

Prostate Testing for Cancer and Treatment (ProtecT) feasibility study

J Donovan*	L Brindle	N Mills
F Hamdy	D Jewell	M Smith
D Neal	P Powell	S Noble
T Peters	D Gillatt	A Lane
S Oliver	D Dedman	

and the ProtecT Study Group: J Anderson, M Benney, S Burton, I Emmerson, J Goepel, L Goodwin, J Graham, D Gunnell, H Harris, B Hattrick, P Holding, C Kennedy, S Kilner, P Kirkbride, H Leung, T Mewes, J Oxley, I Pedley, M Robinson, L Salter, M Sidaway, C Torrington, L Wilkinson, A Wilson

* Corresponding author

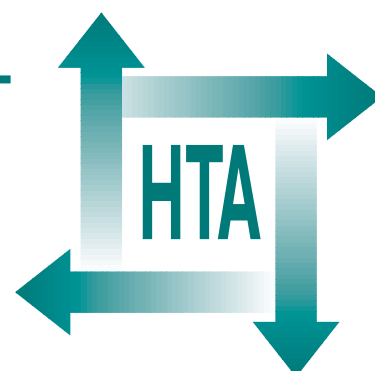
Department of Social Medicine, University of Bristol, UK



Executive summary

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Executive summary

Background

There is currently insufficient evidence to introduce population screening for prostate cancer. While it is accepted that prostate cancer is an important public health problem, there is paucity of evidence on the natural history of the disease, the accuracy of diagnostic tests (e.g. prostate-specific antigen (PSA) testing) and the effectiveness of treatments.

Objectives

The overall aim was to evaluate the feasibility of a randomised controlled trial (RCT) of treatments for localised prostate cancer, including:

- feasibility of ‘case-finding’ in the community (including the reliability and psychosocial impact of PSA testing)
- determining the most efficient and effective design for a major trial of treatments
- randomised trials of recruitment strategies
- piloting outcome measures and procedures for the main trial of treatments.

Methods

The study was an RCT of treatment preceded by case-finding in the community, with qualitative research methods integrated at each stage. Case-finding took place in primary care centres in Sheffield, Newcastle and Bristol. The RCT was undertaken in urology clinics in these same centres. Men aged 50–69 years from specific primary care centres in the three cities were invited to attend a 30-minute prostate check clinic appointment in which they were informed about the study and asked to consent to a PSA test. Men with a raised PSA (initially ≥ 3.0 ng/ml if 50–59 years; ≥ 4.0 ng/ml if 60–69 years; but changed to ≥ 3.0 ng/ml for all men after 1 year) were invited for biopsy. Men with confirmed localised prostate cancer were invited to participate in a randomised trial of recruitment strategies.

Men with confirmed localised prostate cancer were asked to consent to randomisation between a nurse

or urologist for an ‘information’ appointment to discuss recruitment to the treatment trial. In the information appointment, the need for a trial was explained in detail, along with the advantages and disadvantages of each treatment, and the recruiter attempted to randomise the patient to the treatment trial or reach a patient-led preference for a treatment. All men, whether randomised or not, were asked to consent to be followed-up, and these formed a pilot for the proposed main trial.

Main outcome measures

Case-finding

Numbers of men agreeing to attend prostate check clinics and then going on to have a PSA test, biopsy and diagnosis of prostate cancer were calculated. The accuracy of PSA testing was calculated by positive predictive values (PPVs) at various cut-points. The psychosocial impact of case-finding was investigated through the use of the Hospital Anxiety and Depression Scale (HADS) and ICS_{male} (urinary symptoms) questionnaire, completed by all men at baseline and those with raised PSA levels at the time of biopsy.

Randomised trial of recruitment

The primary outcome was the proportion of patients accepting randomisation to the treatment trial. Also calculated were the proportions consenting to randomisation to the three- (radical prostatectomy, radical radiotherapy and ‘conservative’ management) or two-arm (radical options only) trial and those accepting the random allocation. An economic analysis based on the duration of information appointments and recruiter salaries was performed to assess the most cost-effective recruiting staff.

Qualitative research

In-depth interviews were undertaken with several groups:

- men interviewed on several occasions as they progressed through the feasibility study from case-finding to randomisation
- men after they had received PSA test results
- men with confirmed localised prostate cancer after their information appointment.

