Centre for Reviews and Dissemination

What is the most effective strategy for the investigation of adult haematuria?

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Objectives

- Evaluate the effectiveness of screening for haematuria.
- Evaluate the effectiveness of tests to determine the underlying cause of haematuria.
- Determine the diagnostic accuracy of tests used to detect haematuria and to investigate its underlying causes.

Methods

Searches of multiple electronic databases, internet searches, hand searching of journals and conference proceedings were undertaken (up to August 2004), reference lists of included papers were scanned, and experts in the field were consulted. Studies (in any language) had to meet the following inclusion criteria:

Effectiveness studies

- *Screening:* RCTs of the effectiveness of screening programmes, reporting patient outcomes.
- *Further investigation:* RCTs or non-randomised controlled trials (CCTs), reporting patient outcomes.

Diagnostic accuracy studies

- *Design:* Diagnostic cohort or case-control studies, including a clear reference standard.
- *Intervention:* Any test or combination of tests used in the detection or investigation of haematuria.
- *Participants:* Adults with suspected or confirmed haematuria.
- *Outcomes:* Sufficient data to allow construction of a 2*2 table.

Two reviewers independently screened titles and abstracts for relevance. Data extraction and quality assessment were performed using standardised forms and checked by a second reviewer. The quality of the included studies was evaluated using published checklists and criteria.

Data synthesis

- Results were analysed according to test grouping and clinical aim of studies.
- Sensitivity, specificity, likelihood ratios and diagnostic odds ratios were calculated.
- Individual study results were presented graphically in ROC space.
- Heterogeneity was investigated using the Q statistic, through visual examination of study results and regression analyses.

Results

The searches identified over 12,000 potentially relevant studies. A total of 116 studies met the inclusion criteria. (see table 1)

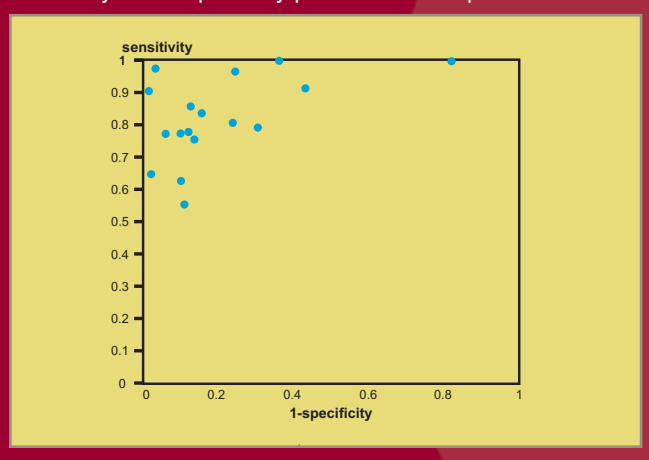
Table 1: Studies included in the systematic review

Study objective		No. studies identified
Effectiveness of screening		0
Detection of haematuria		19
Haematuria as a test for disease presence		6
Further investigation:	Microscopy (localisation)	48
	Tumour markers	13
	Cytology	15
	Imaging	15

Effectiveness of the investigation of haematuria

No studies that evaluated the effectiveness of screening for haematuria or investigating its underlying cause were identified.

Figure 1: Dipstick tests for haematuria: study sensitivity and 1-specificity plotted in ROC spac



Diagnostic accuracy of tests used to detect haematuria and to determine underlying causes

Detection of haematuria

Of 19 identified studies, 18 evaluated dipstick tests. Data from the majority suggested that these are moderately useful in establishing the presence of, but cannot be used to rule-out, haematuria (see figure 1).

Haematuria as a test for the presence of a disease

These studies indicated that the detection of haematuria cannot alone be considered a useful test either to rule-in or rule-out the presence of a significant underlying pathology (urinary calculi or bladder cancer).

Further investigation to establish the underlying cause of haematuria

Microscopy: These addressed methods to localise the source of bleeding (renal or lower urinary tract). The methods and thresholds described in these studies varied greatly, precluding any estimate of a 'best performance' threshold that could be applied across patient groups. However, studies of RBC morphology that used a cut-off value of 80% dysmorphic cells for glomerular disease reported consistently high specificities, (median 96.4%; potentially useful in ruling-in a renal cause for haematuria). The reported sensitivities were generally low.

Tumour markers: The majority of tumour marker studies evaluated NMP22 or BTA. The sensitivity and specificity ranges suggested that neither of these would be useful either for diagnosing bladder cancer or for ruling out patients for further investigation (cystoscopy). However the evidence remains sparse and the diagnostic accuracy estimates varied widely between studies (see figure 2).

