer (either for the whole population of 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 produces a protein called prostate-specific antigen (PSA) that can be measured using a blood test. This is the most common way to start testing for prostate cancer. If the level of PSA in the blood is high, the test is then typically followed by 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.<sup>1</sup> 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%<sup>2</sup>) 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

<sup>1</sup> <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer>

<sup>2</sup> Ibid

majority (76%) of prostate cancer deaths occur in older men (aged 75 and above<sup>3</sup>), 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. A reason why this happens is because 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.<sup>4</sup> It is also more common in men of Black ethnicity compared to White or Asian ethnicity, with Black men having a 1 in 4 lifetime risk of having prostate cancer compared to a 1 in 8 for White men.<sup>5</sup> People are also at higher risk of prostate cancer if they have a close relative who has had the disease and there are some genetic changes (variants or mutations in the BRCA genes) that have been associated with higher risk.

In the absence of a national screening programme, testing for prostate cancer occurs 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 ten 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. It is important to note that screening can do harm, as well as good (benefit). It is also possible for someone to experience both the harms and benefits of screening at the same time. For example, a man can live longer due to their prostate cancer being removed but also live with 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. It can also reduce the 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 diagnosed

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<sup>3</sup> Ibid

<sup>4</sup> <https://cks.nice.org.uk/topics/prostate-cancer/background-information/prevalence/>

<sup>5</sup> <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>

with prostate cancer in England have metastatic prostate cancer at the time of their diagnosis.<sup>6</sup> 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 after beginning treatment,<sup>7</sup> and can persist for a very long time (6 years or more, or possibly a lifetime).<sup>8</sup> For example, after just 6 months:<sup>9</sup>

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

The majority of men (c.80%<sup>10</sup>) whose prostate cancers are identified through screening would not benefit in terms of preventing prostate cancer deaths and metastasis. Many of these men will receive treatment they do not need and the harms of screening will quickly outweigh any benefits. The challenge is how to identify those men who have aggressive prostate cancer while minimising the risks of serious and long-lasting side effects for many other men. 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, it determined that the potential benefits of prostate cancer screening did not outweigh the potential harms, based on the most up-to-date evidence available at that time. Therefore, it did not recommend whole-population screening.

<sup>6</sup> <https://www.natcan.org.uk/reports/npcsa-state-of-the-nation-report-2025/>

<sup>7</sup> <https://www.cancerresearchuk.org/about-cancer/prostate-cancer/treatment/radiotherapy/external-radiotherapy/side-effects-external-radiotherapy>

<sup>8</sup> <https://www.cancerresearchuk.org/about-cancer/prostate-cancer/treatment/surgery/problems-after-prostate-surgery>

<sup>9</sup> <https://www.nice.org.uk/guidance/ng131/chapter/Recommendations#assessment-and-diagnosis>

<sup>10</sup> Expert-derived summary statistic, based on the Göteborg II Screening Study, CAP Screening Trial, and CAESAR studies.

### 2.3. The reasons for reviewing prostate screening again

The UK NSC had previously (in 2020) only examined the evidence on prostate cancer screening across the whole 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.

At the time of the 2020 review, 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 then, 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 topics process asking it 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 process is an opportunity for individuals or organisations to suggest new screening programmes, amendments to existing programmes, or highlight new evidence that might mean an existing recommendation should be reviewed earlier.

Data from 2 large, long-term studies have also been published since the previous UK NSC review:

#### *The UK Cluster Randomised Trial of PSA Testing for Prostate Cancer (CAP Trial)* <sup>11</sup>

- 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.<sup>12</sup> 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 testing and treatment were seen 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<sup>13</sup> 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%.

<sup>11</sup> <https://pubmed.ncbi.nlm.nih.gov/29509864/>

<sup>12</sup> <https://jamanetwork.com/journals/jama/fullarticle/2817322>

<sup>13</sup> <https://pubmed.ncbi.nlm.nih.gov/30824296/>

There were also many cases of overdiagnosis (detecting and treating cancer that would not have gone 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.<sup>14</sup> The study found that prostate cancer screening reduced deaths by 0.22% in absolute terms among men who were screened compared to those who were not. This means that prostate cancer screening using PSA testing can prevent about one prostate cancer death for every 456 men invited to screening over a 20+ years period, demonstrating a very small benefit. Yet the harms associated with the screening offer would remain high as screening increased the number of men diagnosed with prostate cancer by about 30% of which half are likely to be overdiagnosis which would then lead to overtreatment. The study estimated (at current follow up) that for every 1 prostate cancer death averted there are 12 men overdiagnosed who may have received unnecessary treatments and side effects, and many more men with cancer diagnosed at screening for whom screening does not extend their life. These data were published after the economic model was developed. However, the model predictions were compared with these 23 years of follow-up results and were almost identical in the number of overdiagnoses and the reduction in mortality.