In addition, tape-recorded information appointments were examined. Changes to information content and presentation were made and the proportions consenting to be randomised to the treatment trial and accepting the allocation were calculated regularly to examine the impact of these changes.

Proposed main randomised trial of treatment

All men with confirmed localised prostate cancer completed a baseline study questionnaire at the time of case-finding and biopsy. A further questionnaire was completed 6 months after the information appointment, with the major research follow-up to be at 12 months and annually thereafter in the main trial.

Results

Case-finding

A total of 8505 men from 18 primary care centres attended prostate check clinics (56% of those invited), and 7383 had a PSA test. Of these, 861 (12%) had raised PSA levels, and following biopsy, 224 cases of prostate cancer were found (165 clinically localised). The detection rate was 2.2% of clinic attendees. PPVs confirmed that a PSA cut-point of 3 ng/ml was suitable. At the time of PSA testing, levels of depression were low (3.2% 'cases') and anxiety somewhat higher (11.6% 'cases'), but these remained virtually unchanged among those completing questionnaires at the time of biopsy.

Randomised trial of recruitment

Ninety per cent of eligible cases consented to randomisation between a nurse and urologist. Urologists achieved a higher rate of recruitment to the treatment trial (71% compared with 67% for nurses), but this was not statistically significant ($p = 0.60$). As effectiveness was essentially the same between the two arms, a cost-minimisation analysis was performed and showed that the urologist arm was more expensive because greater salary costs outweighed their tendency for shorter appointments and nurses often supported surgeon-led clinics.

Randomised trial of treatment

The three-arm trial was the most popular treatment trial option, with 84% opting for this rather than the two-arm trial ($p < 0.001$). The acceptance of the treatment allocation was 71% within the three-arm trial.

Qualitative research

The offer of PSA testing was construed as an opportunity to discover an unknown condition and the majority of men indicated that they understood that the study involved investigation of treatments. While the majority could recall clearly the principles of randomisation, issues around clinical equipoise caused many considerable difficulty. Recruitment to the treatment trial increased gradually during the feasibility study, from 30–40% at the outset to 70% by the end of the feasibility study. These improvements in recruitment were brought about by changes to the content and presentation of information, particularly avoidance of terms such as 'trial' and 'watchful waiting', and the clear specification of the non-radical treatment arm, as directed by the findings of the qualitative research.

Conclusions

- It is feasible to mount a full-scale three-arm randomised trial of treatment for localised prostate cancer, preceded by a programme of case-finding in the UK.
- The full-scale three-arm Prostate Testing for Cancer and Treatment (ProtecT) randomised trial of treatment has now been commissioned by the NHS R&D Health Technology Assessment Programme. It will be undertaken in nine clinical centres in the UK, involving over 100,000 men, and recruitment will take 5 years, commencing September 2001.

Publication

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NHS R&D HTA Programme

The NHS R&D Health Technology Assessment (HTA) Programme was set up in 1993 to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS.

Initially, six HTA panels (pharmaceuticals, acute sector, primary and community care, diagnostics and imaging, population screening, methodology) helped to set the research priorities for the HTA Programme. However, during the past few years there have been a number of changes in and around NHS R&D, such as the establishment of the National Institute for Clinical Excellence (NICE) and the creation of three new research programmes: Service Delivery and Organisation (SDO); New and Emerging Applications of Technology (NEAT); and the Methodology Programme.

This has meant that the HTA panels can now focus more explicitly on health technologies ('health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long term care) rather than settings of care. Therefore the panel structure has been redefined and replaced by three new panels: Pharmaceuticals; Therapeutic Procedures (including devices and operations); and Diagnostic Technologies and Screening.

The HTA Programme continues to commission both primary and secondary research. The HTA Commissioning Board, supported by the National Coordinating Centre for Health Technology Assessment (NCCHTA), will consider and advise the Programme Director on the best research projects to pursue in order to address the research priorities identified by the three HTA panels.

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The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In particular, policy options in the area of screening will be considered by the National Screening Committee. This Committee, chaired by the Chief Medical Officer, will take into account the views expressed here, further available evidence and other relevant considerations.

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The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 23 8059 5639 Email: hta@soton.ac.uk
<http://www.ncchta.org>

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