Cost effectiveness of chemoprevention for prostate cancer with dutasteride in a high-risk population based on results from the REDUCE clinical trial

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The objective was to examine the cost-effectiveness of dutasteride, compared with placebo, for preventing prostate cancer in men, who were at an increased risk. The authors concluded that despite the cost of a preventive drug, dutasteride 0.5mg per day could be cost-effective. There were limitations to the study, which make the authors’ conclusions uncertain.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
To examine the cost-effectiveness of dutasteride, compared with placebo, in preventing prostate cancer.

Interventions
The usual care plus chemoprevention with dutasteride 0.5mg per day was compared with the usual care plus placebo, for healthy men with no prostate cancer.

Location/setting
USA/primary and secondary care.

Methods
Analytical approach:
A Markov model was developed in Microsoft Excel to compare the costs and outcomes over four years, 10 years, or a lifetime. The population was based on the inclusion criteria for the Reduction by Dutasteride of Prostatic Cancer Events (REDUCE) trial, which included men at an increased risk of prostate cancer. The authors stated the perspective to be that of the US payer.

Effectiveness data:
The primary efficacy data, the four-year risk of prostate cancer with or without treatment, were from the REDUCE trial, which was an international, double-blind, placebo-controlled, multicentre, clinical trial. The risk after four years was assumed to be that recorded in the Surveillance, Epidemiology, and End Results (SEER) database. The risk of benign prostate hyperplasia was assumed to change with age, and the baseline incidence was from the literature. The rates of acute urinary retention and surgery for benign prostate hyperplasia were from the REDUCE trial. Mortality was estimated using SEER data, as no deaths were reported in the REDUCE trial.

Monetary benefit and utility valuations:
The utilities by age and health state were from the literature. They were adjusted for improvement in benign prostate hyperplasia symptoms and improvements due to fewer acute urinary retentions and surgeries for benign prostate hyperplasia that could occur with dutasteride. They were also reduced for adverse effects that could occur with dutasteride.

Measure of benefit:
The model estimated a number of clinical outcomes, such as the number of prostate cancers by high-grade or low-grade tumour, as well as life-years, and quality-adjusted life-years (QALYs) gained. The benefits were discounted at a rate of
3%.

Cost data:
The costs included annual usual care for healthy men, medications, the management of benign prostate hyperplasia, prostate cancer work-up and staging, prostate cancer treatment, adverse events due to prostate cancer treatment, and adverse events due to chemoprevention. All costs, except those for the drugs, were from the Medicare reimbursement schedules. Dutasteride and alpha-blocker costs were based on their recommended dosing and wholesale acquisition costs. Values were reported in 2009 US dollars ($). Where necessary, they were inflated using the medical component of the Consumer Price Index. All costs were discounted at 3% per annum.

Analysis of uncertainty:
To test how robust the model assumptions and parameters were, the authors produced one-way and probabilistic (second-order Monte Carlo simulation) sensitivity analyses. The results were presented in scatter plots and cost-effectiveness acceptability curves.

Results
Over 10 years, there were fewer prostate cancers in patients on dutasteride (251 per 1,000 patients) than in those on placebo (312 per 1,000), but the costs were higher; $15,341 for dutasteride and $12,316 for placebo. The life-years were not substantially affected, but there was an increase in QALYs of 0.14 with dutasteride.

Chemoprevention with dutasteride appeared to be cost-effective, with an incremental cost of $21,781 per QALY gained or $50,254 per prostate cancer avoided. Over four years, the incremental cost per QALY gained was $18,409, and over a lifetime, it was $22,498.

The sensitivity analyses showed that these results were robust to changes in the parameters.

Authors' conclusions
Authors concluded that despite the cost of the preventive drug, dutasteride 0.5mg per day could be cost-effective for men at an increased risk of prostate cancer.

CRD commentary
Interventions:
No explicit justification was provided for the comparator, but it seems to have been the usual care in the authors’ setting. It was not clear if other relevant comparators were available and should have been analysed.

Effectiveness/benefits:
The lack of detail on the clinical trial makes an assessment of its quality and validity impossible. The use of other sources to augment the trial data was appropriate and the SEER database is a widely accepted source. It is not clear whether the utility data or the adjustments made were appropriate for the model population; few details were provided, making a full assessment impossible.

Costs:
The analysis of costs was performed from the perspective of the US payer. It appears that all the relevant categories were analysed. The costs were given as aggregate totals and no resource use data were presented. All values were presented in tables and the sources were given, but their generalisability to alternative settings might be limited.

Analysis and results:
The analytic approach was appropriate for the study objective. The authors presented their results in full and provided a cost-effectiveness plane and acceptability curve. The sensitivity analyses (one-way and probabilistic) suggested that the results were sensitive to a number of parameters, but most sensitive to the reduction in risk of prostate cancer with treatment, and the utilities. The lack of detail in reporting and the resulting uncertainty in the validity of the inputs, makes the results uncertain.

Concluding remarks:
There were limitations to the study, which make the authors’ conclusions uncertain.
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