Another factor prompting the need for an updated review was advances in 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<sup>15</sup> can help to predict the impact a new screening programme may have on people being screened. It assesses the potential harms as well as the potential benefits and costs.

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

- the uptake of the screening test

<sup>14</sup> <https://www.nejm.org/doi/full/10.1056/NEJMoa2503223>

<sup>15</sup> <https://www.gov.uk/government/publications/uk-nsc-disease-clinical-effectiveness-and-cost-effectiveness-modelling>

- 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 is being done now (the status quo – or usual care), or against different approaches to screening to identify which strategy the UK NSC should recommend.

### 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 ERSPP.

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 could then simulate 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 could simulate all men being invited for a one-off PSA test at age 50 years and then estimate how many would:

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

Evidence-based numbers are added to each step of the pathway, from published, peer-reviewed research or from national databases. This includes data, among others, on:

- personal characteristics such as age, ethnicity and family history
- 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

Where data were not certain, the modellers worked with experts to consider a reasonable higher or lower estimate to see whether and how the conclusions changed. 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 estimates how many men may be harmed by the tests and treatment they receive.

All these possible screening pathways are then compared against what's happening now in practice (usual care) to see what difference screening would make.

As requested by submissions to the UK NSC via its open call, the SCHARR economic model looked at:

- population screening in all men (regardless of their risk level)
- targeted screening in Black men
- targeted screening in men with a known BRCA1 and/or BRCA2 (BRCA1/2) gene mutation (or variant)
- targeted screening in men with a relevant family history

### **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 for 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 negative)
- the screening test incorrectly identifies the person as having the disease (false positive)
- 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 many 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 the different experiences and likely outcomes, to determine whether the benefit men 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 a less severe disease, which we do not know for certain would have ever 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 we do not know for certain and he ends up dying 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 to screening but did experience harms. An estimated 61-72% of people with a raised PSA level will experience this false positive scenario.<sup>16</sup>

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 it makes. Limitations and uncertainties in the model inputs and assumptions can affect how confident we can be of its outputs.

### 4.1. Screening age ranges

In considering at what age or ages men should be invited for screening, the model drew data from the Health Survey England (HSE) and created a population of men who started in the model at age of 20 (when the model assumed no men would have prostate cancer) until 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 regular screening (i.e., screening more than once). It also modelled a third approach where the time between screening tests (the screening interval) was based on 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 prostate specific antigen (PSA) test. This test measures the amount of PSA in someone's blood. While it is normal to have

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<sup>16</sup> Expert-derived summary statistic, based on the Göteborg II Screening Study, CAP Screening Trial, and CAESAR studies.

some PSA in the blood, having a higher level than would be expected based on age (because PSA levels tend to increase naturally as men get older) may suggest someone has prostate cancer. However, higher than expected levels of PSA can also be caused by benign (harmless) enlargement of the prostate, ejaculation, or a urine infection.

The PSA test is not a precise test to identify men with prostate cancer as part of a screening programme. The majority of prostate symptoms men experience tend to be related to benign enlargement of the gland rather than prostate cancer, unless the cancer has progressed to severe disease.

Around three quarters (72%) of people with a raised PSA do not have prostate cancer (false positive results).<sup>17</sup> However, current guidelines suggest they should have further tests. These are likely to include an MRI scan and an invasive prostate biopsy that they did not need, and they are likely to experience stress and anxiety at the idea of possibly having cancer.

As many as 1-in-7 men (15%)<sup>18</sup> with prostate cancer may have a PSA test result that is considered 'normal' (false negative results) – so screening using a PSA test would not identify these men.

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). These men may develop severe, life-long side effects such as incontinence or erectile dysfunction.

Despite the PSA test having limitations, it remains the test with the most evidence for use in prostate cancer screening.

In the model, the amount of PSA in the blood across the population was drawn from data from a US screening trial (the PCPT Trial). Though these data are more than ten years old, it is one of the few 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 necessarily accept their invitation to have a screening test. The model assumed the base case – or benchmark – uptake of prostate cancer screening to be 36%, based on data from the UK CAP Trial.

