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Trial of Randomised Approaches for National Screening FOR Men (TRANSFORM)

Submission date
24/09/2025

Recruitment status
Recruiting

Registration date
21/10/2025

Overall study status
Ongoing

Last Edited
30/12/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Each year in the UK, nearly 50,000 men will be diagnosed with prostate cancer and over 12,000 will die of the disease. Prostate cancer often doesn't cause any symptoms until it has started to grow or has spread outside of the prostate, so early detection is critical. However, there is currently no national screening programme for prostate cancer.
A screening programme could save thousands of lives each year, but clear evidence that screening could detect life-threatening prostate cancers early whilst avoiding unnecessary harm is needed. Screening with existing tests like the PSA (Prostate-Specific Antigen) blood test has potential downsides, such as invasive biopsies for men who do not actually have cancer and overdiagnosis and overtreatment of low-risk cancers that may not require medical intervention. There are several highly promising tests that may overcome many of the known harms of PSA-based screening. For example, short Prostagram™ MRI scans performed in the community or saliva-based genetic tests (polygenic risk scores) may detect a similar number of the most serious prostate cancers whilst leading to fewer biopsies and fewer unnecessary treatments. However, the NHS needs strong evidence to decide whether these new screening methods should be introduced and whether they are a good use of NHS resources. TRANSFORM aims to provide the definitive evidence for prostate cancer screening.

Who can participate?
TRANSFORM is an invitation-only trial, which means participants will be randomly selected from participating General Practices and invited through a letter in the post. Men who are aged 50-74 years will be invited. Black men and those with learning disabilities are known to have poorer outcomes from prostate cancer, so will be invited from the age of 45 years.
Men with prostate cancer, or who have had any prostate cancer investigations in the previous 5 years (PSA blood test, prostate MRI, prostate biomarker test, prostate biopsy), or who have had a urinary tract infection in the previous 3 months will not be invited. In addition, men with serious health conditions such as metastatic cancer or severe frailty that is likely to limit their life expectancy to below 10 years will not be invited.

What does the study involve?
The study will have two stages:
Stage 1 (pilot and feasibility) will test four different Prostate Health Checks to decide which is

the optimal screening strategy to take forward to the main trial:
Prostate Health Check 1: PSA blood test. Prostagram™ MRI scan for PSA levels 3.0ng/mL or greater.
Prostate Health Check 2: PSA blood test. Prostagram™ MRI scan for PSA levels 1.0ng/mL or greater.
Prostate Health Check 3: Prostagram™ MRI scan for all.
Prostate Health Check 4: Saliva test for polygenic risk score (PRS). Prostagram™ MRI scan if PRS indicated an elevated risk of developing prostate cancer.
Additionally, Stage 1 will test two different study designs. Design 1 involves a two-stage consent process whereby participants are identified via GP practices and invited to join the TRANSFORM Research Cohort. Those that consent will then be randomised to one of the four Prostate Health Checks or to a control group. In Design 2, men will be identified via GP practice lists then randomised directly to one of the four Prostate Health Checks or to a control group. The optimal trial design will be taken forward to the main study.
Stage 1 will also include setting up Transform Discovery, a tissue repository which will collect samples from consenting participants including blood, urine, saliva, and stool to create a unique "Biodigital Twin" for each participant, allowing real-time testing of novel biomarkers to aid prostate cancer detection.
Stage 2 (main trial) will take forward the most robust design and screening test(s) based on Stage 1 data, in order to assess whether the new screening strategy is beneficial and value for money. Stage 2 will recruit up to 500,000 participants with long-term follow-up through linkage to national databases to assess whether screening men with Prostate Health Checks reduces deaths from prostate cancer without increasing the level of avoidable harms.

What are the possible benefits and risks of participating?
Most men who join the study will not test positive for prostate cancer and will therefore not directly benefit, but participating in the trial will provide vital information to researchers about the best way to screen all men for prostate cancer. Some men will benefit by testing positive for localised prostate cancer which may not have otherwise been identified until it was too late to cure. A smaller group of men will be diagnosed with prostate cancer that is too late to cure.
A small proportion of men will screen positive in the study and will be offered a prostate biopsy (which is a part of standard care for diagnosing prostate cancer). Prostate biopsy has some risks such as blood in the urine, retention of urine, and infection.

Where is the study run from?
The study is run by Imperial College London with support from several leading Universities in the UK.

When is the study starting and how long is it expected to run for?
Stage 1 will start in December 2025 and will enrol participants for around 2 years. Stage 2 will be the much larger main trial starting in 2028. Timelines for Stage 2 will be updated on ISRCTN when it starts.

