May 2026

CANCER RESEARCH UK

Together we are beating cancer

Earlier detection and diagnosis of prostate cancer

A technical summary of the challenges and evidence

Contents

1. Foreword
2. Key points
3. Overdiagnosis and overtreatment are issues for prostate cancer
4. Symptoms aren't a clear indicator of prostate cancer
5. The limitations of Prostate-Specific Antigen
6. The current evidence on prostate cancer screening
7. Evolving diagnostic pathways - pre-biopsy prostate MRI
8. Developments in treatment for low-grade prostate cancer
9. Targeting screening at 'high risk' populations
10. Overview of research and innovation in the pipeline
    a. Screening
    b. Genetics and men considered "high risk"
    c. Diagnostics
    d. Treatment
11. Summary
12. Appendix
13. References

1. Foreword

Prostate cancer is the most common cancer in men in the UK. The early detection and diagnosis of prostate cancer is a topic that is actively debated amongst researchers, clinicians, policymakers and the wider cancer community.

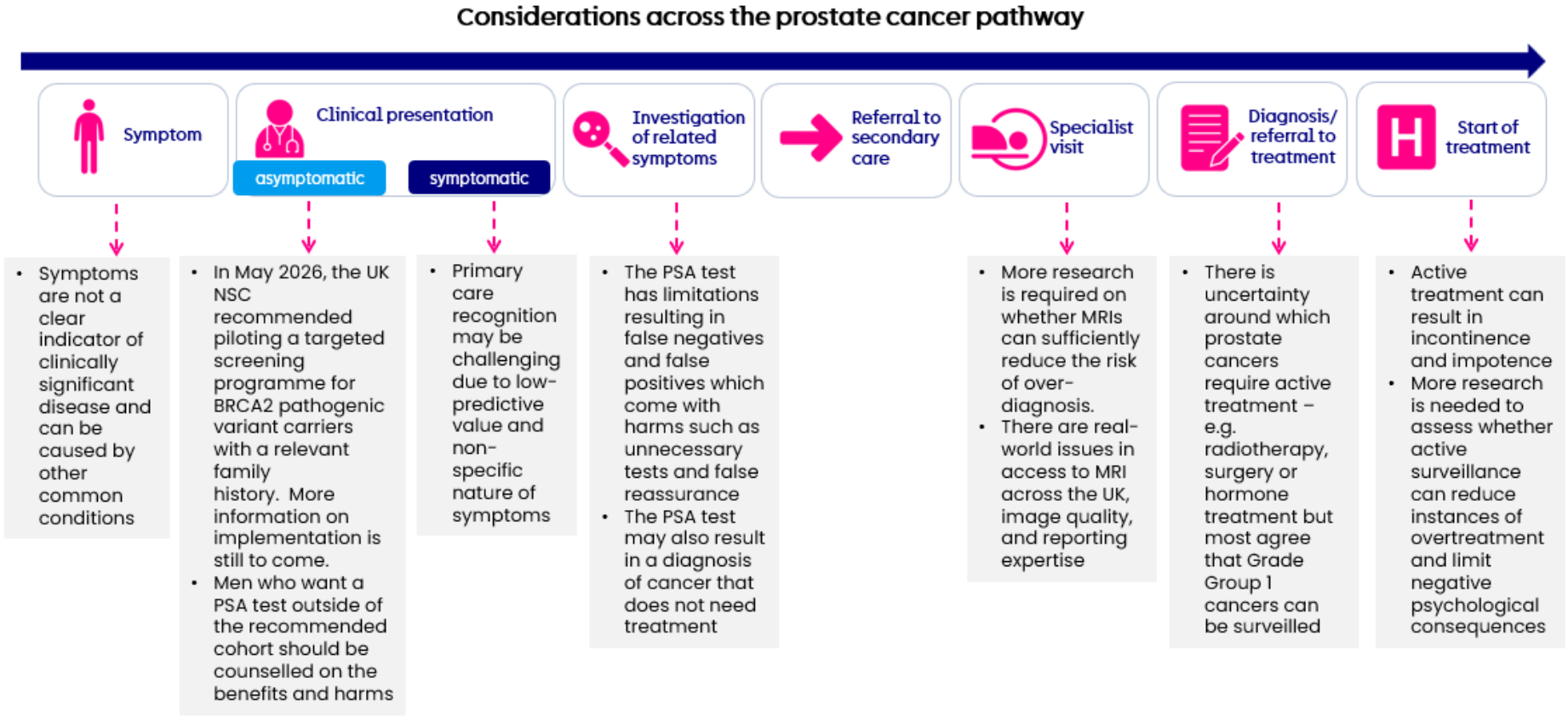
Created by the Strategic Evidence Team, Cancer Research UK.
For any questions or comments contact SEinbox@cancer.org.uk

This is because there are several complexities associated with early detection and diagnosis of this disease. In our article *Detecting prostate cancer: why we need more research* we outline our position and the significant gaps in our understanding of this disease. This technical document expands on these gaps and summarises the existing evidence. The key references at the end represent the current evidence base that we have drawn from, but we are committed to updating this at regular intervals to capture any shifts and developments.

2. Key points

- Overdiagnosis is a significant problem in prostate cancer because not all prostate cancers will progress to cause harm, combined with the lack of an accurate test to identify prostate cancer that requires treatment.
- There are limitations to identification of prostate cancer on the basis of symptoms or the prostate-specific antigen (PSA) test.
- Current screening methods, primarily PSA testing, have not shown consistent benefit in reducing prostate cancer mortality in the general population due to issues with accuracy and contamination in the research trials. There are also harms to consider such as overdiagnosis and overtreatment.
- In May 2026, the UK National Screening Committee (UK NSC) recommended that UK nations implement targeted prostate cancer screening, using the PSA test every 2 years, for men aged 45-61 with a pathogenic variant in the *BRCA2* gene and who have a family history of breast, ovarian, pancreatic, or prostate cancer. They recommended against population-wide screening or targeted screening in other high incidence groups such as Black men, or men with a family history but who do not have a *BRCA2* pathogenic variant.
- New diagnostic pathways, including pre-biopsy MRI (mpMRI), offer improvements, reducing unnecessary biopsies and improving cancer detection, but their ability to reduce overdiagnosis and improve mortality is still under study.
- More research is needed to understand whether other groups should be targeted for screening. This will need to be carefully considered so overdiagnosis is avoided, and there isn't inadvertent exacerbation of health inequalities.

