UK NSC Prostate cancer screening

Yorkshire Cancer Research response, February 2026

Next steps

Comments refer to the 'Next steps' section in the '*UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document (Pages 19-20) which outlines how the NSC will work to address uncertainties and gaps in the evidence.*

The conclusions made by the UK National Screening Committee (UK NSC) highlight a stark need for a more accurate test for prostate cancer as well as improved data availability. It is important that the UK NSC work closely with current and future trials to ensure that the gaps outlined in this review are filled.

Yorkshire Cancer Research currently funds IMProVE, a clinical trial designed to understand whether a new screening approach could work safely and effectively within the NHS. This trial will investigate whether a programme that combines PSA (Prostate-Specific Antigen) blood tests with MRI scans could improve prostate cancer diagnosis, saving lives and if so, how it can be organised to reduce health inequalities. The trial will initially involve 4,500 men in Sheffield and Leeds and may be expanded to other parts of the region. As a pilot study, IMProVE aims to inform the design of a future, larger trial. Its key objectives include assessing the acceptability of the screening approach and determining how best to engage people from Black and socially disadvantaged backgrounds, who are disproportionately affected by prostate cancer.

The UK NSC Research and Methodology Group (RMG) has reviewed IMProVE to ensure the study is designed and delivered in a way that will generate evidence valuable to the UK NSC. IMProVE should therefore be referenced in the 'Next steps' section alongside TRANSFORM, given its potential to help address uncertainties highlighted by the model, inform future research and contribute to improved prostate cancer screening strategies.

The UK NSC concluded that whole-population prostate cancer screening using current tests is not recommended because it is unlikely to be cost-effective and may deliver more harm than benefit. IMProVE aims to address these concerns by piloting a risk-stratified, MRI-enhanced screening approach designed to reduce overdiagnosis and improve cost-effectiveness. Unlike PSA-only strategies, IMProVE combines PSA testing with MRI to identify clinically significant cancers while avoiding unnecessary biopsies, thereby minimising harm. The trial incorporates a comprehensive health-economic model to evaluate cost per QALY, net monetary benefit and resource use across different screening strategies, providing UK-specific evidence on affordability and efficiency. In addition, IMProVE will assess psychological outcomes and model benefits and harms such as impact on life years (lifetime), stage shift, false-positivity rate and overdiagnosis, addressing uncertainty around whether screening improves overall health outcomes.

This trial will also directly address critical uncertainties identified by the UK NSC regarding targeted prostate cancer screening for Black men. IMProVE contributes by generating UK-specific evidence on psychosocial and behavioural factors influencing PSA screening uptake among Black men and those from deprived backgrounds, areas where current knowledge is largely US-based. Through focus groups and co-design workshops, the trial will identify barriers and facilitators to participation and develop tailored recruitment strategies. These findings can inform feasibility, acceptability and equity considerations around prostate cancer screening.

While results from this pilot cannot be directly extrapolated to a population screening programme,

IMProVE remains a critical component of the evidence base needed to inform a prostate cancer screening programme and will directly shape a future, larger trial. Importantly, IMProVE and TRANSFORM were developed to complement each other to avoid duplication and ensure that a wide range of evidence is generated. The two research teams are in regular contact to share progress and learning and where possible to standardise reporting across the two studies.

For these reasons it is important that both IMProVE and TRANSFORM are included in the 'Next steps' section and utilised to fill the remaining gaps in evidence highlighted in this review. The UK NSC should liaise directly with both trials to ensure that evidence collected will contribute effectively to future reviews and larger research trials and enable more accurate modelling of prostate cancer screening. Where additional information may be required to support decision making on prostate cancer screening, that falls outside the remit of the IMProVE and TRANSFORM trials, this should be identified at the earliest opportunity and steps taken to obtain such data.

Yorkshire Cancer Research also recommend that the UK NSC formally call for further research into the possibility of identifying other tests that could either replace the PSA test or be used in combination with it to reduce levels of overdiagnosis.

