NMP22 is a sensitive, cost-effective test in patients at risk for 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
This study evaluated the use of an enzyme immunoassay for nuclear mitotic apparatus protein in voided urine (NMP22) as a marker for the early detection of transitional cell carcinoma of the bladder in patients with hematuria or other indications at risk for malignancy. The sensitivity and specificity of NMP22 were compared with urinary cytology.

Type of intervention
Screening; Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with microscopic or gross hematuria, or other indications for risk of bladder cancer.

Setting
The setting was secondary care. The economic study was carried out in Cleveland, Ohio, USA.

Dates to which data relate
The effectiveness data were collected between April 1997 and February 1998. The dates for the resource use data were not reported. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
Cost data were collected from reimbursement and charge data in the authors' institution.

Study sample
No power calculations were reported to determine the sample size. All patients who were referred to the urology clinic for microscopic or gross hematuria, or other indications for risk of bladder cancer, were asked to provide a urine sample. The samples from 330 patients were tested by both the NMP22 and urology cytology tests, and all of the 330 patients were included in the final analysis.

Study design
The study was a single-centred, controlled trial carried out in the Cleveland Clinic Foundation. All patients were asked to provide a urine sample for the NMP22 test and cytology before cystoscopy. The urine was collected and divided into 2 aliquots, of which one was transported to the urology laboratory for NMP22 analysis, and one to the cytopathology laboratory of the Cleveland Clinic. The urologist and pathologist were masked to the results of the test. The follow-up was limited to cystoscopy for all patients. The authors did not report the time period between the patients providing samples for the tests and cystoscopy. There was no loss to follow-up.

**Analysis of effectiveness**

All patients included in the study were accounted for in the analysis. The primary outcome measures were the sensitivity, specificity, positive predictive value and negative predictive value of both the NMP22 test and the cytology test.

**Effectiveness results**

The sensitivity of NMP22 test was 100% (18/18 true positive tests for bladder cancer) (95% CI: 82 - 100). The sensitivity of the cytology test was 33% (6/18 true positive tests for bladder cancer) (95% CI: 13 - 59).

The specificity of the NMP22 test was 85% (267/312 true negative tests for bladder cancer) (95% CI: 82 - 90), whilst the specificity of the cytology test was 100% (312/312 true negative tests for bladder cancer) (95% CI: 97 - 100).

The positive predictive value of the NMP22 test was 29% (18 true positive tests out of 63 positive tests) (95% CI: 18 - 63), in contrast to the cytology test for which the positive predictive value was 100% (6/6) (95% CI: 54 - 100).

The negative predictive value of the NMP22 test was 100% (266/266) (95% CI: 99 - 100), and that of the cytology test was 96% (312 true negative tests out of 324 negative tests) (95% CI: 94 - 98).

**Clinical conclusions**

The authors concluded that urinary NMP22 is an effective, simple and non-invasive marker for the detection of bladder cancer.

**Measure of benefits used in the economic analysis**

No summary measure of health benefit was defined in the economic analysis. This was therefore a cost-consequences analysis.

**Direct costs**

Costs and quantities were not reported separately. The costs for the hospital were based on the charges and reimbursement levels, rather than prices, for the tests at the institution at which the study was undertaken (Cleveland Clinic Foundation). The following direct costs were included in the analysis: the charge for a NMP22 test ($20 per sample); the charge for an urinary cytology test ($100); the reimbursement cost for each cystoscopy ($106 for MEDICARE and $416 for private insurance carriers). Discounting was not required due to the implicit short time frame of the study. The price year was not reported.

**Statistical analysis of costs**

No statistical analysis of costs was conducted.

**Indirect Costs**

No indirect costs were included in the analysis.
Currency
US dollars ($). No currency conversions were reported.

Sensitivity analysis
No detailed sensitivity analysis was reported, but the authors did explore the impact of the type of reimbursement schedule (Medicare versus private insurance carrier) on costs.

Estimated benefits used in the economic analysis
The reader is referred to the effectiveness results reported earlier.

Cost results
The authors reported that elimination of 267 cystoscopies through the use of urinary NMP22 would result in a cost saving ranging from $28,032 to $111,072 (depending on the type of insurance carrier). For the 330 patients requiring evaluation the authors reported that the cost of NMP22 testing would be $6,600, compared to $33,000 for cytology testing, thus producing an overall cost saving of $26,400. The use of the urinary NMP22 test versus urinary cytology to determine whether cystoscopy is required to eliminate the risk of bladder cancer would result in a cost saving of $54,072 to $137,472, and a saving of at least $3,039 per diagnosis of bladder cancer.

Synthesis of costs and benefits
No synthesis of costs and benefits was reported.

Authors' conclusions
The authors concluded that urinary NMP22 is a simple, non-invasive, cost-effective marker for the detection of bladder cancer.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of comparator used, namely that it represented current practice in the authors' setting. You, as a user of this database, should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a controlled trial design. Urine samples from each patient were divided into two and tested using both of the screening tests. The results for each test were compared to cystoscopy plus biopsy (the gold standard diagnosis tool) to determine the sensitivity and specificity of each. This design was appropriate for the study question. The urologist and pathologist who compared the screening test results to the cystoscopy and biopsy data were masked to the test used to obtain the screening data. The study sample appears to have been representative of the study population. However, the authors did not report the methods used to select patients for participation in the trial, or whether all relevant patients were included. The authors did not report details of the patients excluded from the trial or who refused to participate. The authors did not report the sample size required to detect statistically significant differences. Appropriate statistical analyses were undertaken to take account of potential biases.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit, thus there was no measure of the impact on health status of differences in sensitivity and specificity between the tests. The tests had different profiles in terms of false positive and false negative results. It is important to assess the impact of these differences on the health and social well being of patients.
Validity of estimate of costs
The only costs reported by the authors were the cost per sample of the NMP22 test and urinary cytology and the reimbursement cost of each cystoscopy procedure following a positive screen test results. Costs and quantities were not reported separately. The study used charges rather than unit costs in the cost estimates. Charges do not reflect opportunity cost and the use of charges, without also reporting resource use data, limits the generalisability of the study’s findings. The authors did not report any currency conversions, and discounting was not undertaken because of the short time frame of the study.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, but did not fully address the issue of generalisability to other settings. The study enrolled patients with symptoms of microscopic gross hematuria and other indications for risk of bladder cancer, and this was reflected in the authors' conclusions. The authors did not, however, report any limitations to their study.

Implications of the study
The authors concluded that urinary NMP22 is a simple, non-invasive, cost-effective tumour marker for the detection of bladder cancer. Consequently they propose that the use of NMP22 might replace urinary cytology and reduce the frequency of diagnostic cystoscopy in the future.

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