Figure 1: An overview of current considerations across the prostate cancer pathway



3. Overdiagnosis and overtreatment are issues for prostate cancer

There are different types of prostate cancer

While research is ongoing to better understand prostate tumour biology, it is generally agreed that prostate tumours can come in different forms that progress at different speeds (1,2). Some are 'aggressive' and often progress rapidly before a clinical diagnosis can be made or curative treatment can be considered. Other prostate tumours could be 'slowly progressive', meaning that the tumour could eventually grow and require treatment, whereas some are 'indolent' and are unlikely to ever cause symptoms or be diagnosed clinically in a person's lifetime. An analogy that is often used for these different types are 'birds' (aggressive/progress very fast), hares (can progress but usually treatment is curative if detected in time), and tortoises (so slow-growing that it won't cause harm or need treatment within a person's lifetime).

There are challenges in identifying prostate cancers that will progress

While this is true for many cancers, prostate cancer is unique for a few reasons. First, we are currently unable to distinguish well enough between prostate cancer that requires treatment versus those that do not require treatment. It is also unclear how 'progression' of prostate cancer should be defined, which makes it challenging to know when to treat. Additionally, prostate cancer has been estimated to have a particularly long sojourn time, which is the duration that the cancer is detectable through asymptomatic tests but is not clinically detectable through symptoms. One study estimated the sojourn time for prostate cancer to be between 11.3-12.6 years and the more recent CAP trial estimated a similar number of between 12-15 years depending on patient's age(3,4). In comparison, one study estimated the sojourn time for breast cancer to be between 0-5 years, with a mean of 2 years (5). It should be noted that methods to calculate sojourn time can differ. In general, a longer sojourn time means that cancers that are not harmful at the time, but could go on to cause harm, and may be detected earlier through interventions like screening. However, there is unlikely to be a change to the person's outcome (known as 'lead-time bias'). This means that there was likely no benefit to earlier diagnosis and in many cases, the earlier diagnosis means people are more likely to get treatment prematurely, which can be harmful.

Consequences of overdiagnosis and overtreatment

Overdiagnosis is when cancer is diagnosed that would never have gone on to cause harm in a person's lifetime – i.e., the indolent cancers (6). It is a possible unintended consequence of early detection. Overdiagnosis is associated with psychological harms such as anxiety and stress from the uncertainty of identifying cancer that would not harm a person in their lifetime (7). Negative psychological consequences may be ongoing and linked to regular check-ups or testing appointments that are used to monitor for progression of the disease (8). It can also lead to unnecessary treatment which is associated with physical harms. In the case of prostate cancer, radical treatment (e.g., radiotherapy or surgery) can cause long term consequences such as impotence or incontinence, which significantly decreases a person's quality of life (9,10). In addition to being harmful to individuals, treating cancer unnecessarily takes significant health system resource and can be costly (11). It is therefore important to make efforts to reduce instances of overdiagnosis and overtreatment.

It is difficult to measure overdiagnosis or identify who has been overdiagnosed. In prostate cancer, tumours are often graded using Grade Groups (which are based on Gleason Score – a measure that looks at the histopathology of the tumour tissue) or Cambridge Prognostic Groups (which considers Gleason score, tumour morphology, and other clinical characteristics)(12). These groupings are more specific and give a better indication of whether the tumour is 'clinically significant' (i.e., likely to progress and need treatment) or 'clinically insignificant' (i.e., more likely to be indolent or not require treatment yet). However, there is not a clear consensus amongst clinicians and researchers on where to draw the line between 'significant' and 'insignificant', and research studies to date have used varying definitions. In general, while these categorisations can be a helpful guide, more research is needed to strengthen their accuracy. For example, some tumours initially marked 'clinically insignificant' may still progress and require treatment, which is why regular monitoring is required (13).

Earlier diagnosis efforts can be helpful for the tumours that behave as 'hares' (i.e., tumours that can progress but treatment is usually curative if detected in time) but accurate ways (e.g. symptoms or primary care tests) to distinguish between prostate cancer that is 'indolent' versus prostate cancer that is likely to progress, are lacking.

4. Symptoms aren't a clear indicator of prostate cancer

Progressive prostate tumours may not always present with symptoms, including those symptoms that are currently cited in NG12, the Scottish Referral

Guidelines, and the Northern Ireland Referral Guidance for Suspected Cancer (e.g. symptoms like lower urinary tract symptoms (LUTS), erectile dysfunction, visible haematuria). A 2018 study found that 28.8% of prostate cancer patients had no recorded symptoms prior to diagnosis (14). This could be because symptoms of prostate cancer often emerge when the tumour presses on the urethra, but prostate tumours are found in the peripheral zone 70% of the time, and therefore would be unlikely to press on the urethra (15).

While a subset of tumours may cause LUTS, these symptoms have a low predictive value for prostate cancer (16). LUTS are highly prevalent in the general population, especially as men age, and can be associated with common conditions such as urinary tract infection or benign prostatic hyperplasia, the latter of which is the most common cause (17,18). Overall, this makes it difficult for health professionals to assess which patients need to be referred.

5. The limitations of Prostate-Specific Antigen

In the absence of symptoms, disease-associated biomarkers are another potential indicator of early disease. Analysis of disease-associated biomarkers could be used to screen for the disease. In prostate cancer, the main biomarker is known as Prostate-Specific Antigen (PSA). Serum PSA levels are analysed through a blood test known as the PSA test. However, the PSA test is not accurate enough at distinguishing people who have prostate cancer that is likely to progress, from those that do not have prostate cancer or who have indolent prostate cancer. The PSA test has a high rate of false positives, mainly driven by the fact that it is normal for all men to have some PSA in their blood and levels of this biomarker can be elevated by several common benign conditions/factors, including urinary tract infection, benign prostatic hyperplasia, vigorous exercise, or recent ejaculation (19). One meta-analysis suggests the false positive rate of the PSA test could be as high as 80%, meaning that 80% of people with elevated PSA do not actually have prostate cancer (20).[1] Due to this, many men with elevated PSA levels may undergo unnecessary further investigation that could be invasive such as prostate MRI or

[1] This study used a PSA cut-off threshold of 4ng/mL and only focused on symptomatic men. It should be noted that there is limited evidence for the diagnostic accuracy of the PSA test in the primary care setting, which is where the test is most commonly used. The test accuracy also depends on what PSA threshold is used and whether the patient is presenting with symptoms or not. Current symptomatic guidance (e.g., NICE NG12, NiCaN and SRG) suggest utilising age-specific thresholds as PSA levels rise with age, attributed to the benign enlargement of the prostate gland with age. However, evidence is currently limited on what the 'optimal' age thresholds should be. Therefore, the thresholds suggested in referral guidance are largely based on clinical consensus. For asymptomatic men, most research studies use a fixed threshold of 3 or 4 ng/mL, though this is also contested.

biopsy. This also increases the risk of harm from overdiagnosis and overtreatment. Additionally, there is evidence to suggest that the PSA test could miss aggressive cancers ('false negatives') (19,21). Therefore, the overall utility of PSA for distinguishing between indolent versus potentially harmful prostate cancer as well as between cancer and no cancer is limited. More research and innovation is needed to find a new, more accurate test for prostate cancer or another biomarker that is more specific that can be used as early as possible in the diagnostic pathway.

