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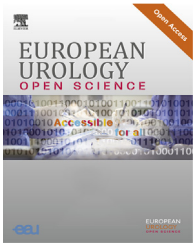

Bladder Cancer

Xpert Bladder Cancer Detection in Emergency Setting Assessment (XESA Project): A Prospective, Single-centre Trial

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Abstract

Background and objective: Bladder cancer (BC) represents a significant health care challenge and is frequently detected during evaluations for haematuria in emergency departments (EDs). Our aim was to evaluate the clinical performance and economic implications of the Xpert BC Detection (BCD) test for patients presenting to the ED with haematuria to address the pressing need for more efficient and accurate diagnostic tools in this setting.
Methods: We conducted a prospective single-centre observational study in the ED of a tertiary university hospital. Patients presenting with gross haematuria as the primary reason for their visit were enrolled. Urine samples collected in the ED were analysed using the Xpert BCD test. The primary outcomes were sensitivity, specificity, and a cost analysis for the Xpert BCD test in comparison to standard diagnostic methods such as urine cytology (UC) and white-light cystoscopy (WLC).
Key findings and limitations: The Xpert BCD test exhibited superior sensitivity to UC, particularly in identifying high-grade tumours. Importantly, Xpert BCD implementation has the potential to significantly reduce the number of unnecessary WLC procedures and streamline diagnostic pathways. The cost analysis also highlighted potential cost savings for Xpert BCD adoption in the ED setting.
Conclusions and clinical implications: Our findings underscore the promise of Xpert BCD for revolutionising the diagnostic approach to BC in the ED for patients with gross haematuria. Its greater sensitivity and efficiency mean that Xpert BCD has the potential to improve patient care, optimise resource use, and alleviate the economic burden associated with unnecessary procedures.

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Patient summary: Xpert Bladder Cancer Detection is a simple urine test that detects the presence of five genes associated with bladder cancer. We found that for patients visiting the emergency department because of blood in their urine, use of this test could save time and money over urine cell analysis (UCA) for ruling out or diagnosing bladder cancer. The test was also more sensitive in detecting higher-grade cancers. More research is needed to confirm our results.

1. Introduction

Bladder cancer (BC) is a globally significant health concern, ranking as the tenth most frequently diagnosed cancer worldwide [1]. BC is frequently diagnosed during evaluations for gross haematuria, a common presentation at emergency departments (EDs) [2]. The majority of patients with haematuria do not actually have BC, yet will require invasive testing to rule out malignancy, leading to a significant health care burden in terms of costs and waiting times, as well as a psychological impact [3].

The current gold-standard methods for identifying BC are white-light cystoscopy (WLC) and urine cytology (UC) [4]. These conventional tools have inherent limitations. UC is characterised by high specificity but variable sensitivity (38–84%), even for high-grade (HG) disease, and notably lower sensitivity for low-grade (LG) BC (20–53%) [5]. Therefore, even with a high negative predictive value (NPV) of 92%, UC cannot be recommended as a standalone diagnostic test [6]. Furthermore, UC requires pathological review, which is not performed on the same day as a clinic visit and is susceptible to inter- and intra-observer variability. WLC has moderate sensitivity and specificity ranging from 47% to 100% and from 64% to 100%, respectively [7]. Nevertheless, WLC cannot differentiate between HG and LG BC, and even benign lesions can be misdiagnosed, so patients may undergo unnecessary surgery [8,9]. Furthermore, WLC frequently causes patient discomfort and urinary tract infections because of its invasive nature. Finally, another issue is the lack of availability of real-time WLC performed by a trained urologist in the ED. Given these considerations, neither WLC nor UC is feasible in the ED setting for patients presenting with gross haematuria. Alternative diagnostic approaches such as bladder ultrasonography (BUS) have good sensitivity for larger lesions but may miss small or flat tumours, even in expert hands, and often require WLC confirmation due to false positivity in case of haematuria with blood clots [10].

