Cost-effective models for flutamide for prostate carcinoma patients: are they helpful to policy makers?
Bennett C L, Matchar D, McCrory D, McLeod D G, Crawford E D, Hillner B E

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.

Health technology
Using first-line hormonal therapy combined with flutamide (CAB) versus first-line hormonal therapy alone (surgical orchiectomy or LhRH analogues) for prostate carcinoma patients with minimal or severe diseases.

Type of intervention
Treatment and secondary prevention.

Economic study type
Cost-utility analysis.

Study population
70 year old male patients with metastatic prostate carcinoma with severe or minimal disease.

Setting
Hospital. The economic study was carried out in the USA.

Dates to which data relate
Effectiveness and cost data were reported from three studies published in 1993 and 1995. No dates for the prices used were stated.

Source of effectiveness data
Effectiveness data were derived from a review of previously completed studies.

Modelling
A decision analysis model using a Markov process was constructed to model the prognosis of patients with metastatic prostate carcinoma over time. The Markov model employed a 3-month cycle.

Outcomes assessed in the review
The outcome assessed in the review was clinical efficacy: progression of disease and overall survival benefits.

Study designs and other criteria for inclusion in the review
Although not reported as an inclusion criterion, in practice a clinical trial and a meta analysis were used as references for the clinical probabilities.
Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Three studies were actively used as the references for the clinical probabilities.

Methods of combining primary studies
The authors used the narrative method to combine the results of the primary studies.

Investigation of differences between primary studies
Not reported.

Results of the review
The following probabilities were used in the model:

probability (range) per 3 month of response to death, 0 (0-0.05);
response or stable to progression for severe disease, 0.12 (0.07-0.20);
response or stable to progression for minimal disease, 0.06 (0.03-0.10);
progression or death, 0.19 (0.15-0.30);
the relative efficacy of flutamide therapy in reducing death, 0.25 (0-0.50).

Methods used to derive estimates of effectiveness
Using a time-trade off instrument, a focus group of 40 physicians (25 urologists and 18 oncologists) were employed to evaluate the quality of life estimates corresponding to the four major states investigated:

(a) asymptomatic (stable disease);
(b) stable disease with gastrointestinal side effects;
(c) moderate pain and fatigue; and
(d) severe pain and fatigue.

Some assumptions were made by the authors regarding the three health states (response with therapy and/or stable state; progression, and death) after the initial 3 months of the start of the disease.

Estimates of effectiveness and key assumptions
Based on the physicians' assessment, the median utility values (and the inter-quartile ranges) for the 4 scenarios
associated with metastatic prostate carcinoma were:

state (a) 0.92 (0.88, 0.96);

state (b) 0.84 (0.75, 0.88);

state (c) 0.83 (0.67, 0.88); and

state (d) 0.42, (0.25, 0.59).

The assumptions made regarding the three health states (response with therapy and/or stable state; progression, and death) after the initial 3 months of the start of the disease were as follows:

(1) the survival after progression was the same, independent of flutamide;

(2) the same probability of progression from response or stable disease was assigned;

(3) it was assumed that 95% of untreated patients with severe and minimal disease would die in 7 and 10 year period, respectively;

(4) orchiectomy and LhRH analogs were assumed to be equally effective;

(5) it was assumed that gastrointestinal toxicity would occur in 15% of patients undergoing flutamide therapy within 3 months of starting the therapy.

Measure of benefits used in the economic analysis

The benefit measure used was Quality Adjusted Life Years (QALYs). A decision analytic model using a Markov process was employed to model the prognosis of prostate carcinoma patients over time. 43 physicians were invited to assess the trade-off between 4 major states of life for patients with metastatic prostate carcinoma with severe or minimal disease. The valuation tool used was time trade-off.

Direct costs

Costs were discounted. Quantities were not reported separately from the costs. The cost calculations and items included were reported in detail in another study published in 1995. The perspective considered in the cost analysis was that of a global payer. All direct health care costs paid by Medicare or the Department of Veterans' Affairs were included in the cost analysis. The date of the price data was not specified.

Indirect Costs

Not considered.

Currency

US dollars ($).

Sensitivity analysis

One-way simple sensitivity analyses were performed on clinical and cost variables.

Estimated benefits used in the economic analysis

The flutamide therapy had an average survival benefit of 5.2 months for men with minimal disease and 4.0 months for men with severe disease, using a baseline relative efficacy of 25% from the NCI trial. The corresponding values in the case of using the overview estimates with relative efficacy were reported as 1.9 months for minimal disease and 1.5
months for severe disease.

**Cost results**
The discount rate in the baseline analysis was 5% and the range was 0-10. The baseline costs per 3 months (range) if flutamide was used were $800 ($600-1,000); for response or stable disease the cost was $300 ($100-1,000); for progressive disease, $3,600 ($1,800-10,000); and for death, $10,000 ($3,000-25,000). The average total cost associate with each strategy was not reported.

**Synthesis of costs and benefits**
The cost per QALY saved had a range from $25,300 (corresponding to a utility score estimate of 1 for early progression disease) for patients with minimal disease to $17,200 (corresponding to a utility score estimate of 0.42 for early progression disease) for patients with severe disease. The cost per QALY saved reported, when the sensitivity analysis was performed, ranged from $9,160 in the case of 25% price reduction of flutamide to $41,000 for patients with severe disease for the case of 10% efficacy.

**Authors’ conclusions**
Using NCI trial data, flutamide has an incremental cost-effectiveness more favourable than most therapies, while estimates based on the PCTCG found a less favourable outcome for the drug. Concerns about out-of-pocket expenditures and efficacy limit flutamide utilisation; quality of life considerations are less cogent.

**CRD COMMENTARY - Selection of comparators**
No justification was provided for the choice of the comparator. You, as a database user, should therefore consider whether this a widely used health technology in your own setting.

**Validity of estimate of measure of benefit**
The internal validity of the estimates of benefit measure can not be assessed due to lack of information regarding the sources used as references for the clinical outcomes in the study. The paper contains no evidence of a comprehensive literature review or of a quality assessment of the studies included in the review.

**Validity of estimate of costs**
Resource utilisation was not reported separately from the costs. Adequate details of methods of cost estimation were not given. A cost analysis from a societal perspective might have been more appropriate.

**Other issues**
Given the apparent lack of a comprehensive literature review and a quality assessment of the studies included therein, full presentation of the sensitivity analysis performed, and statistical analysis of the costs, the results may need to be treated with some caution. The issue of generalisability to other settings was not addressed.

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**Bibliographic details**
Other publications of related interest

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Subject indexing assigned by NLM

MeSH
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