Overdiagnosis, overtreatment and active surveillance

Comments refer to the issue of overtreatment referred to in the 'UK National Screening Committee (UK NSC) Screening for prostate cancer' (Pages 4-6) which is contributed to by the current active surveillance pathway as highlighted in the 'UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document (Page 15).

Overdiagnosis, which can lead to overtreatment, is one of the key reasons given for the UK NSC's recommendation against whole population screening, targeted screening for Black men and targeted screening for men with a relevant family history.

Part of the issue with overtreatment lies with the active surveillance pathway. The review identifies that half of men who start on active surveillance will move on to have more radical treatments such as surgery or radiotherapy over 15 years. This is often due to rising PSA levels. However, rising PSA levels do not necessarily indicate the advancing of cancer and usually reflect the ageing of the prostate. This can result in men unnecessarily opting for treatment. To enable a future prostate cancer screening programme that does not result in men unnecessarily undergoing treatment which could have potential harms, there is a clear need to ensure men remain on the active surveillance pathway for as long as is safe.

Yorkshire Cancer Research are currently funding the FINESSE trial. This trial will look at whether Finasteride, an existing medication known to slow prostate growth, can increase adherence and reduce the need for extensive surgery or radiotherapy in men on the active surveillance pathway. A minimum of 227 men will be randomised into two arms; one arm will receive finasteride and the other usual care. All men will receive active surveillance including PSA testing and MRI scanning. Theoretically, due to slowed prostate growth, men receiving Finasteride will be less likely to opt for radical treatment.

By potentially improving adherence to the active surveillance pathway this trial could be critical for the feasibility of a future prostate cancer screening programme. Yorkshire Cancer Research therefore recommend that the results of this trial should be considered in future reviews to inform considerations around the impact of prostate cancer screening on overtreatment.

Uptake of the PSA test

Comments refer to Page 10 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative document

This section outlines that the model assumes the uptake of the PSA testing using data frothe UK CAP trial, putting the uptake of prostate cancer screening at 36%.

The UK CAP trial recruited through primary care practices, randomising men aged 50 to 69 in each primary care practice into the intervention and control groups. The intervention group received a single invitation to a nurse-led clinical appointment where men were given information about PSA testing and then offered the PSA test. The control group received standard NHS management and information about PSA testing was only provided to men who requested it. In this study, 36% of men within the intervention group accepted the offer of a PSA test. PSA testing within the control group was assumed to be approximately 10%-15%.

Yorkshire Cancer Research request clarity on the assumption that in a screening scenario the uptake would remain at 36%. The UK CAP trial is run in a primary care scenario, amongst a population where asymptomatic PSA testing is already available. As a result, a proportion of men who declined the screening offer may have done so because they had already been tested opportunistically, and some may have been ineligible for trial participation for the same reason. Yorkshire Cancer Research request further information on whether opportunistic screening for asymptomatic men would stop in a screening scenario and therefore whether the uptake of PSA testing in men invited to screening is likely to be higher than 36%. By applying UK CAP trial uptake rate directly, the model may exclude a group of men who currently seek opportunistic screening. These men are likely to have higher levels of health literacy and proactive health seeking behaviour, suggesting they may have above average uptake in a formal screening programme. Their inclusion could feasibly increase overall uptake beyond 36%. Yorkshire Cancer Research would welcome further justification for the use of the UK CAP trial to model uptake of prostate cancer screening given it is likely to miss out the men currently proactively request PSA tests, and for the UK NSC to consider what impact this increased uptake may have in the different screening scenarios explored.

The usual care scenario

Comments refer to Page 11 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative document

The model assumes usual care to include both PSA testing for symptomatic presentation and asymptomatic testing due to PSA test request via GP. However, as stated in the previous comment, Yorkshire Cancer Research would like clarity on whether 'PSA testing via request to their GP' would stop if a national screening programme was rolled out. Men may no longer need to proactively seek a PSA test if all men were invited to screening.