6. The current evidence on prostate cancer screening

Given the need to reduce late-stage diagnosis of clinically significant prostate cancers to improve outcomes, coupled with the high likelihood that many people subsequently diagnosed with prostate cancer may not present with symptoms at all, there is significant interest in establishing a screening programme.

In the UK, the National Screening Committee (UK NSC) conducts independent, expert-led reviews of the evidence to appraise the cost effectiveness, and appropriateness of a screening programme for a condition or disease, considering any benefits and harms carefully. They then issue recommendations to the four UK governments on what screening programmes should be adopted. For a programme to be recommended, there must be high-quality evidence that (1) early intervention improves outcomes such as disease-specific mortality, and this outweighs harms associated from overdiagnosis and overtreatment, (2) there is a safe, effective, and acceptable test available, and (3) there is adequate onward follow-up care for those identified by screening (22).

Based on their 2020 evidence review, the UK NSC concluded that these criteria had not been met and therefore they did not recommend a population-wide prostate cancer screening programme using the PSA test (22). In 2022, the UK National Screening Committee's remit expanded to also include targeted and risk-stratified screening programmes. Therefore, in November 2025, they completed another robust review of the evidence alongside commissioning the Sheffield Centre for Health and Related Research (SCHARR) to conduct modelling for different screening scenarios for prostate cancer. As a result of this, they released a final recommendation in 2026 that UK nations introduce targeted screening programme for men aged 45-61 with a confirmed pathogenic variant in a *BRCA2* gene and who have a family history of breast, ovarian, pancreatic, or prostate cancer. This is discussed more in section 9. The remainder of this section will focus on why they still don't recommend a population-wide screening programme.

In 2020, the UK NSC based their decision on a few reasons, a major one being that most of the screening trials to date have employed the PSA test to screen asymptomatic men, and as noted above, there are inaccuracies and limitations to the test that increase the risk of harm from unnecessary investigations, overdiagnosis, and overtreatment. When considering the results from PSA-based screening trials that have screened all men, regardless of risk level, (see Appendix), overall findings are mixed as to whether PSA testing in asymptomatic men reduces prostate-specific mortality. However, most studies have suggested a significant amount of potential overdiagnosis and excess incidence amongst those screened (24,25). Importantly, there are limitations to these trials, including contamination which are outlined in the Appendix. Additionally, the UK NSC's 2020 review notes that a superior treatment for early-stage prostate cancer has not been identified and radical treatment options come with adverse side effects that can significantly impact quality of life such as impotence and incontinence. It is therefore unclear whether early identification of men with prostate cancer would provide them with a therapeutic advantage. Read our PSA screening article (April 2024) for more information.

In the UK NSC's 2025 review, several screening scenarios were modelled (targeted screening scenarios are discussed more in section 9). Different age ranges were explored for each scenario. Based on the evidence and this modelling, the UK NSC concluded that general population-wide screening, regardless of age, would likely result in more harms than benefits, specifically in regard to overdiagnosis.

It should be noted that within their evidence review, all the trials that employed PSA as a screening test were completed in the context of an older diagnostic pathway. This pathway is considered to be more harmful because all patients with elevated PSA went straight to receiving a transrectal biopsy. Transrectal biopsies can result in complications such as bleeding, infection, and sepsis (26). There are also limitations with diagnostic accuracy because this biopsy technique largely consists of random sampling of prostate tissue (27,28). This means that aggressive cancer can get missed or indolent tumour tissue can get picked up, leading to overdiagnosis.

The next sections will discuss changes in the pathway and how they could impact future screening and the risk of harm through overdiagnosis and overtreatment.

7. Evolving diagnostic pathways - pre-biopsy prostate MRI

In recent years, the prostate cancer diagnostic pathway has evolved to include a pre-biopsy MRI scan of the prostate, known as a multi-parametric MRI (mpMRI) scan, which might mitigate some of the harms associated with the previous pathway, e.g. receiving a PSA test and going straight to transrectal biopsy if elevated (27). There have also been developments in biopsy techniques such as MRI-guided biopsy to help target tissue sampling to areas with high-grade lesions, as well as a shift towards transperineal biopsy which is associated with fewer complications than transrectal biopsy and may be more accurate (29,30).

The introduction of pre-biopsy MRI has likely improved the prostate cancer diagnostic pathway. The key study, known as the PROMIS trial, showed that using mpMRI to triage men for a biopsy reduced unnecessary biopsies by 27% and diagnosed 5% fewer 'clinically insignificant' cancers (defined as a Gleason 4 or higher) (27). A meta-analysis supported the findings of this trial, with results showing that prostate MRI before targeted biopsy is superior to a biopsy-only approach and allows people to avoid unnecessary biopsies (31). While these are positive improvements to the diagnostic pathway for prostate cancer, it's important to consider that some MRI findings can be false negatives or may be indeterminate, meaning that it's unclear whether clinically significant prostate cancer is present (32). These cases present diagnostic challenges, and further invasive investigation such as biopsy may be required.

Pre-biopsy prostate MRI may have potential to form part of a screening strategy, but studies thus far have been varied, which makes it difficult to draw conclusions. The introduction of MRI would likely make screening safer and more effective but research from large-scale screening trials that employ pre-biopsy MRI are still required to establish a mortality benefit and reduction in overdiagnosis through testing this way. Emerging research suggests potential to reduce overdiagnosis, but there is a need to further understand this (33). Consideration must also be given to the feasibility and costs associated with a population-based screening programme that would involve MRI-scanning many more men with elevated PSA. Though some modelling has shown that screening incorporating MRI is likely to be cost-effective (34), it would require significant health system resource, capacity, and infrastructure, which must be weighed up within the context of the already overstretched NHS.

Challenges in access, image quality, and clinical expertise

There are real-world challenges with the current implementation of MRI that may mean that the benefits of it as demonstrated in trials may not be being realised in practice. For example, since the recommendation of pre-biopsy MRI in the prostate cancer diagnostic pathway, there has been variation in access and uptake across the UK. We are not aware of routine, publicly available data on this, but Prostate

Cancer UK (PCUK) made a Freedom of Information (FOI) request in 2019 to find out more. Data showed that while there is widespread coverage of MRI that is up to PROMIS trial standard in England, there are still areas where MRI remains unavailable, is limited in availability, or is not up to PROMIS trial standard (35). As noted in the article, this is more apparent in Wales and Northern Ireland. Scotland publishes its performance of pre-biopsy MRIs in their Quality Performance Indicators. In 2021, 97.1% of patients had a pre-biopsy MRI, however only 77% had a pre-biopsy MRI which was reported on in line with standard guidelines (36).