Xpert Bladder Cancer Detection (Xpert BCD) is a novel mRNA marker test for BC diagnosis; it is an in vitro diagnostic with CE-marked approval for use in patients with haematuria and a suspicion of BC [11]. Previous studies reported overall sensitivity of 78% and specificity of 84%, and sensitivity of 90% for HG cancer [12].

Our aim was to assess the clinical performance of the Xpert BCD test in patients presenting to the ED with haematuria. Specifically, we sought to determine its diagnostic accuracy in comparison to the gold-standard diagnostic workup involving UC and WLC, and to evaluate the economic resource use associated with an Xpert BCD-led diagnostic pathway.

2. Patients and methods

2.1. Study design

This prospective, single-centre, single-arm, observational study involving a nonconsecutive sample of patients presenting to the ED of a tertiary university hospital started in February 2022. The study was approved by the institutional ethics committee and was conducted according to the hospital guidelines for good clinical practice; all participants provided informed consent for participation in the clinical trial (reference ICH-015-3065).

2.2. Population

The inclusion criteria were patients aged ≥18 yr presenting to the ED with gross haematuria within 48 h as the primary reason for admission and a Manchester triage priority code of 4 or 5 [13], indicating a need for medical treatment that could be safely delayed. Participants were required to provide informed consent and agree to undergo the study protocol including UC and WLC.

Exclusion criteria were known BC lesions under active surveillance (AS), a history of bladder chemotherapy, an in situ urinary stent, a Manchester triage priority code of 1–3 (ie, requiring urgent intervention within 2–4 h or a life-saving intervention), or any condition that could interfere with the study protocol. In addition, patients who were unable to provide informed consent because of cognitive impairment or language barriers were excluded from the study.

2.3. Xpert BCD

Xpert BCD (Cepheid, Sunnyvale, CA, USA) is an mRNA urinary biomarker test developed for BC diagnosis. It is based on real-time quantitative polymerase chain reaction (PCR) technology for quantitative measurement of the levels of five mRNAs associated with cell proliferation and survival (IGF2), cell growth and division and signal transduction (ANXA10, ABL1), epigenetic dysregulation (UPK1B), and response to neuroendocrine stress, immunity, and inflammation (CRH) in a voided urine sample. A proprietary linear discrimination analysis algorithm weights the cycle threshold results for the five mRNA targets [12] and a binary "positive" or "negative" result for BC is reported. Each test

cartridge contains internal controls to assess the quality of the starting material and the PCR reaction. The test requires approximately 2 min of hands-on time and ~90 min for results.

2.3.1. Procedures

For each patient, a full medical history was taken and a physical examination was conducted in accordance with good clinical practice. Urinary samples were collected in the ED, either as a midstream sample or via a urethral catheter, after patient enrolment in the study.

All patients received instructions on urine collection for UC, which was performed on three samples (1 sample on 3 consecutive days). All patients also underwent WLC within 20 d of enrolment. In cases with suspected malignant bladder lesions or positive UC, transurethral resection of bladder tumour (TURBT) was performed within 30–45 d. If the Xpert BCD test was positive but WLC was negative, no further immediate intervention was performed.

2.4. Outcomes

2.4.1. Primary endpoint

The primary aim of the study was to evaluate the diagnostic performance of the Xpert BCD test in identifying BC in patients presenting to the ED with gross haematuria, with the final decision on whether to perform TURBT based on WLC results. We assessed the sensitivity, specificity, PPV, NPV, and the area under the receiving operating characteristic curve (AUC). True positives were defined as patients with confirmed BC at TURBT and a positive Xpert BCD test result. True negatives were patients with no evidence of BC at TURBT and a negative Xpert BCD test result.

We also assessed the performance of the Xpert BCD test, UC, WLC, and UC + WLC in identifying ≥pT1 and/or HG BC.