### **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

<sup>17</sup> <https://cks.nice.org.uk/topics/prostate-cancer/diagnosis/assessment/>

<sup>18</sup> Ibid

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:

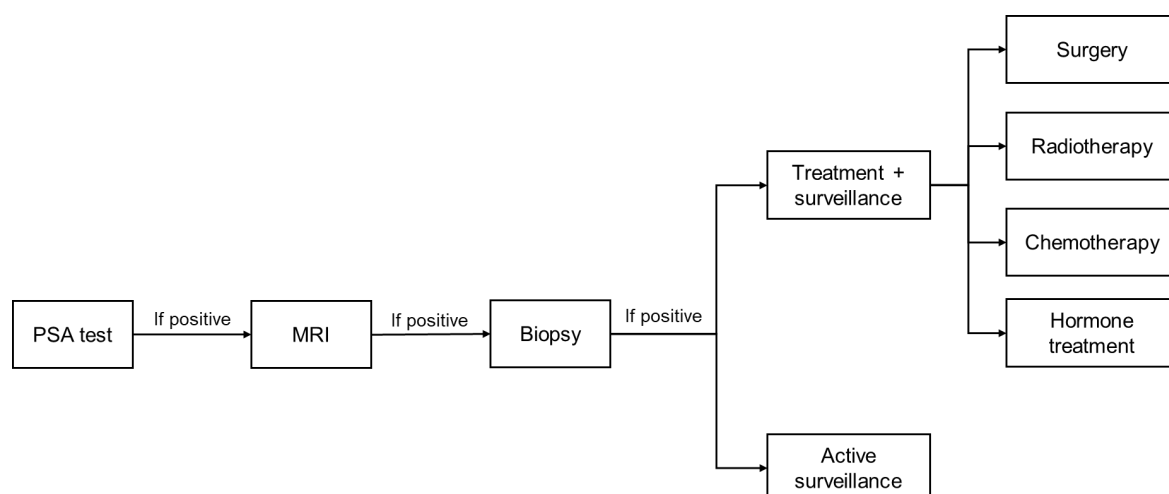
- Symptomatic presentation: where men present at their GP with symptoms that could indicate prostate cancer or other diseases and are then offered a PSA test.
- PSA testing via request to their GP: where some men may have a PSA test carried out as part of their routine care or are offered one based on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

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 the model cannot distinguish between those men who were tested 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 pathway from screening to treatment is illustrated here:



After the PSA test, people who screen positive are offered multiparametric magnetic resonance imaging (mp-MRI) before their biopsy. It was assumed that the uptake of the tests

within the diagnosis pathway would be higher than the screening test, because people are more likely to take up further testing when they think it will directly benefit them. The uptake of the mp-MRI was assumed to be the same as the uptake of the biopsy, drawn from CAP trial data: 85%.

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

- 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 would receive
  - In the first 12-18 months: a PSA test every 3-4 months in the first-year post-diagnosis, a digital rectal examination (DRE) at 12 months, and an mp-MRI at 12-18 months; then
  - From 2 years' on: a PSA every 6 months and DRE every 12 months.

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

Hormone therapy is associated with lifelong physical and emotional harms such as erectile dysfunction, mood changes, osteoporosis, diabetes and heart disease. Surgery (radical prostatectomy) reports common side effects like blood clots, infection and a much higher risk of urinary incontinence following this treatment. Radiotherapy may lead to a higher risk of bowel incontinence as well as erectile problems particularly in the first 6 months, while chemotherapy can lead to hair loss, mouth sores, and possible nerve damage.<sup>20</sup> Those who do not receive treatment but are under active surveillance may also feel distressed by the impression that they have an 'untreated' cancer.

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 cause 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.

<sup>19</sup> <https://www.cancerresearchuk.org/about-cancer/prostate-cancer/treatment>

<sup>20</sup> <https://nejm.org/doi/full/10.1056/NEJMoa2214122>

#### 4.5. Disease 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 assumed that factors such as age, Black ethnicity, and BRCA1/2 carrier 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 stage of the cancer).