MRI scanners must also be appropriately configured, and good MRI scan quality is vital for distinguishing high-grade lesions from low-grade lesions (37,38). A study in 14 hospitals within the Peninsula and Somerset, Wiltshire, Avon, and Gloucestershire Cancer Alliances evaluated prostate mpMRI quality and compliance and found that at least 40% of patients did not have a scan of adequate quality (39). Some urologists note the importance of working alongside radiologists and being attentive to image quality to aid decision-making (40). Evidence also suggests that radiologist and clinician experience in reading and reporting mpMRI scans can impact whether a scan is reported on accurately (41). A formal consensus meeting comprised of UK experts in prostate cancer resulted in detailed recommendations for the implementation of mpMRI, including one that suggests that primarily urologists or radiologists with interest in mpMRI should report scans and that training courses should be offered (37).

Evidence and data suggests that while pre-biopsy prostate MRI is an improvement in the diagnostic pathway, more must be done to ensure that it is implemented effectively and equitably across the UK.

8. Developments in treatment for low-grade prostate cancer

In addition to changes in the diagnostic pathway, there have been advancements in how patients are treated for prostate cancer. Particularly, those diagnosed with low-grade disease that does not require treatment at the time of diagnosis are offered 'active surveillance' instead of radiotherapy or surgery. Active surveillance consists of regularly monitoring the disease for signs of progression (usually through regular PSA tests or prostate MRI) which allows some patients to avoid treatment consequences such as impotence and incontinence that could decrease their quality of life. Although this may reduce some harms associated with overtreatment, it should be noted that there is still uncertainty on how to define 'progression', especially to a point where active treatment is needed. As noted above, there is still an inability to reliably distinguish tumours that are indolent from

tumours that are progressive meaning that sometimes radical treatment will still be needed down the line due to tumour progression or misclassification.

In the UK, the ProtecT trial studied prostate cancer mortality amongst men diagnosed with low-grade prostate cancer who received either active surveillance, surgery, or radiotherapy (42). Results showed no significant difference in prostate cancer mortality across the three groups at 15 years follow up. However, by follow up, over 60% of participants assigned to active surveillance had undergone either surgery or radiation but it's unclear whether this was due to disease progression or other factors such as anxiety or fear. It could be that patients opt for active treatment sooner than they need to because they are worried of progression. Some studies suggest that men on active surveillance feel anxious and uncertain, which could be attributed to the fact that they must cope with the difficult knowledge of being diagnosed with prostate cancer that does not yet need treatment (43,44). Evidence suggests that anxiety peaks around the time for monitoring appointments or due to hypervigilance, indicating that the psychological harms may be present throughout surveillance (8). To note, there is contrasting research which suggests that risk of depression or anxiety does not differ between men who have active treatment versus men who have active surveillance (45). While the introduction of active surveillance can reduce some of the physical harms associated with overtreatment, more qualitative research on the psychological impacts is needed to better understand this issue.

Additionally, active surveillance is not without a healthcare burden, especially with the increasing role of MRI in active surveillance protocols to more accurately monitor patients. One study reported that patients are on active surveillance for at least 5 years (46). Whilst active surveillance is likely to be cost-effective compared to radical treatment initially (47), there needs to be a better understanding of how many people are receiving active surveillance without ever having their tumour progress enough to move towards treatment. The health system resource and costs associated with extended monitoring of this cohort must be considered alongside the opportunity for earlier diagnosis of progressive tumours that do require treatment. The aim must be to improve at diagnosing only tumours that are clinically significant in order to minimise healthcare burden and psychological harm.

9. Targeting screening at 'high risk' populations

Men with a genetic predisposition

There is evidence suggesting that those with pathogenic variants in cancer related genes such as *BRCA1/2* and *MSH2, MSH6* and *MSH1* have a higher incidence of prostate cancer, with some evidence suggesting potentially more aggressive disease(48,49). The IMPACT trial, which is investigating targeted prostate cancer screening in this population, has shown a particularly strong link between *BRCA2* pathogenic variant carriers and aggressive prostate cancer compared to non-carriers. The evidence for the correlation between pathogenic variants in other genes with more aggressive disease is less certain and requires more long-term follow-up.

As of May 2026, the UK NSC recommends that nations introduce a targeted prostate cancer screening programme for men aged 45-61 with a pathogenic variant in the *BRCA2* gene and who have a family history of breast, ovarian, pancreatic, or prostate cancer. The UK NSC recommends using the PSA test to screen men in this cohort every 2 years. This is based on their rigorous review of the evidence and modelling by the SCHARR team which shows that, amongst these men, the benefits are likely to outweigh the harms. For example, the committee propose that it's more likely that targeting this cohort will identify people who have an aggressive, fast-growing cancer before it's progressed to a late stage. Finding cancers like this at an earlier stage means that treatment is more likely to be appropriate and successful, and more lives could be saved. The risk of overdiagnosing slow-growing prostate cancers that would never have gone on to cause people harm is also lower.

If the governments accept this recommendation, there will be lots to work out regarding how a programme like this will be delivered in practice. We recommend reading our cancer news article "UK NSC recommends targeted prostate cancer screening" (May 2026) about the recommendation.

Black men

As mentioned in our *Detecting prostate cancer: why we need more research* (April 2025) article, data suggests that certain groups, such as Black men have approximately a 2-3 times greater incidence of prostate cancer than White men in the UK (50). However, unpicking this picture is slightly more complex.

Firstly, evidence suggests that risk may vary for different groups within broad ethnicity categories (51), meaning that any interventions developed would need to be developed and implemented to take account of this emerging evidence. The UK-based PROCESS study found that Black Caribbean men had a slightly higher incidence of prostate cancer followed by Black African men (52).[2] The reason for higher incidence of prostate cancer among these groups is likely to be as a result

[2] It should be noted that the PROCESS study data is very outdated, with cases only being captured until 2001.

of a mixture of environmental as well as biological factors, including genetics. Studies are attempting to elucidate if there are specific genetic drivers of risk across populations (53).

There is also evidence to suggest that natural PSA levels amongst men without prostate cancer may differ based on ethnicity. One systematic review concluded that Black men without prostate cancer have higher PSA levels than White men without prostate cancer, which could contribute to the higher rates of prostate cancer diagnosis amongst Black men (54). This may have implications for overdiagnosis.