Yorkshire Cancer Research understands that currently the lack of differentiated coding in primary care means it is unknown what proportion of men are PSA tested due to opportunistic screening, symptomatic testing, active surveillance monitoring or PSA tested following prostate cancer treatment. This is acknowledged as an area of high uncertainty within the model, resulting in the model relying on one current care scenario which combines multiple routes to PSA testing.

Yorkshire Cancer Research recommend that the final UK NSC report recommends that data collection in primary care is improved to make future modelling more accurate. Without the ability to separate opportunistic screening, symptomatic testing, active surveillance monitoring or PSA testing following

prostate cancer treatment the model lacks a true 'non-screening' arm to compare against. Separate primary care record codes should be used to differentiate between symptomatic and opportunistic PSA testing, as well as PSA testing done as part of follow-up care following prostate cancer treatment or as part of active surveillance. This would help inform conclusions around overdiagnosis. It is currently unclear how frequently the PSA test is used in different scenarios and how the patient outcomes differ following tests in these different scenarios. Crucially, this data should be made available so it can be used to inform research and future screening programmes.

The diagnosis and treatment pathway

Comments refer to Page 12 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative document

The document notes that, at the time the modelling was undertaken, data from the Stockholm3 test was not yet available. Yorkshire Cancer Research recognises that it is now too late for this evidence to be incorporated into the current modelling. However, as data from the Stockholm3 trial has since become available (as of October 2025), Yorkshire Cancer Research recommends that the UK NSC commit to including this evidence in future reviews, alongside any other emerging developments, to ensure the modelling reflects the most up to date and comprehensive evidence base.

Definition of Black ethnicity

Comments refer to Page 18 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative document

This page identifies the lack of available ethnicity data for people of mixed ethnicity as a limitation, grouping all people of mixed ethnicity together. This means the model is unable to differentiate between different mixed ethnic groups or identify which of those men were of mixed Black ethnicity. Ahead of the next review UK NSC should work with partners to ensure there is improved data and proxy measures to enable the modelling to include men of mixed Black ethnicity.

Definition of BRCA1/2 gene variant carriers and actual BRCA1,2 status allocation

Comments refer to Page 18 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document and Pages 30-32 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk

The accompanying narrative document states that **'someone's knowledge of their BRCA status'** is modelled using a study that looked at the **'uptake of genetic testing** among apparently healthy relatives of people with confirmed BRCA mutations'. It is unclear how, or if, this estimate of 'known BRCA status' for people with a BRCA gene mutation has then been applied to the modelled impact of screening, as section 8.4.5 of the SCHARR report models the impact of screening **all** BRCA1/2 mutation carriers (based on prevalence estimates of 1 in 381 for BRCA 1 and 1 in 277 for BRCA 2). Yorkshire Cancer Research would like to see clarification regarding how or if this model of 'known BRCA status' for people with a BRCA gene mutation has then been applied to the modelled impact of screening.

If this estimate of 'known BRCA status' is used in the model, the Charity have a few potential concerns regarding the use of the Forde et al. study for this purpose. This study measured the uptake of pre-symptomatic genetic testing among relatives of individuals with confirmed BRCA1/2 mutations to derive age-specific probabilities that individuals know their BRCA1/2 status (assuming they are carriers). Based on the study, the model assumes that, for the 45 to 61 age group, known BRCA status is between 33% and 35% (SCHARR report, Page 32, Section 6.4.2, Table 2). This assumes that the proportion of men with an affected relative who accepted an offer of testing reflects the proportion of the population with a BRCA gene mutation who are aware of their BRCA status. In the Forde et al. study there is no stated estimate of BRCA1/2 mutation prevalence following this testing – only that they have accepted BRCA testing. Being tested for a BRCA gene mutation is not the same as being a confirmed carrier, and therefore it is Yorkshire Cancer Research's understanding that a proportion of those in the Forde et al. study will have been found not carry a BRCA gene mutation.

