Economic evaluation of NMP22 in the management of bladder cancer

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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
The use of nuclear matrix protein 22 (NMP22) to detect the recurrence of bladder cancer after the transurethral resection of a bladder tumour (TURBT).

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised individuals who had prior bladder cancer and had undergone a TURBT.

Setting
The analysis used the results from a study by Soloway et al. (see Other Publications of Related Interest), the setting of which was not stated. The economic analysis was carried out in Quebec, Canada.

Dates to which data relate
The dates to which the data related were not reported. The effectiveness data in terms of the sensitivity and specificity of NMP22, and the rate of transitional cell carcinoma recurrence (RTCCR), were obtained from the study by Soloway et al. The resource consumption within each modality was calculated for the first 6 months following initial resection. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study and from the authors' assumptions.

Link between effectiveness and cost data
The costing was carried out retrospectively, but not on the same patient sample as that used in the effectiveness study.

Study sample
There were no sample data available since this study modelled the cost-effectiveness of the proposed modalities. The effectiveness data were estimated from another study. Therefore, no sample size was determined, and power calculations were not carried out. The rate of transitional cell carcinoma (29.5%) was obtained from a prior study. These were the only data related to the study sample.
Study design
This was, in effect, an uncontrolled diagnostic test evaluation. It was supported by the authors' assumptions regarding the perfect accuracy of cystoscopy.

Analysis of effectiveness
The basis for the analysis (intention to treat or treatment completers) only was not reported. The outcome measure was the rate of bladder cancer recurrence detected by the monitoring procedure. Sensitivity, specificity and the rate of recurrence were also reported.

Effectiveness results
The sensitivity (69.7%) and specificity (78.5%) of NMP22 were obtained from a prior study. The rate of recurrence 3 months after TURBT was 29.5%. The rate of detecting recurrence was 0.911 for NMP22.

Clinical conclusions
Under the conditions of recurrence of bladder tumour, and the sensitivity and specificity for NMP22 reported in the study, the NMP22 strategy was less effective in detecting recurrence than the conventional cystoscopy.

Modelling
A model was used to estimate the costs of the proposed alternatives. The purpose of the model was to determine the cost-efficacy of both modalities. The study was performed using a decision-analysis technique that compared a follow-up modality using NMP22 with the conventional follow-up SRMP, for the first 6 months after an initial TURBT. It was stated that, when NMP22 was less than 10 U/mL, the 3-month follow-up cystoscopy was omitted. When the NMP22 was over this amount, the 3-month cystoscopy was performed. The 6-month cystoscopy was performed for both alternatives.

Estimates of effectiveness and key assumptions
The authors made some assumptions. It was assumed that, if there was a recurrence, it would be detected by the routine cystoscopy (SRMP). Therefore, missed recurrences were presumed to occur only when a false negative result was obtained using NMP22.

Measure of benefits used in the economic analysis
The summary measure of benefit was the rate of detecting recurrence.

Direct costs
The resource quantities and the costs were reported separately.

The direct costs considered in the analysis were those of the hospital. The costs included for SRMP were the urologist's fees for patient visits (Can$31) and cystoscopies (Can$45), the hospital costs for cystoscopic examinations (Can$52.61), the pathologist's fees for cytology (Can$12.50), and the laboratory costs for cytologies (Can$14.58). The costs included for NMP22 were for the test (Can$43.78), the laboratory (Can$1.59), and the corresponding costs related to cystoscopy and cytology according to the number of times the patients had to receive them (1 or 2).

The costs for the TURBT were excluded as they were considered to be the same for both modalities, and the analysis looked primarily at the monitoring procedures.

The costs were estimated using actual data. The study reported the average costs. Discounting was not carried out as the costs were incurred over less than 2 years. The costs for a cystoscopic examination were obtained from the current Quebec fee schedules. The hospital costs represented the average hospital cost for an endoscopic examination in a
Quebec hospital following the AS-471 report of the "Ministere de la sante et des services sociaux". The cost of NMP22 was estimated from the NMP22 current Canadian price list (Paladin Labs Inc.). The laboratory costs for NMP22 were for a batch of 39 tests being processed at a time. The price year for the costs of cystoscopy and cytology was 1998. The price year for the costs of NMP22 was not given.

