Authors' objectives
To assess the clinical and cost-effectiveness of methods for the diagnosis, treatment and screening of early localised prostate cancer.

Searching
EMBASE, Cancerlit, MEDLINE, the Social Sciences Citation Index, the Science Citation Index, PsycLIT, DHSS Data and ASSIA were searched from 1990 to 1995 for studies in any language; economic evaluations were sought back to 1986 because of their relative scarcity. A sample of the search terms used was given in the authors' text. In addition, a MEDLINE search on PSA between 1991 and 1994 was also available to the authors. A citation search was conducted on the early treatment trials of the US VACURG team for cross-checking purposes. Review articles and other reviews were identified through bibliographic searches and through DARE (NHS Centre for Reviews and Dissemination). Unpublished information on current projects was identified through the NHS Projects Register, its USA equivalent HSRProj, and through personal contacts or networks of the staff and expert steering group of this project. Some centres were contacted directly (e.g. the Agency for Health Care Policy and Research in the USA.). The director of the publishing house of the Chinese Medical Association was contacted by letter in an attempt to access research from China; however, no reply was received.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and prospective and retrospective cohort studies, focusing on early localised prostate cancer with a study group size greater than 50 but preferably greater than 100, were eligible for inclusion.

Specific interventions included in the review
No inclusion criteria relating to the intervention were specified. The interventions addressed in the review were as follows.

Diagnosis or screening: digital rectal examination (DRE), prostate- specific antigen (PSA), transrectal ultrasound imaging (TRUS) and needle biopsy. The tests were assessed both alone and in combination, e.g. DRE plus PSA.

Treatment: radical prostatectomy, radiotherapy and conservative management.

Reference standard test against which the new test was compared
No inclusion criteria relating to the reference standard were specified for the diagnostic studies. The studies included in this section of the review appear to have used needle biopsy as the reference standard.

Participants included in the review
No inclusion criteria relating to the characteristics of the participants were specified. The participants in the included studies were as follows.

Diagnosis: males who were either volunteers or were referrals for suspected prostate cancer.

Treatment: males with diagnosed prostate cancer.

Screening: volunteers, attendees at clinics, and responders to adverts.

Outcomes assessed in the review
The included studies were required to use outcome measure appropriate to diagnostic techniques or therapeutic interventions. The outcome measures used were as follows.
Diagnosis: sensitivity and specificity.

Treatment: disease progression, mortality, continence and potency.

How were decisions on the relevance of primary studies made?
The lead reviewer mainly made decisions on the relevance of primary studies, but with support from three other reviewers who were each responsible for a specific study area (epidemiology and screening; PSA studies; economic evaluations). Any disagreements were resolved by discussion.

Assessment of study quality
Therapeutic studies were scored for nine criteria on a 0 to 2 scale and an overall score from 0 to 2 was given. It appears that only non-RCTs were assessed for validity. The nine criteria were: recruitment or study group bias; control or comparison group; intended outcome measures; appropriate outcome measures; outcome assessment blind; do results meet study objectives; statistical tests applied; all patients entered in study accounted for at conclusion; centre, practitioner or experience bias.

Economic evaluations were scored similarly using the following criteria: viewpoint (e.g. society, NHS); source of data on probability of main clinical events; type of resource use identified; method of measuring resource use; method of valuation of resource use; type of benefits measured; method of valuation of benefits; discounting applied and rate; sensitivity analysis used and variables employed. The lead reviewer assessed each study for validity. This was supplemented by a blinded, second opinion using the same criteria on a sub-sample of studies (1 out of 8). Any disagreements were discussed.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative discussion.

How were differences between studies investigated?
Differences between the studies were investigated through a narrative discussion.

Results of the review
A total of 432 studies were included in the review.

Diagnosis.

DRE: the sensitivity ranged from 44 to 97% and the specificity from 22 to 96%. Approximately 20% of the cancers that can be identified by PSA were missed, whereas nearly 30% of the cancers with PSA values within the normal range were detectable by DRE.

PSA: the sensitivity varied from 57 to 99% with 70% being the most frequently observed figure; the specificity ranged from 59 to 97%. PSA concentration was directly related to age, which makes it a more sensitive tumour marker for men younger than 60 years.

TRUS: the sensitivity ranged from 52 to 91% and the specificity from 41 to 97%.

Needle biopsy (not guided by TRUS or DRE): random biopsy has been reported to detect between 14 and 94% of the total tumours detected. Complications have been recorded with this technique, and although the event rate is low it is not insignificant.
Staging systems: clinical staging was hampered by a lack of information relating to the natural history of the disease. The technique was relatively insensitive, suffering from subjectivity, potential sampling errors and the lack of a uniformly accepted grading system.

Treatment.

The survival rate was 90% for radical prostatectomy, 60% for radiotherapy, and 80% for conservative management. Short- to medium-term outcomes, particularly morbidity and quality of life issues following treatment, have not been properly addressed.

Screening.

DRE and PSA testing, combined with TRUS and biopsy where indicated, can detect localised prostate cancer in approximately 3 to 5% of men aged over 50 years.

Cost information

A Canadian study estimated an effectiveness ratio of Can$213,000 per life-year gained (1994 prices) for the diagnosis and treatment of screening men aged 50 to 69 years by PSA assay. This was stated to be based on 'insecure data'. An earlier study found a much lower cost per life-year gained, ranging from US$2,267 to $3,687 (1984 prices). Economic studies have not been performed in the UK, but the cost would be likely to be of the order of £500 million to £1.5 billion.

Authors' conclusions

The use of DRE, PSA or TRUS alone to diagnose prostate cancer is not recommended.

DRE is a relatively quick and easy technique, but there are concerns about its accuracy and performance. TRUS-guided biopsy is considered the 'gold' standard; however, it is not completely accurate and complications may occur. The use of PSA testing for all men attending urology clinics cannot be recommended because the comparative effectiveness of treatment options for localised prostate cancer is not known. PSA testing should be limited to men with clinical evidence of prostate cancer who have a life expectancy of at least 10 years, and only following full counselling about the implications and uncertainties of treatment. PSA is, however, recommended in the follow-up of men with known prostate cancer, to monitor tumour progression.

The 'gold' standard for staging localised disease is surgery, including lymphadenectomy. Clinical staging with DRE, PSA and TRUS is unreliable. There is only a 10% difference in survival rate between radical and conservative treatment. Conservative management is, therefore, a reasonable option for men with localised disease. In the absence of evidence from RCTs concerning the relative benefits of treatments, informed patient choice should be a major consideration. The potential costs of a screening programme are huge, and the limited economic evaluations available provide little support for screening. In addition, the efficacy and effectiveness of treatment remain unresolved.

CRD commentary

The full text contains further, relevant information concerning the diagnosis, management and screening of early localised prostate cancer, more than could be included in this abstract. It is highly recommended that those with a specific interest read the full Health Technology Assessment report.

There are few flaws with this extensive review of the literature. Although not a fault of the review, there is a strong bias towards studies conducted in the USA and there is a lack of high-quality randomised trials.

Implications of the review for practice and research

Economic evaluations in the UK are required. A large scale RCT comparing radical prostatectomy with conservative management for men with localised prostate cancer is urgently required to assess the comparative effectiveness and cost-effectiveness of these treatments. This was a thorough review that supported the present Department of Health's guidance on PSA screening.
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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.