Additionally, uptake of testing among relatives cannot be used to infer the proportion of BRCA positive individuals in the wider population who know their status. Relatives of identified carriers have strong behavioural incentives to seek testing, whereas the general population typically learn their BRCA status only following a cancer diagnosis, proactive self referral, referral due to family history, or participation in genetic research. Despite rising levels of genetic testing and awareness of BRCA1/2 status, as noted in the paper, it is unlikely that knowledge of having a BRCA gene mutation among those affected is as high as estimated using the Forde et al study as this study does not indicate whether people are confirmed carriers and applies to a specific population with higher behavioural incentives than the general population. Further justification is required for using this study to infer BRCA awareness in a population where genetic testing is not routinely offered and where many carriers will have no known affected relative.

Definition of BRCA1/2 gene variant carriers

Comments refer to Page 18 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative document

This section of the accompanying document states that there is no reason to suspect that BRCA1/2 mutations are more likely to occur in people of one ethnicity compared to another. Yorkshire Cancer Research recommend the UK NSC call for future research into potential differences in BRCA gene mutation prevalence between different ethnic groups.

Modelling results, building the economic model for prostate cancer screening and actual BRCA1,2 status allocation

Comments refer to Page 8 and Page 19 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document and Pages 30-32 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk

The accompanying narrative document (Page 19) states 'the most cost-effective strategy for screening men with a **confirmed BRCA1/2 gene mutation** is screening every 2 years, from age 45 to age 61'. In addition, Page 8 of the accompanying narrative document states the focus of the economic model is on "men with a **known BRCA1 and/or BRCA2 gene mutation**", that is only those that know they have a BRCA gene mutation. However, this wording appears misaligned with the SCHARR model which indicates that all potential individuals with a BRCA1 or BRCA2 mutation are included in the model rather than only those with a **known** mutation. On Page 30 of the SCHARR

report, it states that BRCA status was allocated to people within the relevant dataset based on assumed prevalence rates (1 in 381 for BRCA1 and 1 in 277 for BRCA2), that is, an estimate of all individuals with a BRCA gene mutation, whether or not they are aware of it.

The language used between these documents appears misaligned and therefore Yorkshire Cancer Research request the language across the documents is updated to make it clear that the modelling for BRCA-related prostate cancer screening was done based on estimated population prevalence of BRCA1 and BRCA2 mutations.

Additional screening costs

Comments refer to Page 74 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk

The modelled invitation costs are based on the invitation costs for bowel cancer screening, including invitation letters, reminder letters for non-responders, helpline services, postage, staff time and overheads. However, Yorkshire Cancer Research request the UK NSC provide further justification for this decision and provide information detailing how the costs of the two programmes are comparable.

BRCA carriers: impact of screening scaled to the population of England

Comments refer to Page 149 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk

Yorkshire Cancer Research welcomes the recommendation to offer prostate cancer screening to men with a BRCA gene mutation. However, given some studies have indicated 97% of people in the general population who are estimated to have a BRCA gene mutation have not yet been identified and that the modelled benefits of a targeted screening programme rely on the assumption that all eligible men have undergone BRCA testing it is extremely important that before the roll out of a targeted screening programme, more must be done to identify people that would be eligible.[1] This can ensure the programme will be cost effective, bring benefit to those that are screened and achieve the modelled level of impact. Yorkshire Cancer Research is funding PROTECT-C, a £3.8 million trial, led by Professor Ranjit Manchanda at Queen Mary University of London. The trial will investigate the risks, benefits and feasibility of introducing genetic testing for all women, regardless of whether they have a relative with cancer. It will also help determine how many people accept the offer of genetic testing and, of them, how many are found to have a genetic change. Crucially, it will assess if and how offering genetic testing to all people can be affordable on the NHS. While this trial is only investigating genetic testing for women, it illustrates key areas for consideration in relation to the recommendation to use BRCA status as a way to target a prostate cancer screening programme.

