Economic impact of screening for bladder cancer using bladder tumor markers: a 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
The study examined the use of a bladder tumour marker, NMP22, in screening for bladder cancer. NMP22 is a nuclear matrix protein marker that uses monoclonal antibodies to detect levels of mitotic apparatus proteins that are increased in cancer cells. Both low- and high-risk populations for bladder cancer were considered.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of individuals (both sexes, all races) aged 50 years or older. A sub-group analysis considered a cohort of individuals at high risk of developing bladder cancer, with risk factors being smoking, haematuria, or dysuria.

Setting
The setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 2003 and 2005. No dates for resource use were reported. The price year was 2005.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A decision tree model was constructed to determine the total cost of screening low- and high-risk populations for bladder cancer using NMP22. Other details of the decision model were not reported, but a short-term horizon appears to have been used.

Outcomes assessed in the review
The outcomes estimated from the literature were the sensitivity and specificity of the cancer marker and incidence rates of bladder cancer for different age groups.
Study designs and other criteria for inclusion in the review
The primary studies appear to have been identified selectively. For the general population, accuracy of NMP22 was derived from a published meta-analysis, while incidence rates came from Surveillance, Epidemiology and End Results (SEERs) data. For the high-risk cohort, accuracy of NMP22 and incidence rates came from a prospective study of 1,331 consecutive high-risk patients.

Sources searched to identify primary studies
Not applicable.

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

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

Number of primary studies included
Three primary studies provided the clinical evidence.

Methods of combining primary studies
The primary studies were not combined since each source provided a single series of estimates.

Investigation of differences between primary studies
Not reported.

Results of the review
In the general population, the sensitivity of NMP22 was 0.73 (95% confidence interval, CI: 0.47 to 0.87) and the specificity was 0.80 (95% CI: 0.58 to 0.91).

In the high-risk cohort, the sensitivity was 0.56 (95% CI: 0.44 to 0.67) and the specificity was 0.86 (95% CI: 0.84 to 0.88).

In the general population, the annual incidence rates per 100,000 individuals were 22.8 in the 50 - 59 year age group, 66.5 in the 60 - 69 year age group, 128.6 in the 70 - 79 year age group, and 153.6 in patients aged 80 years or older.

In the high-risk population, the annual incidence rates per 100,000 individuals were 2,778 in individuals aged 40 years or younger, 1,976 in the 41 - 50 year age group, 4,230 in the 51 - 60 year age group, 8,099 in the 61 - 70 year age group, and 10,317 in the 71 - 80 year age group.

Measure of benefits used in the economic analysis
The summary benefit measure was the number of cases of bladder cancer detected. This was obtained through the decision model on the basis of cancer incidence and the sensitivity and specificity of NMP22.

Direct costs
The analysis of the costs might have been carried out from the perspective of the third-party payer, although this was not explicitly stated. The cost items included in the analysis were NMP22 test, office cystoscopy, cytology, intravenous pyelogram and office visit. The unit costs were reported but the quantities of resources used were not. The costs were
based on Medicare reimbursement rates and a local county hospital. The source of resource consumption was not reported but was probably also based on Medicare. Discounting was not relevant as short-term costs were estimated. The price year was 2005.

**Statistical analysis of costs**
Statistical analyses of the costs were not carried out.

**Indirect Costs**
The indirect costs were not included in the economic analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
Deterministic sensitivity analyses were carried out to assess the impact on the cost-effectiveness ratios of variations in cancer incidence, tumour marker sensitivity and specificity, and cost estimates. Both one- and two-way sensitivity analyses were carried out. Ranges of values were defined on the basis of published evidence or authors' opinions.

**Estimated benefits used in the economic analysis**
The number of cases of bladder cancer detected was not reported.

**Cost results**
The total costs were not reported.

**Synthesis of costs and benefits**
The costs and benefits of the screening programme were combined by calculating the cost per cancer detected with NMP22. The average cost-effectiveness ratio appears to have been estimated.

