

# Clinical and cost-effectiveness of new and emerging technologies for early localised prostate cancer: a systematic review

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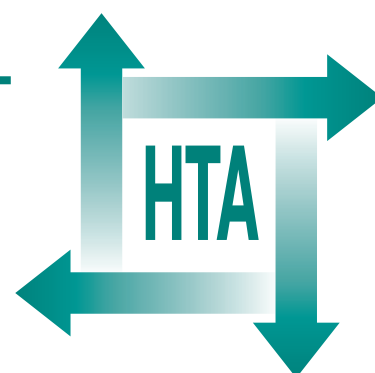
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## *Executive summary*

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# NHS R&D HTA Programme

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## Executive summary

### Background

Cancer of the prostate is the second most common cancer in men in England and Wales with an incidence rate of approximately 71 per 100,000. In 1999 there were 8500 deaths from prostate cancer, accounting for approximately 12% of cancer-related deaths and 3% of all deaths in men. Following the availability of prostate-specific antigen (PSA) testing, which allows symptom-free detection of the disease, there has been a sharp rise in the reported incidence of prostate cancer.

Current management of early prostate cancer includes watchful waiting, radical prostatectomy or radiotherapy. All treatments for prostate cancer may cause unwanted side-effects, including impotence and incontinence. A number of relatively new treatments are being studied in an attempt to develop therapies for early localised cancer that are effective and minimally invasive and result in fewer side-effects. New and emerging treatments include developments in radiotherapy [including brachytherapy, three-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated conformal radiotherapy], new techniques in cryosurgery and hormonal therapies. Other therapies, including gene therapy, are in the very early stages of development.

### Objectives

This report is a review of the clinical and cost-effectiveness of new and emerging technologies for early, localised prostate cancer. A systematic review was undertaken to identify new and emerging technologies and to evaluate clinical and cost-effectiveness through assessment of the best available evidence. The review aimed to assess clinical effectiveness in terms of survival, disease-free survival, quality of life (QoL), including complications and adverse events) and acceptability.

### Methods and results

The first stage of the literature search identified 15 interventions for inclusion in the review:

- *neoadjuvant hormonal therapy* (NHT)
- *adjuvant hormonal therapy* (AHT)
- hormonal monotherapy
- *brachytherapy*
- *3D-CRT*
- *intensity-modulated conformal radiotherapy* (IMRT)
- *cryotherapy*
- high-intensity focused ultrasound (HIFU)
- interstitial microwave thermal therapy (IMTT)
- transperineal radiofrequency interstitial tumour ablation (RITA)
- laser photocoagulation
- gene therapy
- high linear energy transfer radiation
- radionuclide therapy
- vaccine therapy.

Those treatments in italics are selected for discussion.

Further systematic searching was undertaken to identify all literature relating to these interventions. In total, 104 studies evaluating 12 interventions were included in the review of clinical effectiveness. The majority of evidence was of poor quality in the form of case series. No evidence was identified relating to high linear energy transfer radiation, radionuclide therapy or vaccine therapy.

The highest quality evidence identified [13 randomised controlled trials (RCTs)] evaluated the effectiveness of NHT. No evidence of benefit was seen in terms of biochemical disease-free survival. One RCT and three case series evaluated AHT. There was no evidence of benefit in terms of survival, but there was some conflicting evidence that higher risk patients may benefit. The largest number of studies, most of which were descriptive case series, reported results for brachytherapy. There was some evidence to suggest that brachytherapy may be more effective than standard treatments for lower risk patients, although less effective for intermediate- and high-risk patients, in terms of biochemical disease-free survival. Evidence in terms of complications was mixed. Lower quality evidence reported fewer complications than for standard treatments. Higher quality evidence suggested that disease-specific QoL for brachytherapy patients was lower

than for patients receiving standard treatments. The review of 3D-CRT identified four RCTs evaluating treatment-related morbidity. 3D-CRT achieved significantly fewer gastrointestinal complications than standard radiotherapy. Evidence in the form of case series suggested that higher radiation doses achieved better disease control, although patient characteristics were often reported as independent indicators of control. The review of IMRT was based on several case series, the largest of which suggested that IMRT may reduce late gastrointestinal toxicity compared with 3D-CRT. The review of cryotherapy was based on case-series evidence which reported high rates of impotence. Owing to the paucity and poor quality of evidence identified for the remaining interventions (hormonal monotherapy, HIFU, IMTT, RITA, laser photocoagulation and gene therapy), conclusions regarding their clinical effectiveness cannot be drawn.

The results of the clinical effectiveness review should be viewed in the context of the quality of the available evidence. Very few RCTs were identified, with the majority of included studies being descriptive case series, open to patient selection bias and measuring surrogate end-points with short-term follow-up. It is difficult therefore to draw conclusions on the relative benefits or otherwise of the newer technologies owing to the lack of substantive evidence of any quality and the lack of comparisons between the newer technologies and with standard treatments.

No relevant cost-effectiveness studies were identified. An economic model was therefore developed to explore the potential cost-effectiveness of newer treatments. Owing to the lack of disease-free survival data both for the treatments included in the review and for traditional treatments, cost-effectiveness estimates were based on the impact of adverse events on quality-adjusted life-years (QALYs). Owing to the paucity of evidence relating to adverse events for the majority of interventions, the assessment of cost-effectiveness was restricted to brachytherapy,

3D-CRT and cryotherapy compared with standard treatments. Of the new treatments included in the analysis, only cryotherapy appeared potentially not to be cost-effective compared with traditional treatments, owing to the associated high incidence of impotence. The economic analysis is based, however, on the assumption that newer and traditional treatments are equally effective in terms of survival and results are sensitive to the estimates of adverse events and utility values.

## Recommendations for research

Given the lack of high-quality clinical evidence with long-term follow-up and the uncertainty surrounding the assumptions in the economic analysis, the following areas are recommended for further research:

- RCTs with sufficient follow-up to measure benefits in terms of overall survival to include QoL measurement to establish trade-offs between potential adverse events and benefits of treatment.
- The identification of prognostic risk factors among men diagnosed with early prostate cancer.
- QoL studies to compare the utility of health states among patients on active monitoring, patients receiving treatment and the comparable healthy population.
- The relationship between surrogate end-points and survival.
- The adoption of standard definitions for adverse events.

## Publication

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