Comparison of molecular and conventional strategies for followup of superficial bladder cancer using decision analysis

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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.

Health technology
Two alternative follow-up strategies for the management of recurrence in patients with a history of superficial bladder cancer were examined. The strategies were cystoscopy and cytology versus urinary markers.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients of any age with disease-free status at first follow-up visit and pathological stage Ta or T1 transitional cell carcinoma of the bladder with no evidence of carcinoma in situ. The patients required surveillance for disease recurrence.

Setting
The setting was secondary care. The economic study was carried out at the Toronto Hospital, Toronto (ON), Canada.

Dates to which data relate
No dates for the effectiveness evidence were reported. The resource use data were gathered from 1987 to 1997. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from authors' assumptions and a single study.

Link between effectiveness and cost data
The costing was performed on a different sample of patients from that used in the effectiveness study.

Study sample
Power calculations to determine the sample size were not performed. A single group of patients was included in the effectiveness study. There were 361 patients with a mean age of 64.9 years (range: 29.3 - 93.2 years). Of these, 300 patients were in the Ta stage and 61 in the T1 stage. The method used to select the sample was unclear. No comparison group was considered.
**Study design**
The effectiveness data came from a review of case series. The patients were identified from a single centre, the Toronto Hospital. The average length of follow-up was 17.6 months (range: 0.1 - 119 months). It was unclear whether some patients were lost to follow-up.

**Analysis of effectiveness**
It appears that all the patients included in the initial study group have been considered in the effectiveness study. The analysis of effectiveness aimed to assess the sensitivity and specificity of the urinary marker test and the disease recurrence rate. A correlational analysis of survival estimates was carried out to identify the factors that had a significant impact on recurrence-free survival.

**Effectiveness results**
The sensitivity of the urinary marker test was 95% and the specificity was 77%.

The hazard rates for recurrence in the cohort were not reported.

The statistical test suggested that tumour stage, (p=0.0036), and grade, (p=0.007), were significantly associated with recurrence-free survival.

**Clinical conclusions**
The effectiveness study provided the data that were used in the decision model.

**Modelling**
A decision tree model was used to estimate the overall costs associated with the two follow-up strategies over a 3-year period. The model was populated with probability data derived both from both authors’ assumptions and from a cohort of patients followed at the study centre.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions that were used in the decision model. The most critical assumption concerned the impact of the two interventions on patient survival.

**Estimates of effectiveness and key assumptions**
The authors assumed the following:

- the two follow-up strategies were equally effective in terms of their impact on patient survival;
- the strategy of cystoscopy and cytology was the 'gold' standard with a 100% specificity and sensitivity;
- some tumours would test marker negative and might continue to be negative despite recurrence, which would lead to false-negative results;
- a positive result from the urinary marker would need confirmatory cystoscopy;
- about 20% of tumours progressed silently;
- all patients with progression required radical cystectomy;
- the patients underwent a follow-up evaluation every 3 months in year 1, every 6 months in year 2, and once in year 3;
- the risk of recurrence after treatment was the same as the initial risk of recurrence.
Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic evaluation since the two interventions were considered equally effective. Therefore, a cost-minimisation analysis was carried out.

Direct costs
Discounting could have been relevant since the time horizon of the analysis was 3 years. However, it was not applied. The unit costs were presented, but the quantities of resources used were not. The health services in the economic evaluation were cystoscopy (e.g. professional fee, facility and equipment), cytology (e.g. technical and professional fees), radical cystectomy (e.g. professional and institutional fees such as hospital wards, blood bank, laboratory, radiological expenses), and urinary marker. The cost/resource boundary of the study appears to have been that of the health service payer. The source of the unit costs was not stated, but is likely to have been the study centre. The resource use data were estimated on the basis of assumptions made in the decision tree and the sample of patients used in the effectiveness study. The price year was not reported.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were performed to assess the impact of variations in the key model inputs on the estimated costs of the two surveillance strategies. Plausible ranges were derived from the literature or were derived from authors’ assumptions. Univariate and multivariate analyses were performed. The cost thresholds (points at which the two strategies had equal costs) were estimated for a range of specificity and sensitivity values of the urinary marker test, using the stage and degree of disease as the main covariates.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The cost of cystoscopy and cytology was $240 for every follow-up visit during the 3-year period.

The cost of urinary marker testing was highest at the first follow-up visit, $228 for stage Ta and $237 for stage T1. However, it decreased over time (until $158 for stage Ta and $159 for stage T1).

In any case the expected cost of urinary marker testing was lower than the expected cost of cystoscopy and cytology.

The sensitivity analysis showed that the probability of recurrence and the specificity and sensitivity values had a strong impact on the estimated costs.

For urinary marker testing to have a cost-advantage it required a minimum sensitivity of 70% at the 18-month follow-up. The minimum specificity required was 37% at the 36-month follow-up.
Despite variations in treatment patterns, the cumulative costs were lower among patients in the urinary marker group.

**Synthesis of costs and benefits**
The costs and benefits were not combined because a cost-minimisation analysis was carried out.

**Authors' conclusions**
Over a 3-year period, the use of urinary marker testing for patients with superficial bladder cancer led to cost-savings in comparison with the standard approach of cystoscopy and cytology. This conclusion held under several scenarios that were considered in the study.

**CRD COMMENTARY - Selection of comparators**
The authors justified the choice of the interventions that were compared in the study. The strategy of cystoscopy and cytology were considered the gold standard, although it represented an invasive approach that was associated with some morbidity and pain. Urinary marker testing was a more recent strategy for recurrence surveillance, and the fact that only a voided urine specimen was required represented an advantage. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness was characterised by the assumptions of equal effectiveness (survival) of the two surveillance strategies. This assumption was derived from the authors' opinion and was not supported by a panel of experts or other studies. The authors stated that some differences could have been observed in terms of quality of life, but this was beyond the scope of the study. Therefore, the assumption that survival was comparable between the two interventions was not explicitly justified. Most of the effectiveness data were used as model inputs and came from authors' assumptions and data derived from a series of patients observed at the study hospital. However, no explicit control group was used in the analysis and only a few details of the data source were provided. Further, most of these data were not reported and uncertainty surrounding the assumptions was not investigated in the sensitivity analysis. These issues tend to limit the internal validity of the analysis.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the analysis because a cost-minimisation analysis was conducted.

**Validity of estimate of costs**
The actual perspective adopted in the study is likely to have been different from that stated by the authors. In fact, the indirect costs were not included in the economic evaluation and only those costs relevant to the health service payer were considered. The analysis of resource use used data derived from the sample of patients involved in the effectiveness study, but some assumptions were also made in the decision model. Details of the unit costs were provided, but the information on resource use was limited. The price year was not reported, thus making reflation exercises in other settings difficult. The costs were calculated for groups stratified by disease stage, which had a substantial impact on the economic outcomes. Discounting was not performed, but it could have been relevant since the costs per patient were incurred during more than 2 years.

**Other issues**
The authors did not compare their findings with those from other studies. They also did not explicitly address the issue of the generalisability of the study results to other settings. However, sensitivity analyses were performed to consider variations in urinary marker equipment across different medical centres. This enhanced the external validity of the analysis. The authors stated that most of the assumptions made in the analysis favoured the gold standard strategy, therefore their findings were conservative.
Implications of the study
The authors suggested that future studies with larger sample size should assess the role played by other prognostic factors. A further interesting area of research would be a subgroup analysis aimed at identifying those patients who may receive more benefits from the surveillance programme.

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