Importantly, whilst Black men may have a higher incidence of prostate cancer, it is unclear whether they are at a higher risk of mortality compared to White men. An English study calculated that Black men had double the lifetime risk of dying of prostate cancer compared to White men, however Black men also had the highest incidence of prostate cancer (55). When comparing the lifetime risk of dying from prostate cancer to being diagnosed with it, a similar ratio was observed across different ethnic groups (55).

Additionally, there is conflicting evidence on the link between advanced stage diagnosis and ethnicity. The 2025 National Prostate Cancer Audit reports that Black African and Black Caribbean men aged 65-84 with a recorded stage at diagnosis had a greater number of diagnoses per 1,000 across all stages, including stage 3 and 4, compared to White men (56). In contrast, an analysis of stage at diagnosis in England found that Caribbean and African men with prostate cancer had a decreased chance of late-stage cancer compared to the White-British cohort (57). Another study which looked at men with a raised PSA result found that the likeliness of diagnosis at an advanced stage was similar for Black and White men (58). The relationship between ethnicity and advanced stage diagnosis needs to be further explored in studies using tumour grading to provide a better understanding of potential overdiagnosis.

Another study in England found that living in a more deprived area was associated with higher risk of advanced stage prostate cancer diagnosis (59). Therefore, we need to understand more about how intersectionality and how the presence of multiple inequalities may impact the risk of being diagnosed with late-stage prostate cancer.

All of the uncertainties and complexities in the evidence base need to be addressed and considered before a targeted screening programme can be considered for Black men, otherwise there is a risk of exacerbating existing health inequalities.

Men with a family history

Other groups that have a higher incidence of prostate cancer include men with a family history of prostate cancer, but who do not have a confirmed pathogenic variant. However, this definition of family history requires more specificity as it is well-evidenced that degree of relatedness and patterns of disease influence risk. For example, men with affected first-degree relatives have a higher risk than those with second-degree or more distant relatives. Risk is further increased when first-degree relatives are diagnosed younger than age 60.

Although men with a family history of prostate cancer may have a higher incidence of prostate cancer, evidence is conflicting on whether these men have a higher likelihood of developing clinically significant disease or dying from it. Some studies show mortality to be lower amongst these men compared to men without a family history. This is commonly attributed to an increased awareness of the disease and therefore a higher likelihood to request and receive a PSA test (60,61). One US-based study suggests that risk of lethal prostate cancer is higher amongst those with a family history of prostate cancer (60), though more specific research and data on tumour grade is required within this group. There is also some evidence suggesting that those with a family history of breast cancer could be at slightly higher risk of prostate cancer though similar research and data gaps exist (60). Genetic drivers of risk in this cohort are still largely unclear but are currently being investigated within studies like the PROFILE study which is explained more within the next section (62).

Although this group of men are known to be at higher incidence, the range of risk is still broad. Furthermore, more research is needed to determine drivers of risk and assess whether existing early intervention strategies are beneficial for this group.

Crucially, for all screening, including targeted approaches, we require better diagnostic technology that can distinguish indolent cancer from progressive cancer.

10. Overview of research and innovation in the pipeline

There is clearly a lot of complexity within prostate cancer early detection. However, there is promising research ongoing which might help resolve some of the uncertainty that currently exists.

Screening

CRUK supports the upcoming TRANSFORM trial, funded by PCUK and the National Institute for Health and Care Research (NIHR), which will study the effectiveness of different tests for prostate cancer screening, including PSA, MRI, and polygenic risk scores (PRS). This trial has begun recruitment in 2025 and results will show whether prostate screening in the context of the new diagnostic pathway and with new diagnostic tools could be a possibility. It will be important to ensure that the TRANSFORM trial can limit contamination within the study in light of different efforts e.g. case-finding initiatives.

Genetics and men who are considered 'high-risk'

Additionally, the PROFILE study is ongoing to better understand the role of pathogenic variants (including in *BRCA1, BRCA2, ATM, PALB2, MLH1, MSH2, MSH6, CHEK2*) in risk of prostate cancer in men who have a family history of prostate cancer and men of Black African or Black African-Caribbean ancestry without a family history. This study will help shed light on which men might be at higher risk so that targeted screening and diagnostic strategies which consider genetics may be developed. CRUK is also part funding the RelMAGINE trial which combines the use of MRI, genotyping of prostate cancer cells, and genetic changes in the blood to predict clinically significant cancers. The BARCODE 1 study, also part-funded by CRUK, is assessing PRS to risk stratify men for targeted prostate cancer screening and initial findings have recently been published (63), but follow-up is still ongoing. As mentioned above, PRS will also be explored in the TRANSFORM trial. CRUK is also part funding the IMPACT study which is looking at screening men with a pathogenic variant in *BRCA1* or *BRCA2* genes, or Lynch syndrome genes, for prostate cancer.

Diagnostics

There are also developments occurring within pre-biopsy MRI, such as a shift from mpMRI towards bi-parametric MRI (bpMRI). The main difference between the two scans is that mpMRI utilises a contrast agent to complete the scan whereas bpMRI does not, which means that bpMRI is less expensive, quicker to complete, and does not have a risk of allergy or negative reactions to the contrast agent. The PACIFIC and PRIME trials are currently evaluating whether the diagnostic accuracy of bpMRI is similar to that of mpMRI, and if so, a shift may occur such that bpMRI is used instead which may save health system resource and costs. This may also have implications for the use of MRI in screening. Research is also evaluating the potential for MRI in active surveillance. For example, the ATLAS trial will explore whether MRI can improve detection of prostate cancer progression in patients undergoing active surveillance.

Treatment

There is research ongoing to find kinder and more effective treatments for prostate cancer, especially for late-stage disease which is associated with worse outcomes. An example of this is the STAMPEDE trial that has been ongoing since 2005 and has since produced results that have significantly changed standard practice (e.g., adding docetaxel, a type of chemotherapy, or abiraterone, a type of hormone therapy, to improve disease control and life-expectancy) (64). CRUK are also jointly funding STAMPEDE2 which is testing treatments for metastatic hormone sensitive prostate cancer.

11. Summary/conclusion

There are several complexities associated with early detection and diagnosis of this disease. Key drivers are limitations in existing interventions to distinguish between tumours that are likely to progress from those that are indolent. This means that there are significant concerns about harms associated with overdiagnosis and overtreatment, which is exacerbated by the fact that symptoms are not a good predictor of disease, and the significant limitations to the PSA test.