The other measure considered was the aggressiveness of cancer. The level of aggressiveness of a cancer is referred to as its grade. For prostate cancer, grades are categorised into groups called Gleason Grade Groups (GGG), where a higher grade (GGG4 or GGG5) indicates a more aggressive and possibly faster growing cancer, while a lower grade (GGG1 or GGG2) suggests the cancer may be slow growing. However, the GGG is not perfectly predictive: not all high GGG cancers will necessarily progress to severe disease and some 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.<sup>21</sup>

The GGG of prostate cancer when it is first diagnosed will vary between individuals and be influenced by factors such as age, ethnicity and genetic factors. This means that older men are likely to be diagnosed with a higher GGG as well as people with a BRCA1/2 gene mutation.

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 uncertainty as to whether these data apply to a UK context. For example, men in the USA may present to healthcare later in their disease progression due to barriers to accessing privately-funded healthcare rather than any natural predisposition to more aggressive prostate cancer, so this trend may not be visible in the UK. This is an area of uncertainty and may mean the model overestimates the aggressiveness of prostate cancer in Black men and therefore the benefit associated with screening in this group. All other non-White ethnicities were assumed to have the same probability of a GGG as those from a white ethnicity.

People with BRCA1/2 gene variants are also modelled to be more likely to have a higher GGG cancer at diagnosis based on published reviews, but it was assumed that this increased risk did not vary with age.

The model made a pragmatic assumption that cancers would progress sequentially from stage 1 through to stage 4. In reality, this is not fully understood. For cancer grades, it is also

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<sup>21</sup> <https://pubmed.ncbi.nlm.nih.gov/39288333>

not known whether higher GGG cancers all start out as low GGG cancers or whether they are higher grade from the beginning. This is another source of uncertainty within the model.

#### **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 a lifetime (70 years) had only a small impact on cost-effectiveness.

#### **4.7. Predicting the benefits and harms of screening**

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 (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 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 (compared to 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 cancer is found but it would never have caused harm over the person's lifetime).

These may sound simplistic, but they include a whole range of harms, including the physical and emotional impact of cancer diagnosis and treatment-related side effects.

Even if a man lives longer due to his cancer being detected and treated, he may still experience poorer 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 of life lived and the health of those remaining years of life (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 health across 5 domains: mobility, self-care, usual activities, pain and anxiety.

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

- 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 onto having radical treatments (surgery or radiotherapy) over 15 years<sup>22</sup> – for some men, this is due to anxiety – and experience the associated benefits and harms. This will be included within EQ-5D.
- At 6 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 to 4% will be incontinent of faeces (unable to control their bowels).<sup>23</sup> 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.

<sup>22</sup> <https://www.nejm.org/doi/full/10.1056/NEJMoa2214122>

<sup>23</sup> <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-MRI
  - 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.
- 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 4 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 £0 or above (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 currently used by the National Institute for Health and Care Excellence (NICE) to determine the cost-effectiveness of tests or treatments. 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, screening models predict outcomes decades ahead. Diagnosis and treatment changes frequently so this is also an area where a WTP threshold is difficult to ascertain and compare.

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 the model describes older diagnostic and treatment pathways and needs to use the past to predict 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 compared to usual care. All scenarios explored (one-off screening tests at different ages and repeat screening tests) resulted in substantial overdiagnosis.

For whole-population screening for prostate cancer, regardless of age, this level of overdiagnosis means that screening is likely to 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, ethnicity is self-reported by participants and is recorded against categories from the 2011 census. In the model, men of Black ethnicity therefore included any men who identified as: 'African,' 'Caribbean,' or 'Any other Black, African or Caribbean background.' These men have a higher risk of prostate cancer. In contrast,

published evidence suggests that men of South Asian and East Asian ethnicity generally have lower rates of prostate cancer compared with White men.

A limitation to the data is that all people of mixed ethnicity were grouped together into a single category of 'any mixed race.' It was therefore not possible to identify which of those men were of mixed Black ethnicity, meaning these men were not included within this target group. Therefore, the model is unlikely to fully reflect the diversity or risk profile of this group.

### **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 what the benefits and harms are of screening Black men, and if and how prostate cancer progresses differently in Black men.

As with the other risk groups, many different screening strategies were explored. Screening Black men every 4 years between the ages of 50 and 62 had the lowest uncertainty about the benefit-to-harm balance. But it is still very uncertain.

## **5.3. Targeted screening for men with a known BRCA1/2 gene variant**

### **5.3.1. Definition of BRCA1/2 gene variant carriers**

This population includes any man with a known BRCA1 or BRCA2 gene variant. The model assessed the cost-effectiveness of screening in a combined group of BRCA1/2 carriers.