In the general population, the cost per cancer detected was $783,913 in the 50 - 59 year age group, $269,028 in the 60 - 69 year age group, $139,305 in the 70 - 79 year age group, and $116,696 in patients aged 80 years or older.

In the high-risk population, the cost per cancer detected was $6,690 in individuals aged 40 years or younger, $9,245 in the 41 - 50 year age group, $4,530 in the 51 - 60 year age group, $2,341 in the 61 - 70 year age group, and $2,090 in the 71 - 80 year age group.

The cost per cancer detected in the high-risk population was $3,310.

The results of the sensitivity analysis showed that cancer incidence had the greatest influence on the model results. If the annual incidence was higher than 4% (which represents a cohort of high-risk individuals), the cost per cancer detected was less than $5,000. In the cohort of high-risk patients and under the most unfavourable scenario, the cost-effectiveness ratio was below a value of $20,000.

**Authors' conclusions**
The implementation of an NMP22-based bladder cancer screening programme for all asymptomatic individuals was not cost-effective in the USA. However, application to an appropriate high-risk target population could achieve a cost-effectiveness ratio (i.e. cost per cancer detected) comparable with currently used screening programmes for prostate, colon and breast cancer.
CRD COMMENTARY - Selection of comparators
The analysis implicitly compared the screening strategy with no screening, which represents the actual pattern of care in the authors’ institution. The authors discussed the advantages and disadvantages of using cytology as a screening tool. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The authors did not report the methods and conduct of a systematic review of the literature. Therefore, the primary studies used to provide the clinical data could have been identified selectively. The authors provided a rough description of the primary studies. One was a meta-analysis, which usually is associated with a high internal validity; another was a large prospective study that did not enrol a purely asymptomatic population. SEERs data were used to derive the incidence of disease. Differences between the primary studies were not discussed, but the issue of uncertainty in the clinical estimates was addressed in the sensitivity analysis.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. It will not be comparable with the benefits of other health care interventions. The analysis focused on a screening programme, thus an intermediate measure (i.e. the number of cancers detected) was used. The impact of the programme on other aspects of health such as survival or quality of life was not addressed. The authors noted that no randomised trial has compared survival with and without a screening strategy for bladder cancer.

Validity of estimate of costs
Given the source use to derive the costs, the perspective of the analysis appears to have been that of a third-party payer. A breakdown of the cost items was provided, as well as the unit costs. However, information on resource consumption was less clear. This limits the possibility of replicating the analysis in other settings. The costs were treated deterministically but some sensitivity analyses were carried out. The price year was reported, thus enabling the analysis to be replicated in other time periods. Key cost estimates were varied in the sensitivity analysis.

Other issues
The authors made only a few comparisons of their findings with those from other studies. They did not explicitly address the issue of the generalisability of the study results to other settings. Some sensitivity analyses were carried out, which to some extent enhances the external validity of the analysis since alternative scenarios for costs and epidemiological data were considered. The results of the cost-effectiveness analysis were reported selectively in that the total costs and the expected number of cancer cases detected were not reported. However, cost-effectiveness ratios were given for sub-groups of patients. The analysis was carried out for a short-term horizon, and future costs associated with bladder cancer and long-term mortality were not considered. This would appear to represent a limitation of the study given that the long-term effects of a screening strategy that is likely to reduce future costs and deaths are relevant in estimating the true value for money of NMP22. Finally, only average cost-effectiveness ratios were estimated. In fact, although NMP22 was implicitly compared with no screening, the number of cancers detected with no screening was not explicitly reported and no incremental analysis was performed.

Implications of the study
The study results suggest that the use of NMP22 for bladder cancer screening might be cost-effective in appropriately selected high-risk patients. Further studies should be undertaken to assess the accuracy of bladder tumour markers in detecting bladder cancer in a completely asymptomatic cohort.

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None stated.
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Other publications of related interest


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