Who is funding the study?
1. Prostate Cancer UK (PCUK)
2. National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
Prof. Hashim U Ahmed, transform@imperial.ac.uk

Contact information

Type(s)
Scientific

Contact name
Mrs Natalia Klimowska-Nassar

Contact details
-
-
United Kingdom
-
-
n.klimowska@imperial.ac.uk

Type(s)
Principal investigator

Contact name
Prof Hashim Ahmed

ORCID ID
https://orcid.org/0000-0003-1674-6723

Contact details
Imperial College London
B Block
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0NN
+44 (0)20 7594 1660
hashim.ahmed@imperial.ac.uk

Type(s)
Scientific

Contact name
Ms Francesca Rawlins

Contact details
Imperial College London
B Block
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0NN
+44 (0)20 7594 1660
f.rawlins@imperial.ac.uk

Type(s)
Scientific

Contact name
Mr Nikhil Mayor

Contact details
Imperial Prostate
Imperial College London
London
United Kingdom
-
-
n.mayor@imperial.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
343441

Central Portfolio Management System (CPMS)
57097

Protocol serial number
Grant Code: MA-BD22-001

Study information

Scientific Title
Trial of Randomised Approaches for National Screening FOR Men (TRANSFORM)

Acronym
TRANSFORM

Study objectives
Stage 1: pilot and feasibility
Trial design optimisation:
1. Assess feasibility of pre- and post-randomisation consent designs in terms of screening uptake (overall and in specific sub-groups) and rates of contamination in the control groups.
2. Investigate which recruitment approaches are most effective in terms of rate of recruitment, number of men recruited in specific sub-groups and uptake of screening.
3. Investigate barriers and facilitators to participation in, and compliance to, screening interventions at each screening round within different socio-economic, ethnic and vulnerable groups in the community and if necessary, create strategies to improve participation and compliance.

Pilot prostate health checks:
1. Evaluate biopsy rates, early-stage high, intermediate and low risk prostate cancer detection

rates and model cost-effectiveness of the different intervention arms.
2. Management of prostate cancer, testing and treatment relative adverse events and side effects.

TRANSFORM Discovery:
Operationalise TRANSFORM Discovery through optimisation and establishment of a bio-digital twin comprising a trial related tissue collection, multi-omic tissue processing, digital pathology and imaging data matched with clinical data from the main TRANSFORM database.

Stage 2: main trial:
Long term cancer outcomes:
1. Evaluate prostate cancer mortality and prostate cancer metastases.
2. Evaluate prostate cancer incidence.
3. Biopsy rates, early stage high, intermediate and low risk prostate cancer detection, management of prostate cancer, testing- and treatment-related adverse events and side effects.

Costs and cost-effectiveness:
1. Estimate the cost-effectiveness of strategies based on the screening intervention, compared with the current UK standard of care and update these estimates as the trial progresses.
2. Carry out a care pathway analysis and budget impact analysis to determine resource and manpower implications of a screening recommendation within the UK healthcare system.

TRANSFORM Discovery:
TRANSFORM Discovery will deliver digital data and biospecimen collection from the trial and undertake (i) biomarker testing at scale and pace, (ii) accelerate translational & discovery science, and (iii) establish a sustainable long-term Bio-Digital Twin model.
Biomarker testing will be undertaken, with embedded health economic evaluations, to deliver rapid real-time testing of biomarkers in collaboration with academic and commercial partners.
TRANSFORM Discovery will facilitate exploratory simulations of novel strategies of healthcare delivery though data modelling to inform development of new hypotheses for prostate cancer management.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 29/08/2025, Wales REC5 Health and Care Research Wales (Castlebridge 5, Cardiff, CF11 9AB, United Kingdom; +44 (0)2922 940910, 02922 940954, 02922 941106; Wales.REC5@wales.nhs.uk), ref: 25/WA/0197

Primary study design
Interventional

Study design
Randomized controlled study

Study type(s)
Screening

Health condition(s) or problem(s) studied
Prostate cancer

Interventions
In this multi-arm multi-stage randomised platform trial, eligible men will be invited via their GP practice for a community-based screening intervention. The trial will involve two stages. In Stage 1 (pilot), two pre-consent randomisation designs will be evaluated. In Design 1, participants will be approached to express interest in joining the TRANSFORM Research Cohort. Consenting participants will be randomised to one of four screening pathways ("Prostate Health Checks") or to a control group. Design 2 follows a "Zelen" approach, whereby participants are randomised prior to consent to one of four Prostate Health Checks or to a control. Participants in the control groups in both designs will follow usual care. The aim is to evaluate which method is most feasible in terms of screening uptake to power the main trial (Stage 2), taking into account potential contamination (rates of PSA testing in the control groups) where possible.

The optimal trial design and Prostate Health Check will be taken forward to Stage 2 for evaluation on a larger group of men. Stage 1 will incorporate a single screening round and Stage 2 will include at least two rounds of screening.

In parallel, the Transform Discovery Biodigital Twin (BDT) will collect biological specimens to guide translational research and real-time assessment of novel biomarkers.