The number of people with (prevalence) BRCA1/2 gene mutations was taken from NHS England estimates and discussed with a geneticist.

Importantly, not all men with a BRCA1/2 gene mutation may know they have one. In the model, it was assumed that someone's knowledge of their BRCA status would increase by age. These data were estimated based on a study that looked at the uptake of genetic testing among apparently healthy relatives of people with confirmed BRCA mutations. However, there has been a rapid rise in genetic testing in recent years and the model is therefore likely to underestimate the current levels of BRCA awareness.

Another limitation of these data is that our understanding of genetic risk is limited by who participates in large genetic research studies. There is no reason to suspect that BRCA1/2 gene mutations are more likely to occur in people of one ethnicity compared to another. However, major genetic testing studies have been mostly of people of European ancestry and that has determined most of our understanding of these mutations.

There is also some evidence to suggest that the relationship between BRCA2 and prostate cancer might be stronger than for BRCA1. This will be explored further.

### **5.3.2. Modelling results**

The model is more conclusive about the balance of benefits and harms compared to cost of screening men with a known BRCA1/2 gene mutation. It is estimated that the offer to screen this group would result in less overdiagnosis compared with usual care. This is because men with BRCA1/2 mutations may develop more aggressive cancers and so the benefits to screen would outweigh the harms when compared to the general population or other risk groups. The most cost-effective strategy for screening men with a confirmed BRCA1/2 gene mutation is screening every 2 years, from age 45 to age 61.

It is important to note that the economic model did not consider the cost of BRCA gene testing within the costs of the overall targeted screening programme, whether screening is better targeted at one or both BRCA genes, or whether genetic testing to identify who has a BRCA gene mutation is cost-effective. A better understanding of a pathway to identify people with BRCA1/2 mutations will help to describe the possible challenges to implementing this screening strategy.

## **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 first-degree 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 men whose relatives had their cancer diagnosed at a younger than expected age.

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

### **5.4.2. Modelling results**

The balance of benefit and harm compared with costs of screening men with a familial risk was highly uncertain and similar to findings for whole-population screening, with about half (48-50%) of screen-detected cases at the age of 60 being overdiagnosed compared to usual care. Screening at a younger age did not appear more cost-effective (meaning that the incremental NMB was below 0).

## **6. Next steps**

### **6.1. Consultation**

The SCHARR model was developed to examine whether a national screening programme for prostate cancer for the whole population or specific target groups would do more good than harm at reasonable cost, compared to current care.

The model was developed with input from different experts through UK NSC workshops including clinicians, economists, and public representatives. Feedback from experts supported the modelling work but raised and emphasised outstanding concerns about data reliability, GGG score accuracy, and the need to better explain overdiagnosis risks. Experts also supported the UK NSC's engagement with the TRANSFORM trial (see below) to help address uncertainties highlighted by the model in order to help improve prostate cancer screening strategies.

On reviewing the model predictions for each screening strategy, the UK NSC was concerned with the high levels of harms and very significant uncertainty that remain in prostate cancer screening, including overdiagnosis, unnecessary testing and treatment, and the physical lifelong impact and psychological harms that may arise.

The findings of the model of whole-population screening for prostate cancer mean that this approach is not recommended. Using currently available tests, it is very unlikely to be cost-effective and it is not clear whether it would result in more good than harm.

Of the targeted screening strategies considered, the findings of the model suggest that screening for prostate cancer in men with known BRCA1/2 gene mutations is the approach most likely to do more good than harm. The UK NSC will consult on a draft recommendation for this screening strategy.

There is still too much uncertainty over the benefits and harms of a targeted screening programme for prostate cancer in Black men, so this screening strategy cannot be recommended. Further research is critical to help understand disease onset and progression (natural history), whether Black men are more likely to have more aggressive cancers than men of other ethnicities, and the long-term benefits and harms of screening in this group. The UK NSC is working closely with the TRANSFORM trial with a view to gathering more evidence on prostate cancer in Black men.

Additionally, there is still too much uncertainty over the harms and benefits of a targeted screening strategy for prostate cancer in men with a relevant family history. More data should become available over time – from the TRANSFORM trial and as prostate screening for men with a known BRCA1/2 gene mutation is explored.

Based on the current modelling data presented, the UK NSC will go out to public consultation on whether a targeted screening programme should be recommended for men with a confirmed BRCA gene mutation every 2 years, from age 45 to age 61.

## **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 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. 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.