Urine cytology: Studies evaluating urine cytology as a test for urinary tract malignancies were heterogeneous and poorly reported. Specificity values were generally high, suggesting some possible utility in confirming malignancy. However, the evidence suggests that urine cytology has no application in ruling-out malignancy or excluding patients from further investigation (see figure 2).

Imaging: Techniques (CT, IVU or US) to detect the underlying cause of haematuria. The target condition and the reference standard varied greatly between these studies. The diagnostic accuracy data of several individual studies appeared promising (see figure 3) but meaningful comparison of the available imaging technologies was impossible.

Figure 2: Laboratory tests for investigating the cause of haematuria: study sensitivity and 1-specificity plotted in ROC space

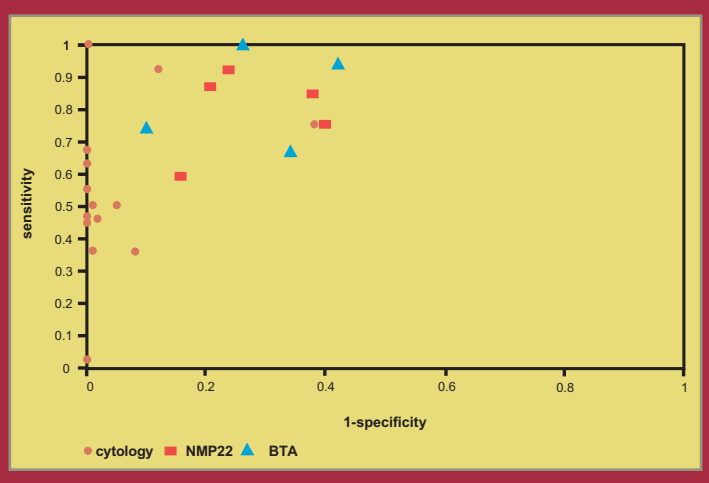
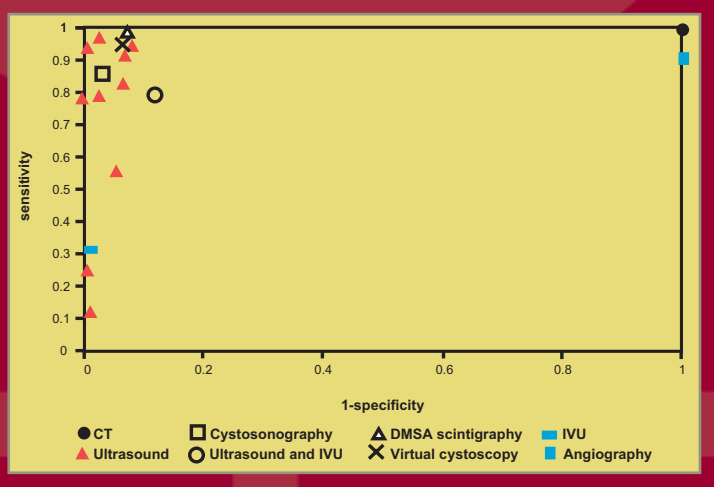


Figure 3: Imaging tests for investigating the cause of haematuria: study sensitivity and 1-specificity plotted in ROC space



Conclusions

There is currently insufficient evidence to develop a purely evidence based strategy for the investigation of adult haematuria. Quality of studies was generally poor. Future studies should follow the STARD guidelines for reporting of diagnostic accuracy studies.

The following major outstanding questions for future research were identified:

- Is screening/testing for haematuria effective?
- Is investigation of the cause of haematuria effective?
- Which patients with asymptomatic haematuria need full investigation, and is there a subset of patients who require fewer or no further investigations?
- What is the most effective means of following those with haematuria who test negative on all initial investigations?
- What is the impact of sample degradation with time on the performance of microscopy for the detection of haematuria?
- What would be the incremental benefit of routinely using urinary blood cell morphology techniques alongside simple renal function tests (e.g. proteinuria) in order to improve direct referral to nephrology?
- What is the clinical and economic impact of delayed detection of life-threatening causes of haematuria through the use of non-reference standard tests with follow-up screening using reference tests?

Areas where further research may be useful are:

- The accuracy of dipstick tests in detecting haematuria.
- Factors that affect the performance of urine cytology.
- Diagnostic accuracy of tumour markers.
- The cumulative diagnostic effect of conducting imaging studies.

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