Intervention Type
Other

Primary outcome(s)
Stage 1: Feasibility outcomes
1. Proportion who receive the Prostate Health Check (PHC) in each screening intervention arm (Design 1 and Design 2, separately) at the end of the trial
2. Proportion with PSA test in each of the control groups (Design 1 and Design 2, separately) measured through linkage to national databases at the end of the trial

Stage 1: Prostate health checks intervention pilot outcomes
In each PHC group:
1. Proportion diagnosed with intermediate-risk prostate cancers (NCCN*) [also collected in control groups] at the end of the trial
2. Proportion diagnosed with low-risk prostate cancers (NCCN*) [also collected in control groups] at the end of the trial
3. Proportion having a prostate biopsy [also collected in control groups] at the end of the trial
4. Costs and cost-effectiveness modelling of each PHC intervention (from first visit to diagnosis /treatment)

Key secondary outcome(s)
Stage 1: feasibility outcomes:
1. Proportion who provide Stage 1 consent (Design 1)
2. Proportion with Black ethnicity invited (Designs 1 and 2 combined)
3. Cost per successful consent (Design 1 and Design 2 separately):
4. Proportion who provide Stage 1 consent (Design 1) by age group, ethnicity, IMD quintile
5. Proportion of men with learning disability or severe mental illness who provide Stage 1 consent (Design 1)
6. Proportion undergoing PHCs in each screening intervention arm by age, ethnicity, IMD quintile (Design 1)
7. Performance indicators, including compliance with further assessment and compliance with treatment

Stage 1: prostate health checks intervention pilot outcomes:
In each randomised PHC group:

Timelines:
Time (days) from randomisation to a) undergoing the first part of each PHC to b) receiving the result of the first test to c) undergoing Prostagram™ to d) receiving the result of the Prostagram™ to e) having a prostate biopsy in those advised to undergo a prostate biopsy

Detection:
1. Proportion diagnosed with high-risk prostate cancers (NCCN*)
2. Proportion diagnosed with low/intermediate/high-risk prostate cancer according to NICE risk groups* (* based on Cambridge Prognostic Group, low-risk = CPG1, intermediate-risk = CPG2-3, high-risk = CPG4-5, ref: ww.nice.org.uk/guidance/ng131)
3. Proportion diagnosed by ISUP Grade Group: GG1, GG2, GG3, GG4, GG5 prostate cancer
4. Proportion diagnosed by T stage
5. Proportion diagnosed with any amount of Gleason 4+3=7 or more
6. Proportion diagnosed with ≥ Gleason 4+3 OR Gleason 3+3=6 of ≥6mm (PROMIS definition 1)
7. Proportion diagnosed with ≥ Gleason 3+4 OR Gleason 3+3=6 of ≥4mm (PROMIS definition 2)
8. Proportion of GG2 cancers in each of the following categories of percentage pattern 4 involvement: ≤10%, 11-20%, 21-30%, 31-40%, 41-50%

In those diagnosed with prostate cancer:
1. Maximum cancer length on biopsy in millimetres
2. Gleason Score Ratio of GS6 to GS7+
3. Proportion with lymph node cancer involvement of the pelvis (N1) only
4. Proportion with distant / metastatic disease by individual stage categories: distant lymph nodes (M1a), bones (M1b) and organs such as the liver, brain or lungs (M1c) stratified by N0 or N1 status
*NCCN Guidelines Version 4 (2024)59 will be used to define prostate cancer risk groups where indicated.

Biopsy-related harms:
1. Biopsy-related harms measured by PROBE questionnaire score
2. Proportion with culture-proven infection related to biopsy/within 90 days of biopsy
3. Proportion with infection treated with antibiotics (in the absence of culture confirmation) related to biopsy/within 90 days of biopsy
4. Proportion with sepsis related to biopsy/within 90 days of biopsy
5. Proportion with urinary retention requiring catheterisation (permanent or intermittent) related to biopsy/within 90 days of biopsy
6. Proportion with bleeding requiring catheterisation or hospital admission related to biopsy /within 90 days of biopsy
7. Proportion with vasovagal episode requiring hospital review or admission related to biopsy /within 90 days of biopsy
8. Proportion whose death is related to biopsy/within 90 days of biopsy
9. Rate of hospital admissions within 90 days after biopsy