**Statistical analysis of costs**
No statistical analysis of the costs was reported.

**Indirect Costs**
The indirect costs were not reported.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
As sample data were unavailable, the robustness of the results was tested using a series of one-way sensitivity analyses. These were carried out on:

- the probability of recurrence (20, 40%);
- the sensitivity and specificity of NMP22 (using the results of other studies); and
- the costs of cystoscopic examination (+/- 50%) and NMP22 testing (the cost of an additional visit).

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

**Cost results**
The average total costs for the 6-month follow-up were Can$257 for NMP22 and Can$311 for SRMP.

The incremental cost for SRMP was Can$55.

The costs derived from the 3-month delay in the diagnosis of a recurrence for patients with an NMP22 false negative result were excluded.

**Synthesis of costs and benefits**
The incremental cost-efficacy ratio was Can$613. This represents the additional cost to detect an additional recurrence by changing from the NMP22 strategy to the conventional strategy. The sensitivity analyses showed a cost-efficacy maximum of Can$1,020 with recurrence at 20%.

**Authors’ conclusions**
The use of nuclear matrix protein 22 (NMP22) can be less expensive than the standard recommended monitoring procedure (SRMP), and it can decrease the patients’ discomfort by reducing the need for cystoscopy. In addition, since it can be performed a few days after the transurethral resection of a bladder tumour (TURBT), residual or recurrent tumours can be identified earlier than at the scheduled cystoscopy and can therefore be treated earlier.
CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used. SRMP was considered because it represented the current recommended monitoring procedure in the diagnosis of bladder cancer after TURBT.

Validity of estimate of measure of effectiveness
The analysis was based on a decision analysis, using the results of an uncontrolled study. This seems to have been appropriate for the study question. However, since there were no sample data available, it is not possible to assess whether the sample was representative of the study population, or of what design the study of Soloway et al. was. Also, the authors assumed that cystoscopy would be perfectly accurate.

Validity of estimate of measure of benefit
The measure of benefit was the rate of detecting recurrence, which was derived from the decision model. This was appropriate for this technology, but it does not allow comparison with others. However, the main problem was that the authors, in their conclusions, do not appear to have placed any value on this measure, in that they advocate the least beneficial technology. These conclusions were drawn entirely on the basis of lower cost, and the unsupported suggestion of reduced discomfort through a reduced need for cystoscopy.

Validity of estimate of costs
Although it was stated that a health service perspective was used for the analysis, it would have been useful to have considered the indirect costs. These indirect costs were related to the 3-month delay in the diagnosis of a recurrence for patients with a false negative NMP22. However, the omission of these costs does not seem to have affected the results since the authors stated that NMP22 was 100% sensitive in detecting invasive disease. Therefore, they stated that the consequence of not identifying these recurrences until the next scheduled cystoscopy would be minimal. Moreover, although SRMP was assumed to detect any recurrence, the authors warned that cystoscopy is an invasive procedure and may cause significant discomfort to the patient. The use of NMP22 reduced the need for cystoscopic examination for those patients with a result of less than 10 U/mL.

Another fact to be considered is that the cost of NMP22 was estimated on the basis that 39 tests could be processed at a time. A reduction in the number of tests would increase the estimated laboratory costs for this modality. However, given the results of the sensitivity analysis, this does not seem to have altered the results of the study significantly.

The costs and the quantities were reported separately. This enhanced the generalisability of the results to other settings. The average costs were estimated from published sources. No statistical analysis of the quantities or costs was performed. Nevertheless, the one-way sensitivity analysis showed that the results obtained for some of the parameters were robust. However, these analyses seem not to have been used, given that the authors did not show how their conclusions could be attained by the results. For example, it might be reasonable to consider recommending NMP22 when the cost increase to use the conventional strategy becomes very large, compared with the gain in detecting recurrences.

Other issues
The authors did not make appropriate comparisons of their results with the findings from other studies. They warned that the analysis used a limited number of studies and a relatively small number of patients.

The authors did address the issue of generalisability, and stated that a comparable analysis could be conducted using the sensitivity, specificity and costs for other tumour markers. The authors did not present their results selectively. The scope of the analysis (the comparison of cost and cost-efficacy between NMP22 and SRMP after a TURBT) was reflected in the authors’ conclusions. The authors reported some limitations to their study. In particular, the limited number of studies on which their findings were based and the relatively small number of patients.

Implications of the study
The authors recommend considering the implementation of NMP22 as a routine follow-up monitoring procedure, particularly for patients with low-grade tumours. This recommendation should be viewed with caution given the evidence showing a reduced detection of tumour recurrence, despite it being cost-saving.

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**Other publications of related interest**


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