Evidence to support widespread screening for prostate cancer using the PSA test is currently lacking, due to the risk of harm from overdiagnosis and overtreatment, coupled with the uncertain mortality benefit. However, a targeted screening programme for men aged 45-61 with a *BRCA2* pathogenic variant is a promising step forward in this space. New diagnostic technologies and innovation such as MRI and genetic tools, alone or in combination with PSA, may have potential in forming a future diagnostic and screening strategy, but more research is required to evaluate this in relation to the UK NSC's criteria for a screening programme.

12. Appendix

Trial name	Key findings	Notes and limitations
The Cluster Randomised Trial of PSA Testing for Prostate Cancer ('the CAP trial')	• After 15-years of follow-up, there was a 0.09% reduction in mortality amongst those screened compared to the control group. This equates to less than 1 life be saved for every 1,000 men invited for screening.	• Only employed a one-off test as opposed to repeat testing • Compliance with screening intervention was low (36%) • Contamination estimated to be 10-15%

	• 15% (nearly 1 in 6) of men diagnosed through screening were likely to have been overdiagnosed	
European Randomised Study for Prostate Screening (ERSPC)	• After 23 years of follow-up, prostate cancer mortality was 13% lower in the screening group compared to the control group. The absolute risk reduction was 0.22%. The absolute excess incidence of prostate cancer due to screening was 27 cases per 1000 men.	• Conducted repeat testing, though frequency varied between centres/countries • PSA threshold used was reduced over time at some centres • Mortality reduction driven by Sweden and the Netherlands • Contamination rate quoted to be as high as 62.7%
The Prostate, Lung, Colorectal, and Ovarian Cancer Screening trial (PLCO)	• No difference in mortality was found amongst those screened compared to those in the control group.	• Employed repeat testing • High contamination rate, quoted to be 54.8% in the rapid review for PLCO, but a re-evaluation concluded this was closer to 90%

13. References

1. Mishra SC, Satish D, Mishra C. A discussion on controversies and ethical dilemmas in prostate cancer screening. J Med Ethics [Internet]. 2021 Mar 1 [cited 2025 Feb 17];47(3):152–8.
2. Waterbor JW, Bueschen AJ. Prostate cancer screening (United States). Cancer Causes Control [Internet]. 1995 May [cited 2025 Feb 17];6(3):267–74.
3. Pashayan N, Duffy SW, Pharoah P, Greenberg D, Donovan J, Martin RM, et al. Mean sojourn time, overdiagnosis, and reduction in advanced stage prostate cancer due to screening with PSA: implications of sojourn time on screening. Br J Cancer [Internet]. 2009 Apr 7 [cited 2025 Mar 12];100(7):1198.
4. Martin RM, Turner EL, Young GJ, Metcalfe C, Walsh EI, Lane JA, et al. Prostate-Specific Antigen Screening and 15-Year Prostate Cancer Mortality: A Secondary Analysis of the CAP Randomized Clinical Trial. JAMA [Internet]. 2024 May 7 [cited 2024 Aug 30];331(17):1460–70.
5. Wu D, Kim S. Inference of Onset Age of Preclinical State and Sojourn Time for Breast Cancer. Med Res Arch [Internet]. 2022 [cited 2025 Mar 12];10(2):2665.

6. Cancer Research | UK Overdiagnosis | Screening for health professionals [Internet]. [cited 2025 Feb 17]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-screening/overdiagnosis

7. Sandhu GS, Andriole GL. Overdiagnosis of Prostate Cancer. J Natl Cancer Inst Monogr [Internet]. 2012 Sep [cited 2025 Feb 17];2012(45):146.

8. Eymech O, Brunckhorst O, Fox L, Jawaid A, Van Hemelrijck M, Stewart R, et al. An exploration of wellbeing in men diagnosed with prostate cancer undergoing active surveillance: a qualitative study. Supportive Care in Cancer [Internet]. 2022 Jun 1 [cited 2024 Sep 9];30(6):5459.

9. Donovan JL, Hamdy FC, Lane JA, Mason M, Metcalfe C, Walsh E, et al. Patient-Reported Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer. New England Journal of Medicine [Internet]. 2016 Oct 13 [cited 2025 Feb 17];375(15):1425–37.

10. Fanshawe JB, Wai-Shun Chan V, Asif A, Ng A, Van Hemelrijck M, Cathcart P, et al. Decision Regret in Patients with Localised Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol Oncol [Internet]. 2023 Oct 1 [cited 2025 Feb 17];6(5):456–66.

11. Aizer AA, Gu X, Chen MH, Choueiri TK, Martin NE, Efstathiou JA, et al. Cost Implications and Complications of Overtreatment of Low-Risk Prostate Cancer in the United States. Journal of the National Comprehensive Cancer Network [Internet]. 2015 Jan 1 [cited 2025 Feb 17];13(1):61–8.

12. Cancer Research UK. Grade Groups for prostate cancer [Internet]. 2022 [cited 2024 Aug 29]. Available from: https://www.cancerresearchuk.org/about-cancer/prostate-cancer/stages/grades

13. Tilki D, Chen MH, Huland H, Graefen M, D'Amico A V. Mortality Risk for Patients with Biopsy Gleason Grade Group 1 Prostate Cancer. Eur Urol Oncol [Internet]. 2024 Dec 1 [cited 2025 Feb 17];7(6):1520–6.

14. Zakkak N, Barclay ME, Swann R, McPhail S, Rubin G, Abel GA, et al. The presenting symptom signatures of incident cancer: evidence from the English 2018 National Cancer Diagnosis Audit. Br J Cancer [Internet]. 2024 Feb 10 [cited 2025 Feb 17];130(2):297–307.

15. Gnanapragasam VJ, Greenberg D, Burnet N. Urinary symptoms and prostate cancer—the misconception that may be preventing earlier presentation and better survival outcomes. BMC Med [Internet]. 2022 Dec 1 [cited 2025 Feb 17];20(1):1–6.

16. Hamilton W, Sharp DJ, Peters TJ, Round AP. Clinical features of prostate cancer before diagnosis: a population-based, case-control study. The British Journal of General Practice [Internet]. 2006 Oct [cited 2025 Feb 17];56(531):756.

17. Irwin DE, Milsom I, Kopp Z, Abrams P, Artibani W, Herschorn S. Prevalence, severity, and symptom bother of lower urinary tract symptoms among men in the EPIC study: impact of overactive bladder. Eur Urol [Internet]. 2009 Jul [cited 2024 Aug 30];56(1):14–20.

18. Lim K Bin. Epidemiology of clinical benign prostatic hyperplasia. Asian J Urol [Internet]. 2017 Jul 1 [cited 2025 Feb 17];4(3):148.

