UK National Screening Committee

UK National Screening Committee (UK NSC)

Screening for prostate cancer

Contents

1. Aim

To ask the UK National Screening Committee (UK NSC) to open a public consultation on the findings from the Sheffield Centre for Health and Related Research (SCHARR) modelling study that estimated the clinical and cost effectiveness of various prostate cancer screening strategies, as submitted via the UK NSC's annual call and to update the established recommendation on whole population screening.

2. Background

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

The 2020 review found that PSA as a screening test should not be offered within a national programme as it did not meet several of the UK NSC criteria. In particular, there were concerns about high levels of overdiagnosis, overtreatment and false positive results as consequences of PSA screening.

2.1 Concern with PSA testing

Screening can be beneficial to a lot of people by helping to detect the disease early, allowing earlier treatment and potentially improving morbidity and mortality. However, screening is not without harm. The harms can be less obvious but must be carefully weighed when looking at whether a screening programme should be introduced.

The main screening test available for prostate cancer is the Prostate-Specific Antigen (PSA) blood test. A concern with this test is that it is not very reliable. Many men with a high PSA level do not have cancer, whereas some men who do have prostate cancer can still have a normal PSA result. Another major concern with PSA based screening has been that a positive test result leads to an invasive diagnostic pathway and the results of this are unable to reliably distinguish between cancers which are aggressive and which cancers are slow-growing and harmless. Because of this, PSA screening can lead to overdiagnosis and unnecessary treatment, which may cause more harm than benefit to many men. The main risks of PSA-based screening include:

- **False positives:** this is when a high PSA result suggests that cancer is present when it is not. This can lead to unnecessary tests such as prostate biopsies, which carry a risk of rectal bleeding, blood in urine, blood in semen, infection, urinary difficulty, pain and worry.

- **Overdiagnosis:** true positive PSA results for cancers that would never have caused symptoms or affected length of life. Overdiagnosis causes unnecessary worry to men and other psychological harms such as anxiety, fear of cancer, and undue stress lasting long periods of time. It also exposes men to unnecessary treatment, which can sometimes cause lifelong side effects.

2.2 Prostate cancer treatments and risks

Prostate surgery

The most common lifelong harms associated with surgery include urinary incontinence such as leakage when coughing, exercising or lifting (where incontinence pads may need to be worn) and erectile dysfunction – the inability to have or hold an erection due to nerve damage. Other surgical complications could arise include bleeding, infection, blood clots or damage to nearby organs (bladder, rectum). All of these can cause harm that significantly affects someone's quality of life: physically, emotionally and psychologically.

Radiotherapy

Radiotherapy can irritate the bladder and urinary tract, and this can lead to multiple issues such as the frequency of passing urine, experiencing pain when passing urine and suffering from incontinence. The treatment can also lead to bowel problems

such as rectal bleeding and chronic rectal inflammation. Another common side effect is erectile dysfunction. All these physical effects can also lead to psychological harms that affect quality of life.

Chemotherapy

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

Hormone treatment

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

2.3 International screening

As part of the 2020 review, the reviewers also looked at the international offer of prostate cancer screening and reported that, in 2012, the United States Preventative Services Task Force (USPSTF) had strongly advised against prostate cancer screening because of various screening trials failing to show that screening reduced prostate cancer mortality. A more recent look at prostate cancer screening internationally found that Lithuania appears to be the only country with a national approach to offering PSA-based early detection in primary care for men aged 50-74 years. Sweden offers a regional organised prostate cancer testing programme for men aged 50-74 years. Various countries offer opportunistic PSA testing or, as in the UK, provide guidance that supports individual decision making for men on PSA testing. Although there is variation in how prostate cancer testing is offered internationally, organised national programmes are rare. This may reflect a shared concern.

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

Since the 2020 review, the UK NSC's remit has been formally expanded to include targeted and risk-stratified screening. Through the 2022 annual call, the UK NSC received six submissions requesting that several different screening strategies for

prostate cancer be explored. The proposed screening strategies that the UK NSC was asked to look at was for: population screening and targeted screening in black men, men with relevant family histories and carriers of BRCA gene variants.

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

3. Modelling project

The economic model was developed by the Sheffield Centre for Health and Related Research (SCHARR) on the basis of a large body of published scientific evidence and official statistics, and received input from clinical experts, technical experts, PPV members. The economic model was then validated against 2 large long-term studies that looked at using PSA testing to screen for prostate cancer. This collaborative process ensured the model reflected high quality evidence, real-world clinical practice and was informed by different perspectives.

The findings of the model have been shared with the ARG of the UK NSC as well as with clinical experts, economists, and PPVs at dedicated workshops. The report on the economic model and an accompanying narrative document (which provides a high-level summary of the purpose, methods and conclusions of the model) form part of the consultation suite of documents and have been shared and discussed with experts, the ARG and the UK NSC.

