Neural network using combined urine nuclear matrix protein-22, monocyte chemoattractant protein-1 and urinary intercellular adhesion molecule-1 to detect 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
A neural network for the detection of bladder cancer was examined. The network was based on a combination analysis of three tumour markers, specifically urinary intercellular adhesion molecule-1 (UIAM1), nuclear matrix protein-22 (NMP22) and monocyte chemoattractant protein-1 (MCP1). These were measured in urine using commercially available enzyme-linked immunosorbent assays. An algorithm was created with three sets of cut-off values, modelled to be 100% sensitive for superficial bladder cancer, 100% specific for superficial bladder cancer, and 100% specific for muscle invasive cancer.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients presenting to the urology clinic for cystoscopic evaluation.

Setting
The setting was a hospital. The economic study was carried out at the Division of Urology of the Albany Center in Albany (NY), USA.

Dates to which data relate
The effectiveness and resource use data were gathered from November 1999 to September 2000. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was performed prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations were conducted on the basis of prior studies. The calculations suggested that a minimum sample size of 108 patients was required to achieve a 99% confidence value, (p=0.01). The method of sample selection was not reported. The study sample included 253 patients with a mean age of 62.9 years (age range: 18 - 89), of which 182 were...
men. The sample was split into two groups. Group 1 comprised 98 patients with a history of bladder cancer, while group 2 comprised 155 patients undergoing initial cystoscopy. Each group was then randomised into two sub-groups with comparable demographics.

**Study design**
This was a randomised double-blind study, which was carried out in a single centre. The method of randomisation was not reported. The patients were not followed after cystoscopy was performed. No loss to follow-up was reported. The physicians were blinded to the results of the urine test or cystoscopy.

**Analysis of effectiveness**
It appears that all the patients included in the initial study sample have been taken into account when estimating the effectiveness (i.e. intention to treat). The primary health outcomes used in the analysis were the specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV). The authors stated that the study groups were comparable at baseline.

**Effectiveness results**
For haematuria, the sensitivity was 92.6%, the specificity 51.8%, the PPV 18.7%, and the NPV 98.3%.

For cytology, the sensitivity was 66.7%, the specificity 81%, the PPV 29.5%, and the NPV 95.3%.

For NMP22 alone, the sensitivity was 70.4%, the specificity 45.6%, the PPV 13.4%, and the NPV 92.8%.

For MCP1, the sensitivity was 14.8%, the specificity 96.5%, the PPV 33.3%, and the NPV 90.5%.

For UIAM1, the sensitivity was 14.8%, the specificity 96.5%, the PPV 33.3%, and the NPV 90.5%.

For the cancer-sensitive algorithm, the sensitivity was 100%, the specificity 75.7%, the PPV 32.9%, and the NPV 100%.

For the cancer-specific algorithm, the sensitivity was 22.2%, the specificity 100%, the PPV 100%, and the NPV 91.5%.

For the muscle invasive algorithm, the sensitivity was 80%, the specificity 100%, the PPV 100%, and the NPV 99.6%.

**Clinical conclusions**
The effectiveness analysis showed that the diagnostic characteristics of the neural network were superior to those observed with the standard approaches.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was used. A cost-consequences analysis was therefore conducted.

**Direct costs**
Discounting was not relevant since the costs were incurred during a short time. The unit costs were analysed separately from the quantities of resources used. The health services included in the economic evaluation were cytology (including slide preparation and pathologist reading), office cystoscopy, and the combined assay. The cost/resource boundary of the analysis was that of the study hospital. The costs were estimated on the basis of assumptions made by the authors. Resource use was based on the test's hypothesis and results. The price year was not reported.

**Statistical analysis of costs**
The costs were treated deterministically.

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

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were not conducted.

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

**Cost results**
According to current guidelines, cytology and cystoscopy would both be performed on 178 patients, thus the total costs would be $61,054.

Following the proposed approach, the assay would be performed on 178 patients and cystoscopy only on 65 patients, in which case the total costs would be $36,450.

**Synthesis of costs and benefits**
Not relevant because a CCA was performed.

**Authors' conclusions**
The new approach to screening for bladder cancer was effective in detecting the disease, thus reducing the discomfort of unnecessary invasive procedures in false-positive patients. Cost-savings were also observed in comparison with the current cancer screening protocol of haematuria and cytology.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear. Haematuria and cytology were selected as the basic comparator because they represented the standard protocol for the detection of bladder cancer at the authors' institution. You should decide whether they represent an appropriate comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness used a double-blind randomised study, which was appropriate for the study question. However, the random allocation procedure was used only to define the algorithm cut-off levels, because the study intervention was then applied to all individuals included in the initial study sample. Thus, the effectiveness study appears to have been based on a within-group comparison since all patients underwent both the standard and the new approaches. It was unclear whether the study sample was representative of the study population since there were few details of either the study sample or the method used to select it. The method of randomisation was not reported. Power calculations were performed in the preliminary phase of the study. Hence, the sample size was appropriate for the study question. These issues tend to enhance the internal validity of the effectiveness study.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the economic analysis. The analysis was therefore categorised as a cost-consequences analysis.

**Validity of estimate of costs**
The economic analysis was conducted from the perspective of the hospital. Only those costs strictly related to the performance of the tests were included in the analysis. The unit costs and the quantities of resources used were reported separately, thus simplifying the reproducibility of the study in other settings. The costs were treated deterministically and no sensitivity analyses were conducted. Thus, the cost estimates were specific to the study setting. The cost data were derived from assumptions made by the authors. The adoption of a wider perspective and the subsequent inclusion of more cost items would have been helpful. The price year was not provided.

**Other issues**
The authors made some comparisons of their findings with those from other studies. However, they did not address the issue of the generalisability of the study to other settings. Sensitivity analyses were not performed, thus the external validity of the analysis was low. The authors stated that their model may not be applicable to all clinical settings because of the procedures and speed required to analyse the specimens.

**Implications of the study**
The study results suggested that tumour markers might be useful in detecting bladder cancer and in avoiding unnecessary invasive procedure in patients with no cancer, thus having important implications for the patient's quality of life. The authors noted that their new approach might be useful for monitoring patients with a history of bladder cancer, by modifying the sensitivity and specificity of the screening test on the basis of cut-off levels.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
12576812

**DOI**
10.1097/01.ju.0000051322.60266.06

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adolescent; Adult; Aged; Aged, 80 and over; Biomarkers, Tumor /urine; Carcinoma, Transitional Cell /diagnosis /pathology; Chemokine CCL2 /urine; Double-Blind Method; Enzyme-Linked Immunosorbent Assay; Female; Hematuria; Humans; Inter cellular Adhesion Molecule-1 /urine; Male; Middle Aged; Neural Networks (Computer); Nuclear Proteins /urine; Predictive Value of Tests; Sensitivity and Specificity; Urinary Bladder Neoplasms /diagnosis /pathology

**AccessionNumber**
22003000366