ASCO 2024: Prostate cancer spit test better for men with high genetic risk than standard blood test

https://www.icr.ac.uk/news-archive/asco-2024-prostate-cancer-spit-test-better-for-men-with-high-genetic-risk-than-standard-blood-test

A spit test, where a sample can be collected at home, is more accurate at identifying future risk of prostate cancer for one group of men than the current standard blood test, a new study reports.

The BARCODE 1 study calculated the risk of prostate cancer from DNA extracted from saliva – called a polygenic risk score. For the men with the highest risk score, the study found this to be a better tool than the blood test which measures levels of a protein called prostate-specific antigen (PSA), which can be elevated if someone has prostate cancer.

The PSA test detects low-risk cancers

The current PSA test is used to identify men who are at higher risk of prostate cancer – due to their age or ethnicity – and men presenting with symptoms. Men with a high PSA result will be sent for further tests to detect cancer. The PSA test falsely indicates prostate cancer in men three out of four times, and detects cancers which grow so slowly they are unlikely to ever be life-threatening – meaning that men may undergo unnecessary MRI scans, invasive biopsies, and treatments.

Researchers at The Institute of Cancer Research, London, and <u>The Royal Marsden NHS</u> Foundation Trust trialled their new DNA test which looks for genetic variants linked to prostate cancer.

For the men with the highest genetic risk, the test falsely identified fewer people with prostate cancer than the PSA test, picked up people with cancer who would have been missed by the PSA test alone, and picked up a higher proportion of the aggressive cancers than the PSA test. The test also accurately identified men with prostate cancer that was missed by an MRI scan.

The researchers are presenting findings from the study at the <u>American Society of Clinical</u> <u>Oncology (ASCO)</u> annual meeting in Chicago. The research received funding from the <u>European</u> <u>Research Council</u>, the <u>Bob Willis Fund</u>, <u>Cancer Research UK</u>, The Peacock Trust and the <u>National Institute for Health and Care Research (NIHR) Biomedical Research Centre (BRC)</u> <u>at The Royal Marsden and The Institute of Cancer Research (ICR).</u>

Saliva test to detect genetic variants linked to prostate cancer

The study calculated the polygenic risk score (PRS) of 6,142 European men recruited from their GP surgeries, aged 55-69 – an age at which risk of prostate cancer is increased. The score is based on 130 genetic variations in the DNA code that are linked to prostate cancer, and it was developed by studying the DNA of hundreds of thousands of men. Since the study began, an international research team has identified more risk variants for men of Asian and African ancestry, and the ICR team intend to trial a saliva test for this population.

The men with the highest 10 per cent of risk scores – who have inherited many of these variants and are most at risk of developing the disease – were invited to further screening.

Following an MRI and prostate biopsy, 187 (40 per cent) of the 558 men with a high PRS were diagnosed with prostate cancer. This compares with the PSA test, in which 25 per cent of men with a high PSA level will actually have prostate cancer.

PRS saliva test identified aggressive cancers

Of these 187 men, 147 (77.8 per cent) had a PSA level below 3.0ug/L, which is considered 'normal' and would usually indicate that no further screening is required.

Previous studies have shown that the PSA blood test picks up many people who have cancers that are not of concern and would not require treatment. The PRS saliva test identified a higher proportion of aggressive cancers – which are fast growing and likely to spread – than the PSA test. Of the 187 cancers detected, 55.1 per cent were aggressive cancers compared with 35.5 per cent identified by a PSA test, in a recent study.

The PRS test is also more accurate than an MRI scan for these men with high genetic risk, as 119 men (63.6 per cent) had prostate cancer confirmed by a biopsy that was not detected by the MRI.

Following the detection of prostate cancer, 62 of the 187 cancers required further treatment and the rest were actively monitored.

Additional screening tool

As the PSA test is often inaccurate, the PRS saliva test could offer an additional screening tool to be offered to men at higher risk of prostate cancer, or those presenting with symptoms. Future research will follow-up the men with high PRS scores to monitor if they go on to develop prostate cancer.

The £42million <u>TRANSFORM trial</u>, which is being partly led by the team at the ICR, will directly compare the PRS saliva test to the PSA blood test and MRI scan, to assess whether those with a low genetic risk may benefit from an alternative screening tool.

Sparing men at lower risk from unnecessary treatments

<u>Professor Ros Eeles</u>, Professor of Oncogenetics at The Institute of Cancer Research, London, and Consultant in Clinical Oncology and Cancer Genetics at The Royal Marsden NHS Foundation Trust, said:

"With this test, it could be possible to turn the tide on prostate cancer. We have shown that a simple, cheap, spit test to identify men at higher risk due to their genetic makeup is an effective tool to catch the cancer early. Building on decades of research into the genetic markers of prostate cancer, our study shows that the theory does work in practice – we can identify men at risk of aggressive cancers who need further tests, and spare the men who are at lower risk from unnecessary treatments.

"Our next step will be for us to test the genetic markers we have identified that are associated with a risk of prostate cancer in diverse populations, to ensure this test can benefit all men. We are currently comparing the saliva test to other potential screening options, as part of the TRANSFORM trial, to assess the most cost-effective and accurate way to screen men for prostate cancer."

Genetic testing can play a role in saving lives

<u>Professor Kristian Helin</u>, Chief Executive of The Institute of Cancer Research, London, said: "Cancers that are picked up early are much more likely to be curable, and with prostate cancer cases set to double by 2040, we must have a programme in place to diagnose the disease early. We know that the current PSA test can cause men to go through unnecessary treatments and, more worryingly, it's missing men who do have cancer. We urgently need an improved test to screen for the disease. This research is a promising step towards that goal, and it highlights the role that genetic testing can play in saving lives."

Katie Willis, daughter of Bob Willis, former England Cricket Captain who died from prostate cancer, and co-founder of the <u>Bob Willis Fund</u>, said:

"The Bob Willis Fund has proudly supported this important work for the past two years. The potential of genetics to significantly improve early diagnosis of prostate cancer in men is huge. Although the PSA test is effective for some, it did not work for Bob. If this research can save even one life, establishing the Fund would have been a worthwhile endeavour for our family. We commend Professor Eeles and her team at the ICR for their outstanding efforts and look forward to our continued partnership together."

Naser Turabi, Director of Evidence and Implementation at Cancer Research UK, said:

"Prostate cancer is the second biggest cancer killer of men in the UK, taking around 12,000 lives a year. Right now, there's no reliable method to detect aggressive prostate cancer, but this study brings us a step closer to finding the disease sooner in those people who need treatment.

"It's encouraging to see that genetic testing might help to guide a more targeted approach to screening based on someone's risk of developing prostate cancer. More research is now needed to confirm if this tool can save lives from the disease so that it can be rolled out to improve diagnosis."

A study saving lives already

Dheeresh Turnbull, 71, from Brighton, was diagnosed with prostate cancer through the BARCODE 1 study three years ago.

He was referred to The Royal Marsden where he underwent robotic surgery to remove part of his prostate and is currently doing well.



Image: Dheeresh (right) and his brother Joel (left) at The Banham Marsden March at Sutton 2022. Credit: Dheeresh Turnbull. Dheeresh said:

"I was completely shocked when I received my diagnosis as I had absolutely no symptoms at all, so I know I would never have been diagnosed at this stage if I hadn't joined the trial. Because the saliva test revealed that I had a high genetic risk of developing the disease, my younger brother, who would have been too young to join the study directly, signed up and discovered that he also had an aggressive tumour in the prostate. It's incredible to think that because of this study two lives have now been saved in my family."