4. Modelling summary of strategies

An explanation of the economic model, including how it was built and what data were input into it, can be read in the narrative report. Full, technical details of the model are available in the economic model report.

The key findings from the economic model were:

4.1 Whole population screening

Screening all men for prostate cancer in the UK, regardless of their risk, would only slightly reduce the number of deaths but would cause a very large number of men to be overdiagnosed – meaning many would be treated for a cancer that would never have caused them harm. It is estimated that around 40-50% of prostate cancer cases detected by PSA screening will be slow growing. Offering screening, further testing and treatment for these slow growing cancers would lead to high levels of overdiagnosis and overtreatment, causing unnecessary anxiety and lifelong side

effects such as incontinence, erectile dysfunction and bladder problems for a cancer that would never have caused harm. A more accurate test than PSA is needed.

The model reported that the risk of unnecessary treatment increases with age. 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. The economic model also looked at the impact of one-off PSA testing or repeat testing. All of these strategies led to substantial overdiagnosis and therefore uncertainty about whether such screening would be cost-effective. As a result, whole-population screening may well do more harm than good.

4.2 Targeted screening for Black men

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

One of the strategies that had the lowest uncertainty of the benefit to harm balance was screening Black men every 4 years from the age of 50 to 62. In this scenario, the model predicted that, over a 15-year period, an additional 571 prostate cancers would be detected and around 7 to 11 deaths prevented. Unfortunately, there is still significant uncertainty about this scenario as there is a lack of strong evidence from large trials about the balance of harms and benefits for this group of men.

4.3 Targeted screening for men with a known BRCA 1/2 gene variant

Screening men with a confirmed BRCA 1/2 gene variant is the strategy that the model estimates to be effective and remains effective using some clinically agreed assumptions. Offering screening to this group would result in less overdiagnosis of prostate cancer as men with a BRCA gene variant are more likely to develop faster growing and aggressive cancers at an earlier age. Detecting and treating such cancers earlier, and compared to other modelled strategies, treating such cancers earlier is more likely to improve outcomes and outweigh the potential harm from overdiagnosis or unnecessary treatment, compared to men in the general population or from other risk groups. Based on the model's findings, the screening strategy to pursue would be in men with a confirmed BRCA gene variant every 2 years, from age 45 to age 61.

4.4 Targeted screening for men with a relevant family history

Men with a family history of prostate, breast, or ovarian cancer make up about a third of all men. While they are considered to be at a higher risk of developing prostate cancer, the model indicated that all strategies for screening within this group were subject to high levels of uncertainty (similar to that reported in whole-population

screening). As in the general population many cancers would be overdiagnosed and overtreated.

5. TRANSFORM

On 21 November 2025, the TRANSFORM trial was launched. This is a large, randomised control trial that has been designed with UK NSC input to recruit hundreds of thousands of men to screen using various testing strategies. The study aims to develop more accurate testing strategies than the PSA test, using MRI and genetic risk. The idea is a better test will detect more life-threatening cancers and fewer cancers which are likely to be overdiagnosed. It will then measure whether screening using the best new testing strategy does more good than harm. The trial has been designed to specifically address inequalities in age and ethnicity, with a commitment that at least 10% of the study invitations will be for Black men. The committee will continue to work closely with the trial team and as research progresses. The TRANSFORM trial anticipates that it will be able to share data in the next three years.

6. Next steps

The screening strategies that the UK NSC is consulting on and will seek views on:

- against population screening for men (at any age)
- against screening for black men
- against screening for men with a family history
- in favour of screening men with a known gene variant of BRCA1 and BRCA2

The strategy that the UK NSC is in favour to consult on and pursue is screening for men with variants of the BRCA1 and BRCA2 genes every 2 years, from age 45 to age 61. However, we welcome comments on all strategies considered.

It is proposed that the UK NSC should seek stakeholder views on whether to pursue a targeted screening strategy in men with higher genetic risk. As part of the consultation and review of the suite of documents, the UK NSC would welcome specific views on:

- screening for prostate cancer overall and on the standard of the modelling study
- whether the evidence and data used in the model are appropriate
- whether the conclusions drawn from the evidence, data and model are appropriate, in particular:
    - whether targeted screening in men with higher genetic risk should be pursued

  - towards this end, which questions might be addressed by further evidence synthesis work such as reviews and modelling
  - whether a strategy focusing on genetic risk should include men with BRCA 1 and 2 variants or just BRCA 2 variants
  - how research and evaluation might help develop and define a screening strategy based on genetic risk

- any other views

7. Draft Recommendation

The main reason that the UK NSC is not recommending whole population screening using the PSA test is that it is likely to cause more harm than good.

The reason that the UK NSC is not recommending screening Black men for prostate cancer is due to the uncertainties in the data. The UK NSC will work closely with the TRANSFORM trial to resolve these uncertainties as soon as possible.

In the meantime, the draft recommendation from the UK NSC is to go out to public consultation on whether 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.