Is cytology required for a hematuria evaluation?  
Hofland C A, Mariani A J

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 urine cytology (CPT 88108) to detect urothelial malignancy in the evaluation of patients with asymptomatic microscopic haematuria. The full evaluation included excretory urography (IVP; CPT 74400), cystoscopy (CPT 52000), serum creatinine (CPT 80048) and urine culture. Urine cytology, renal ultrasound, retrograde pyelogram and other tests were performed, as indicated.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with one episode of gross haematuria or microscopic haematuria. Haematuria was defined as 3 red blood cells per high-powered field on 2 of 3 properly collected urinalyses.

Setting
The setting was secondary care. The economic study was conducted in Honolulu (HI), USA.

Dates to which data relate
The effectiveness data were from 1976 to 1985. The resource use and cost data related to 2002. The price year was 2002.

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

Link between effectiveness and cost data
The cost data appear to have been calculated retrospectively for the same sample of patients as that included in the effectiveness analysis.

Study sample
The study sample comprised 1,000 sequential patients who underwent a standardised haematuria evaluation. The use of power calculations to determine the sample size was not reported. No sub-groups were formed since the patients received a suite of tests that were compared for diagnostic yield and, as such, acted as their own controls.
Study design
This was a cohort study that was conducted at a single centre. The cytology samples consisted primarily of voided urine collected during an office visit, but some were barbotaged samples collected during cystoscopy. The samples were prepared according to a standard protocol. "Atypical cells" and interpretations other than TCC were considered negative. The charts of patients with TCC were reviewed to determine whether urine cytology yielded unique information that led to the diagnosis. The charts of patients with a life-threatening diagnosis were carefully examined to determine which single test was most responsible for the diagnosis. The length of follow-up was to the point of diagnosis. No patients were lost to follow-up.

Analysis of effectiveness
The form of the analysis was not stated, but the results were based on all patients included in the study. Since all of the patients undertook the evaluation, the issue of comparability was not relevant. The health outcome was the diagnosis of a life-threatening malignancy (TCC). The sensitivity and specificity of urine cytology in the detection of TCC were also calculated.

Effectiveness results
From the sample of 1,000 with a haematuria evaluation, 660 (66%) underwent urine cytology. Urine cytology was obtained in 40 of the 71 patients eventually diagnosed with TCC of the bladder or upper tracts.

Urine cytology was positive in 25 (3.8%) of the 660 patients.

There were 3 false-positive results in patients with cystitis.

False-negative results were found in 18 of the 40 patients with TCC who were tested.

In this cohort, the sensitivity of urine cytology to detect TCC was 55% and the specificity was 99.5%.

In total, 88 patients were diagnosed with a life-threatening condition. For those with TCC, urine cytology, IVP, cystoscopy and serum creatinine directly contributed to the diagnosis.

Clinical conclusions
In this cohort, 4 patients were identified in whom urine cytology provided information that prompted further evaluation or surveillance and was responsible for the diagnosis of TCC.

Measure of benefits used in the economic analysis
The measures of benefits used in the economic analysis were the cases of life-threatening conditions correctly diagnosed and the tests providing unique diagnostic information. These were obtained directly from the effectiveness results.

Direct costs
Discounting was not conducted, but this was appropriate due to the short duration of the study (less than one year). The costs and the quantities were reported separately. The costs to diagnose a life-threatening condition were determined by multiplying the cost of each test by the number of tests performed. The cost data were derived from the Medicare reimbursement schedule for the state of Hawaii. The cost for unique information was calculated as described earlier, except that the number of each test that provided unique information was used as the divisor. The price year was 2002.

Statistical analysis of costs
The cost data were not treated stochastically since only point estimates were provided.
Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was undertaken.

Estimated benefits used in the economic analysis
Urine cytology was performed in 660 patients and was diagnostic for a life-threatening condition in 21 cases (3.3%).

IVP was performed in 966 patients and was diagnostic for a life-threatening condition in 53 cases (5.5%).

Cystoscopy was performed in 956 patients and was diagnostic for a life-threatening condition in 68 cases (7.1%).

Serum creatinine was performed in 931 patients and was diagnostic for a life-threatening condition in 2 cases (0.2%).

The numbers of tests that provided unique information were 4 (0.6%) for urine cytology, 16 (1.7%) for IVP, 64 (6.7%) for cystoscopy, and 2 (0.2%) for serum creatinine.

Cost results
The total cost for each test was not provided. In fact, the total cost was $33,467 (660 x $50.71) for urine cytology, $89,836 (966 x $93.02) for IVP, $206,442 (956 x $216.54) for cystoscopy, and $6,582 (931 x $7.07) for serum creatinine.

Synthesis of costs and benefits
The costs to diagnose a life-threatening condition were $1,521 for urine cytology, $1,695 for IVP, $3,044 for cystoscopy, and $3,291 for serum creatinine.

The costs to provide unique information were $8,367 for urine cytology, $5,616 for IVP, $3,235 for cystoscopy, and $3,291 for serum creatinine.

Authors’ conclusions
Urine cytology is a useful test for adjusting a clinician's index of suspicion for patients undergoing a haematuria evaluation. The cost per life-threatening diagnosis for cytology was slightly less than that for excretory urography (IVP), cystoscopy and serum creatinine. The cost of unique information was slightly higher for cytology, but comparable to the other tests used in the algorithm.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. Urine cytology was compared with other tests that were included in the diagnostic algorithm for haematuria. This enabled a comparative analysis of its diagnostic value in detecting life-threatening causes of haematuria, particularly TCC.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from a single cohort, which was appropriate for the study question. The patients were followed up to determine the diagnostic yield in terms of detecting TCC and other life-threatening conditions. As
such, each patient potentially received all the tests in the algorithm (although only 660 patients received urine cytology due to their risk profile). The analysis appears to have been handled credibly in order to minimise bias and error in relation to the collection and evaluation of the urine samples. Few details of the clinical and demographic details of the sample were given, although the four cases with TCC detected by urine cytology were described in full in the paper.

**Validity of estimate of measure of benefit**
The benefit measure was intermediate in nature, considering the diagnosis of a life-threatening condition and unique information for each test. Whilst this provides a measure of the efficiency of the tests to detect TCC, longer run analyses that include a health outcome would help.

**Validity of estimate of costs**
The cost data were clearly presented and the unit costs and the quantities were reported separately. The source and price year were also given. However, no statistical or sensitivity analyses were performed, although this may be expected when using reimbursement cost data. It is possible that charges were used to proxy real costs and, if so, this will hinder the generalisability of the cost data to other settings.

**Other issues**
The authors did not compare their results with those of other studies and did not address the issue of generalisability. However, the authors placed their results in the context of the AUA Best Practice Policy for Asymptomatic Microscopic Hematuria. Their findings suggested that, had these guidelines been adhered to (i.e. urine cytology only undertaken on the high-risk members of the cohort) fewer cytologies would have been performed. In addition, the costs would have decreased, all cases detected in this series would have been included, and the cost of unique information would have been lower.

**Implications of the study**
The findings of this study supported the use of urine cytology on high-risk patients in accordance with the AUA guidelines. All four patients in the present series would have been tested, and unique information would have been provided at a lower cost.

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