19. Assessment | Diagnosis | Prostate cancer | CKS | NICE [Internet]. [cited 2025 Feb 17]. Available from: https://cks.nice.org.uk/topics/prostate-cancer/diagnosis/assessment/

20. Merriel SWD, Pocock L, Gilbert E, Creavin S, Walter FM, Spencer A, et al. Systematic review and meta-analysis of the diagnostic accuracy of prostate-specific antigen (PSA) for the detection of prostate cancer in symptomatic patients. BMC Med [Internet]. 2022 Dec 1 [cited 2024 Aug 29];20(1):1–11.

21. Thompson IM, Pauler DK, Goodman PJ, Tangen CM, Lucia MS, Parnes HL, et al. Prevalence of prostate cancer among men with a prostate-specific antigen level < or =4.0 ng per milliliter. N Engl J Med [Internet]. 2004 May 27 [cited 2024 Sep 9];350(22):2239–46.

22. Criteria for a population screening programme - GOV.UK [Internet]. [cited 2025 Feb 17]. Available from: https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes/criteria-for-appraising-the-viability-effectiveness-and-appropriateness-of-a-screening-programme

23. UK National Screening Committee. Gov.UK. 2021 [cited 2024 Aug 29]. Adult screening programme - Prostate cancer. Available from: https://view-health-screening-recommendations.service.gov.uk/prostate-cancer/

24. Ilic D, Djulbegovic M, Jung JH, Hwang EC, Zhou Q, Cleves A, et al. Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. BMJ [Internet]. 2018 Sep 5 [cited 2024 Aug 29];362.

25. Ilic D, Neuberger MM, Djulbegovic M, Dahm P. Screening for prostate cancer. Cochrane Database of Systematic Reviews [Internet]. 2013 Jan 31 [cited 2024 Aug 29];2013(1).

26. Loeb S, Vellekoop A, Ahmed HU, Catto J, Emberton M, Nam R, et al. Systematic Review of Complications of Prostate Biopsy. Eur Urol. 2013 Dec 1;64(6):876–92.

27. Ahmed HU, El-Shater Bosaily A, Brown LC, Gabe R, Kaplan R, Parmar MK, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. The Lancet [Internet]. 2017 Feb 25 [cited 2024 Sep 9];389(10071):815–22.

28. Wei JT. Limitations of a Contemporary Prostate Biopsy: The Blind March Forward. Urol Oncol [Internet]. 2010 Sep [cited 2025 Apr 10];28(5):546.

29. Xiang J, Yan H, Li J, Wang X, Chen H, Zheng X. Transperineal versus transrectal prostate biopsy in the diagnosis of prostate cancer: A systematic review and meta-analysis. World J Surg Oncol [Internet]. 2019 Feb 13 [cited 2025 Feb 17];17(1):1–11.

30. Bryant RJ, Marian IR, Williams R, Lopez JF, Mercader C, Raslan M, et al. Local anaesthetic transperineal biopsy versus transrectal prostate biopsy in prostate cancer detection (TRANSLATE): a multicentre, randomised, controlled trial. Lancet Oncol [Internet]. 2025 Mar [cited 2025 Mar 28];0(0).

31. Elwenspoek MMC, Sheppard AL, McInnes MDF, Merriel SWD, Rowe EWJ, Bryant RJ, et al. Comparison of Multiparametric Magnetic Resonance Imaging and Targeted Biopsy With Systematic Biopsy Alone for the Diagnosis of Prostate Cancer: A Systematic Review and Meta-analysis. JAMA Netw Open [Internet]. 2019 Aug 2 [cited 2024 Sep 9];2(8):e198427–e198427.

32. Pausch AM, Ghafoor S, Kluckert J, Rupp NJ, Eberli D, Hötker AM. Risk factors for prostate cancer in men with false-negative mpMRI: A retrospective single center cohort study of image quality scores and clinical parameters. Eur J Radiol. 2024 Jan 1;170:111227.

33. Hugosson J, Månsson M, Wallström J, Axcrona U, Carlsson S V., Egevad L, et al. Prostate Cancer Screening with PSA and MRI Followed by Targeted Biopsy Only. New England Journal of Medicine [Internet]. 2022 Dec 8 [cited 2025 Mar 27];387(23):2126–37.

34. Faria R, Soares MO, Spackman E, Ahmed HU, Brown LC, Kaplan R, et al. Optimising the Diagnosis of Prostate Cancer in the Era of Multiparametric Magnetic Resonance Imaging: A Cost-effectiveness Analysis Based on the Prostate MR Imaging Study (PROMIS). Eur Urol [Internet]. 2018 Jan 1 [cited 2025 Apr 10];73(1):23–30.

35. Prostate Cancer UK. mpMRI before biopsy - a step change in prostate cancer diagnosis for men [Internet]. [cited 2024 Sep 9]. Available from: https://prostatecanceruk.org/about-us/projects/mpmri

36. Public Health Scotland. Prostate Cancer Quality Performance Indicators [Internet]. 2022 [cited 2024 Sep 9]. Available from: https://publichealthscotland.scot/publications/prostate-cancer-quality-performance-indicators/prostate-cancer-quality-performance-indicators-patients-diagnosed-from-july-2018-to-june-2021/

37. Brizmohun Appayya M, Adshead J, Ahmed HU, Allen C, Bainbridge A, Barrett T, et al. National implementation of multi-parametric magnetic resonance imaging for prostate cancer detection – recommendations from a UK consensus meeting. BJU Int [Internet]. 2018 Jul 1 [cited 2025 Mar 14];122(1):13.

38. Fütterer JJ, Tempany C. Prostate MRI and image quality: The radiologist's perspective. Eur J Radiol [Internet]. 2023 Aug 1 [cited 2024 Sep 9];165:110930. Available from: /pmc/articles/PMC10466385/

39. Papoutsaki MV, Allen C, Giganti F, Atkinson D, Dickinson L, Goodman J, et al. Standardisation of prostate multiparametric MRI across a hospital network: a London experience. Insights Imaging [Internet]. 2021 Dec 1 [cited 2024 Sep 9];12(1).

40. Khan A, Moore CM, Minhaj Siddiqui M. Prostate MRI and image quality: The urologist's perspective. Eur J Radiol. 2024 Jan 1;170:111255.

41. Kang HC, Jo N, Bamashmos AS, Ahmed M, Sun J, Ward JF, et al. Accuracy of Prostate Magnetic Resonance Imaging: Reader Experience Matters. Eur Urol Open Sci. 2021 May 1;27:53–60.

42. Hamdy FC, Donovan JL, Lane JA, Metcalfe C, Davis M, Turner EL, et al. Fifteen-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer. New England Journal of Medicine [Internet]. 2023 Apr 27 [cited 2025 Feb 17];388(17):1547–58.