Yorkshire Cancer Research request clarity on the mechanism by which people with a BRCA gene mutation will be identified as being eligible for prostate cancer screening, and subsequently invited to screening. Yorkshire Cancer Research welcomed the introduction of the National Inherited Cancer Predisposition Register (NICPR) last year and request further information on whether the UK NSC plan to work with NDRS and use this platform within the recommended prostate screening programme for men with a BRCA gene mutation. Without using a centralised database such as the NICPR, it is unclear how this type of targeted screening programme would work from a logistical perspective.

Data limitations and requirements

Comments refer to Page 180 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk

In general, the model requires much more up to date and UK applicable data. For example, the model is based on 2018 incidence data (Page 217). It is likely that this is an underestimation of the current UK incidence and does not capture the spike in testing and diagnosis associated with the 'Fry Turnbull' effect. It seems 2018 data was chosen to align with HSE data used elsewhere within the model (Page 225). However, this could mean that estimates of the additional number of people that might be diagnosed through screening become less relevant as more asymptomatic people are already being diagnosed through usual care.

The costing data used is also based on outdated numbers. These have been inflated but only to 2022/23 costs. This is done without any acknowledgement that the inflation rate has changed since 2022/23. Any conclusions made on the basis of these costs are likely to be outdated.

It is clear there are significant gaps in the data which could impact the conclusions of the model. The UK NSC should work with researchers conducting trials on prostate cancer and prostate cancer screening, as well as the NHS to ensure the necessary, high quality, UK data is collected and available to use in future reviews.

Building the economic model for prostate cancer screening

Comments refer to Page 8 of the UK National Screening Committee Prostate Cancer Screening Economic Model: Accompanying Narrative' document

This section outlines that the UK NSC requested submissions for economic modelling for the following groups: population screening in all men (regardless of their risk level), targeted screening in Black men, targeted screening in men with a known BRCA1 and/or BRCA2 (BRCA1/2) gene mutation (or variant) and targeted screening in men with a relevant family history. Based on this modelling it was concluded that the Committee could only recommend targeted screening in men with a known BRCA1 and/or BRCA2 (BRCA1/2) gene mutation.

In line with the SCHARR report's suggestion (Page 186) that it is worth exploring targeted screening of men with multiple risk factors, Yorkshire Cancer Research recommend that future reviews also look at combined risk factor groups such as Black men who also have a relevant family history. While it may not currently be cost effective for either of these groups alone, there may be sufficient evidence for screening those who fall under multiple categories.

Modelling results: PSA screening with threshold 3ng/ml

Comments refer to Pages 93 - 150 of the SCHARR report: Cost-effectiveness of Prostate Cancer Screening for Men of Average and High Risk

This section outlines the modelling results for PSA screening with threshold 3ng/ml for general population, men of Black ethnicity, men with familial risk and BRCA carriers. However, the graphs in this section are not always clearly labelled and the necessary information is not always provided. For example, Figure 24 and Figure 39 show the equivalent graph for different populations, that is the overdiagnosis rate with repeated screening in general population and men of Black ethnicity respectively. However, Figure 24 has labelled bars and Figure 39 does not, making it difficult to compare overdiagnosis rates between these populations. This makes it difficult to follow the model and understand how conclusions of the model are reached. Yorkshire Cancer Research recommend

that an updated report is published, providing a comparison table for all modelling scenarios that look at the impact of screening scaled to the population of England across the different groups outlining additional cases/fewer deaths, estimated overdiagnosis rates, and net monetary benefit (NMB) etc.

The general population modelling is the clearest with the overdiagnosis rates clearly labelled (Figure 24) and additional cases/fewer deaths set out for the probabilistic and deterministic analysis of the impact of screening scaled to the population of England.