Treatment:
1. Proportion receiving active surveillance, focal therapy, prostatectomy, and radiotherapy (with and without ADT) as first option by low, intermediate and high-risk disease subgroups (NCCN*). Proportion having ADT and type of ADT as monotherapy to be reported.
2. Proportion receiving active surveillance, focal therapy, prostatectomy and radiotherapy (with

and without ADT) as first option by low, intermediate and high-risk disease subgroups (NICE risk groups). Proportion having ADT and type of ADT as monotherapy to be reported.
3. Proportion receiving active surveillance, focal therapy, prostatectomy and radiotherapy (with and without ADT) as first option by ISUP Grade Groups (GG1, GG2, GG3, GG4, GG5). Proportion having ADT and type of ADT as monotherapy to be reported.
4. Proportion receiving active surveillance, focal therapy, prostatectomy and radiotherapy (with and without ADT) as first option by T stage. Proportion having ADT and type of ADT as monotherapy to be reported.
5. In those diagnosed with ISUP GG2 prostate cancer, proportion receiving active surveillance, focal therapy, prostatectomy and radiotherapy (with and without ADT) as first option by pattern 4 percentage categories (≤10%, 11-20%, 21-30%, 31-40%, 41-50%). Proportion having ADT and type of ADT as monotherapy to be reported.
6. In men undergoing active surveillance, proportion who progress on biopsy or on imaging.
7. In men undergoing active surveillance, proportion who go on to receive focal therapy, prostatectomy and radiotherapy. Proportion having ADT and type of ADT as monotherapy to be reported.
8. In each of the following categories of stage of disease, proportions of type of local prostate treatment by focal therapy, surgery, radiotherapy and type of systemic treatment: ADT, chemotherapy, androgen receptor inhibitors (ARIs), other drugs for prostate cancer treatment and type of treatment directed at distant disease.
NB: Breakdown of type of modality used for focal therapy to be collated.
NB: Radiotherapy will be divided into numbers undergoing external beam radiotherapy, external beam radiotherapy with neoadjuvant ADT, external beam radiotherapy with adjuvant ADT (and duration), low dose rate brachytherapy and combination radiotherapy (high dose rate or low dose rate brachytherapy combined with external beam radiotherapy and ADT). Numbers undergoing proton therapy and stereotactic ablative radiotherapy (SABR) will also be collected.

Treatment-related harms:
1. Rate of hospital admissions within 90 days after treatment
2. Focal therapy-related harms graded by Clavien-Dindo severity category
3. Surgery-related harms graded by Clavien-Dindo severity category
4. Radiotherapy-related harms graded by CTCAE severity category
5. Other treatment-related harms graded by CTCAE severity category
6. Investigations/ tests for treatment related symptoms, interventions for complications, death

Patient reported outcome measures (PROMS):
1. PROMS on urinary, sexual and bowel function measured by EPIC-26 Short Form
2. Prostagram Questionnaire – all participants who received an MRI
3. PROBE – adapted for Specification, Perceptions and General questionnaires
4. In participants from sexual minority group, Sexual Minorities and Prostate Cancer Scale (SMACS)61
5. Health Service Use (in draft)
6. Health related quality of life measured by EQ-5D-5L
7. For participants with mild or moderate learning disability, the modified version of EQ-5D-3L62 Learning Difficulty and for those with severe learning disability, the proxy (informant) version 2 of the EQ-5D-5L
8. Demographics Questionnaire
9. Health Behaviour and Family History Questionnaire
10. Anxiety measured by the GAD-7 and Cancer Worry Scale (CWS) adapted to prostate cancer
11. Health Literacy measured by the SILS
12. Risk perception of developing prostate cancer measured on 4 items
13. Acceptability of the received prostate health check measured (prospectively and

retrospectively) on the TFA Questionnaire
14. Participant Satisfaction Measure Questionnaire

Health economics:
1. Proportion using health services
2. Costs falling on men and their families

TRANSFORM Discovery BDT:
1. Define and initiate first wave biomarker validations
2. Define consent rates to TRANSFORM Discovery and metrics of tissue (including quality assurance of biological measures), digital pathology, imaging collection and integration with clinical data.

Completion date
01/12/2027

Eligibility

Key inclusion criteria
Stage 1:
1. Men in the general population aged 50-74 years.
2. Additionally, men aged 45-49 years who self-identify in GP practice lists as of Black ethnicity.
3. Additionally, men aged 45-49 years who are on the GP learning disability Quality Outcome Framework (QOF) register.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
45 Years

Upper age limit
74 Years

Sex
Male

Total final enrolment
0

Key exclusion criteria
1. History of prostate cancer (clinical diagnosis or histological).
2. Known history of one or more PSA tests, prostate MRI scans, prostate biomarker tests or prostate biopsies in the preceding 5 years.

3. Urinary tract infection in the 3 months before screening.
4. Significant co-morbidities or other cancers likely to impact their life expectancy in the next 10 years.

Date of first enrolment
21/11/2025

Date of final enrolment
01/06/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
England
W2 1BL

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
England
NW1 2PG

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Charity

Funder Name
Prostate Cancer UK

Alternative Name(s)
Prostate Cancer, Prostate Action, ProstateUK, prostatecanceruk

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
National Institute for Health and Care Research

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date