43. Biddle S. The psychological impact of active surveillance in men with prostate cancer: implications for nursing care. Br J Nurs [Internet]. 2021 May 27 [cited 2025 Mar 14];30(10):S30–7.

44. Rittenmeyer L, Huffman D, Alagna M, Moore E. The experience of adults who choose watchful waiting or active surveillance as an approach to medical treatment: a qualitative systematic review. JBI Database System Rev Implement Rep [Internet]. 2016 Feb 1 [cited 2025 Mar 14];14(2):174–255.

45. Sypre D, Pignot G, Touzani R, Marino P, Walz J, Rybikowski S, et al. Impact of active surveillance for prostate cancer on the risk of depression and anxiety. Scientific Reports 2022 12:1 [Internet]. 2022 Jul 28 [cited 2025 Mar 14];12(1):1–7.

46. Shill DK, Roobol MJ, Ehdaie B, Vickers AJ, Carlsson S V. Active surveillance for prostate cancer. Transl Androl Urol [Internet]. 2021 Jun 1 [cited 2024 Sep 9];10(6):2809.

47. Sharma V, Wymer KM, Borah BJ, Barocas DA, Thompson RH, Karnes RJ, et al. Cost-Effectiveness of Active Surveillance, Radical Prostatectomy and External Beam Radiotherapy for Localized Prostate Cancer: An Analysis of the ProtecT Trial. J Urol [Internet]. 2019 [cited 2025 Feb 17];202(5):964–72.

48. Bancroft EK, Page EC, Brook MN, Thomas S, Taylor N, Pope J, et al. A prospective prostate cancer screening programme for men with pathogenic variants in mismatch repair genes (IMPACT): initial results from an international prospective study. Lancet Oncol [Internet]. 2021 Nov 1 [cited 2025 Nov 28];22(11):1618–31.

49. Page EC, Bancroft EK, Brook MN, Assel M, Hassan Al Battat M, Thomas S, et al. Interim Results from the IMPACT Study: Evidence for Prostate-specific Antigen Screening in BRCA2 Mutation Carriers. Eur Urol [Internet]. 2019 Dec 1 [cited 2025 Nov 28];76(6):831–42.

50. Kheirandish P, Chinegwundoh F. Ethnic differences in prostate cancer. Br J Cancer [Internet]. 2011 Aug 8 [cited 2024 Sep 9];105(4):481.

51. McHugh J, Saunders EJ, Dadaev T, McGrowder E, Bancroft E, Kote-Jarai Z, et al. Prostate cancer risk in men of differing genetic ancestry and approaches to disease screening and management in these groups. British Journal of Cancer 2021 126:10 [Internet]. 2021 Dec 18 [cited 2025 Mar 14];126(10):1366–73.

52. Ben-Shlomo Y, Evans S, Ibrahim F, Patel B, Anson K, Chinegwundoh F, et al. The risk of prostate cancer amongst black men in the United Kingdom: the PROCESS cohort study. Eur Urol [Internet]. 2008 Jan [cited 2024 Sep 9];53(1):99–105.

53. Wang A, Shen J, Rodriguez AA, Saunders EJ, Chen F, Janivara R, et al. Characterizing prostate cancer risk through multi-ancestry genome-wide discovery of 187 novel risk variants. Nature Genetics 2023 55:12 [Internet]. 2023 Nov 9 [cited 2024 Sep 16];55(12):2065–74.

54. Barlow M, Down L, Mounce LTA, Merriel SWD, Watson J, Martins T, et al. Ethnic differences in prostate-specific antigen levels in men without prostate cancer: a systematic review. Prostate Cancer and Prostatic Diseases 2022 26:2 [Internet]. 2022 Dec 1 [cited 2025 Mar 12];26(2):249–56.

55. Lloyd T, Hounsome L, Mehay A, Mee S, Verne J, Cooper A. Lifetime risk of being diagnosed with, or dying from, prostate cancer by major ethnic group in England 2008–2010. BMC Med [Internet]. 2015 Jul 30 [cited 2025 Mar 14];13(1):171.

56. National Prostate Cancer Audit State of the Nation Report. 2025 [cited 2025 Mar 14]; Available from: https://www.hqip.org.uk/national-programmes

57. Fry A, White B, Nagarwalla D, Shelton J, Jack RH. Original research: Relationship between ethnicity and stage at diagnosis in England: a national analysis of six cancer sites. BMJ Open [Internet]. 2023 Jan 26 [cited 2024 Sep 16];13(1).

58. Down L, Barlow M, Bailey SER, Mounce LTA, Merriel SWD, Watson J, et al. Association between patient ethnicity and prostate cancer diagnosis following a prostate-specific antigen test: a cohort study of 730,000 men in primary care in the UK. BMC Med [Internet]. 2024 Dec 1 [cited 2024 Aug 30];22(1):1–10.

59. Barclay ME, Abel GA, Greenberg DC, Rous B, Lyratzopoulos G. Socio-demographic variation in stage at diagnosis of breast, bladder, colon, endometrial, lung, melanoma, prostate, rectal, renal and ovarian cancer in England and its population impact. Br J Cancer [Internet]. 2021 Mar 30 [cited 2024 Sep 16];124(7):1320–9.

60. Barber L, Gerke T, Markt SC, Peisch SF, Wilson KM, Ahearn T, et al. Family history of breast or prostate cancer and prostate cancer risk. Clin Cancer Res [Internet]. 2018 Dec 12 [cited 2024 Sep 16];24(23):5910.

61. Brook MN, Ní Raghallaigh H, Govindasami K, Dadaev T, Rageevakumar R, Keating D, et al. Family History of Prostate Cancer and Survival Outcomes in the UK Genetic Prostate Cancer Study. Eur Urol. 2023 Mar 1;83(3):257–66.

62. The PROFILE Study [Internet]. [cited 2025 Mar 12]. Available from: https://www.icr.ac.uk/research-and-discoveries/icr-divisions/genetics-and-epidemiology/oncogenetics/the-profile-study

63. McHugh JK, Bancroft EK, Saunders E, Brook MN, McGrowder E, Wakerell S, et al. Assessment of a Polygenic Risk Score in Screening for Prostate Cancer. New England Journal of Medicine [Internet]. 2025 Apr 10 [cited 2025 Apr 11];392(14):1406–17.

64. “25 at 25”: Transforming prostate cancer treatment through the STAMPEDE clinical trial | MRC Clinical Trials Unit at UCL [Internet]. [cited 2025 Mar 12]. Available from: https://www.mrcctu.ucl.ac.uk/news/news-stories/2024/september/25-at-25-transforming-prostate-cancer-treatment-through-the-stampede-clinical-trial/