The men of Black ethnicity modelling section requires more detail and data labelling of Figures throughout to bring it in line with the labelling provided in the general population section. The NMB and overdiagnosis rates are not stated for screening Black men at ages 50 to 62 every 4 years which is outlined in the 'impact of screening scaled to the population of England' section as the preferred scenario. Figures 38 and 39 do include this scenario, but these graphs lack the necessary data labels to be able to follow the conclusions made on their basis. Justification is needed for why this scenario is chosen given the NMB is not the highest for this group, nor is the overdiagnosis rate the lowest. Further it is unclear if any adjustments have been made to the assumptions made to the data displayed in Figure 47 as the percentage change between each step of screening in this population is different to that of the general population data displayed in Figure 29. It was not possible to calculate percentage change for every step for men of Black ethnicity due to lack of data labels provided however using the few values provided in the corresponding text it seems the percentage change is not equivalent between steps for men in the general population compared to Black men. The corresponding text for Figures 29 and 47 refers to the number of 'follow-up mpMRI procedures'. To calculate the percentage change between each step for men of Black ethnicity the Charity has assumed 'follow-up mpMRI procedures' refers to the number of **positive** mpMRI despite the wording between the two statements not aligning. This assumption is made on the basis of the Figure 29 and its corresponding text.

Overall, more justification would be valuable for not recommending screening for Black men. The NMB data in Figure 36 is very similar, if not more favourable to that displayed in Figure 72 for the BRCA population. Also, the overdiagnosis rates in Figure 37 are again similar to those in Figure 73 for the BRCA population. Whilst there is an acknowledged level of uncertainty in the data supporting the modelling for Black men, there remains a clearly identifiable population who can self-identify as eligible for screening in contrast to the BRCA scenario, which first requires men with a BRCA gene mutation to be identified. Yorkshire Cancer Research request that additional data to underpin the model for prostate cancer screening in Black men is a acquired as a priority to ensure screening is not being withheld from a population that could greatly benefit. The lifetime risk of prostate cancer in Black men is 1 in 4 while the lifetime risk in White men is 1 in 8, highlighting the increased need in this population. Further it will be critical to understand data relating to stage at diagnosis, aggressiveness of disease and survival for Black men and how this differs to White men in England.

The modelling for men with familial risk also lacks clarity. For example, NMB and overdiagnosis rates are not stated for screening men with familial risk at ages 58 and 60. Figures 56 and 57 do include this scenario, but again these graphs lack the necessary data labels to be able to follow the conclusions made on their basis. It is therefore unclear why it has been decided to use this scenario in the modelled impact of screening scaled to population of England. Furthermore, Figures (such as Figure 65) need data labels adding to align with the equivalent Figures in the general population section. Additionally, the Accompanying Narrative document (Page 19) states that "A family history was taken to mean any first-degree relative with breast, ovarian or prostate cancer". Yorkshire Cancer Research request to see the other definitions of family history considerations and the rationale behind the decision to go with the stated definition.

Finally, the modelling for men with BRCA1/2 mutations lacks some of the necessary details to understand the recommendation. For example, Figures 74 and 75 lack data labels needed to read the NMB and overdiagnosis rates. On the basis of this model it is recommended that a targeted screening programme should be pursued for men with a confirmed BRCA1 and BRCA2 variant every 2 years, from age 45 to age 61. However, at no point in the text (only on the graphs which are unlabelled) does the model state the NMB nor overdiagnosis rate for screening BRCA carriers biennially from ages 45 to 61. For the data displayed in Figure 83, again it would be helpful to understand the assumptions upon which these numbers are based as the percentage change between each step of screening in this population is different to that of the general population data displayed in Figure 29.

References

1. Manchanda R, Blyuss O, Gaba F, Gordeev VS, Jacobs C, Burnell M, et al. *Current detection rates and time-to-detection of all identifiable BRCA carriers in the Greater London population*. Journal of Medical Genetics. 2018;55(8):538-45.