2.4.2. Secondary endpoints

Secondary endpoints included evaluation of the feasibility of the Xpert BCD test in the ED setting and estimation of the reduction in unnecessary WLC/TURBT procedures. The number of unnecessary procedures was calculated by comparing Xpert BCD test results with conventional test results (UC and WLC). If the Xpert BCD test is negative but UC or WLC is positive and subsequent TURBT confirms no BC, then WLC is deemed unnecessary. We also conducted a cost analysis comparing resource consumption between the Xpert BCD test and the standard pathway to highlight potential value-based health care benefits (Supplementary Fig. 1).

2.5. Statistical analysis

Results for continuous variables are summarised using the mean and standard deviation for normally distributed data, and the median and interquartile range for non-normally distributed data. Results for categorical variables are presented as the frequency and proportion.

We assessed the diagnostic performance of the Xpert BCD test, UC, WLC, and UC + WLC in terms of the sensitivity, specificity, PPV, NPV, and AUC and the corresponding 95% confidence interval.

To compare the diagnostic tests, McNemar's test for paired proportions was applied to assess differences in sensitivity and specificity between the Xpert BCD test, UC, and WLC. The overall performance of each test was evaluated as the AUC, with comparisons made using the DeLong test. All reported p values were derived from these statistical tests, with significance set at $p < 0.05$.

3. Results

3.1. Study population

A total of 110 patients were enrolled between February 2022 and December 2023. Of these, 15 were excluded because they withdrew consent, and 19 did not complete the diagnostic pathway (13 did not undergo either UC or WLC, while 6 had an invalid Xpert BCD result). Therefore, data for 76 patients who completed the diagnostic process, including the Xpert BCD test, UC, and WLC, were analysed (Fig. 1). Demographic and clinical data are summarised in Table 1.

3.2. Diagnostic test results

Conventional WLC identified 24 patients (31.5%) with suspected BC, including four (5.3%) who had positive UC and subsequently underwent TURBT. At final pathology after TURBT, eight patients (33.3%) had negative histology for BC, with findings of chronic cystitis, while 16 patients (66.7%) had positive pathology confirming BC, of which seven cases were LG pTa and nine were ≥pT1 and/or HG BC.

For identification of any BC, the Xpert BCD test had sensitivity of 93.8%, specificity of 51.7%, a PPV of 34.1%, and an NPV of 96.9%. For this scenario the sensitivity was 25% with UC, 100% with WLC, and 100%, with UC + WLC. For identification of ≥pT1 and/or HG BC, the Xpert BCD test had sensitivity of 100%, specificity of 47.8%, a PPV of 20.5%, and an NPV of 100%. For this scenario the sensitivity was 44.4% with UC, 100% with WLC, and 100% with UC + WLC. There was no significant difference in AUC between the Xpert BCD test and UC for detection of any BC (0.72 vs 0.63%; $p = 0.13$) or detection of ≥pT1 BC (0.74 vs 0.72; $p = 0.86$). Conversely, there were significant differences in AUC between the Xpert BCD test and WLC (0.72 vs 0.93; $p = 0.00$) and between the Xpert BCD test and WLC + UC (0.72 vs 0.93; $p = 0.00$) for detection of any BC. There were also significant differences in AUC between the Xpert BCD test and WLC (0.74 vs 0.89; $p = 0.00$) and between the Xpert BCD test and WLC + UC (0.74 vs 0.89; $p = 0.00$) for detection of ≥pT1 BC. However, these comparisons are limited to patients with positive WLC, as no TURBT was performed in patients with negative WLC results. Table 2 presents diagnostic accuracy results for all tests in detecting any BC and high-risk BC.

3.3. Xpert BCD as a screening test

Table 3 compares the sensitivity, specificity, PPV, and NPV for the Xpert BCD test and UC in the subgroup of patients with suspicious BC at WLC. The sensitivity of Xpert BCD versus was 93.8% versus 25% for detection of any BC, and 100%

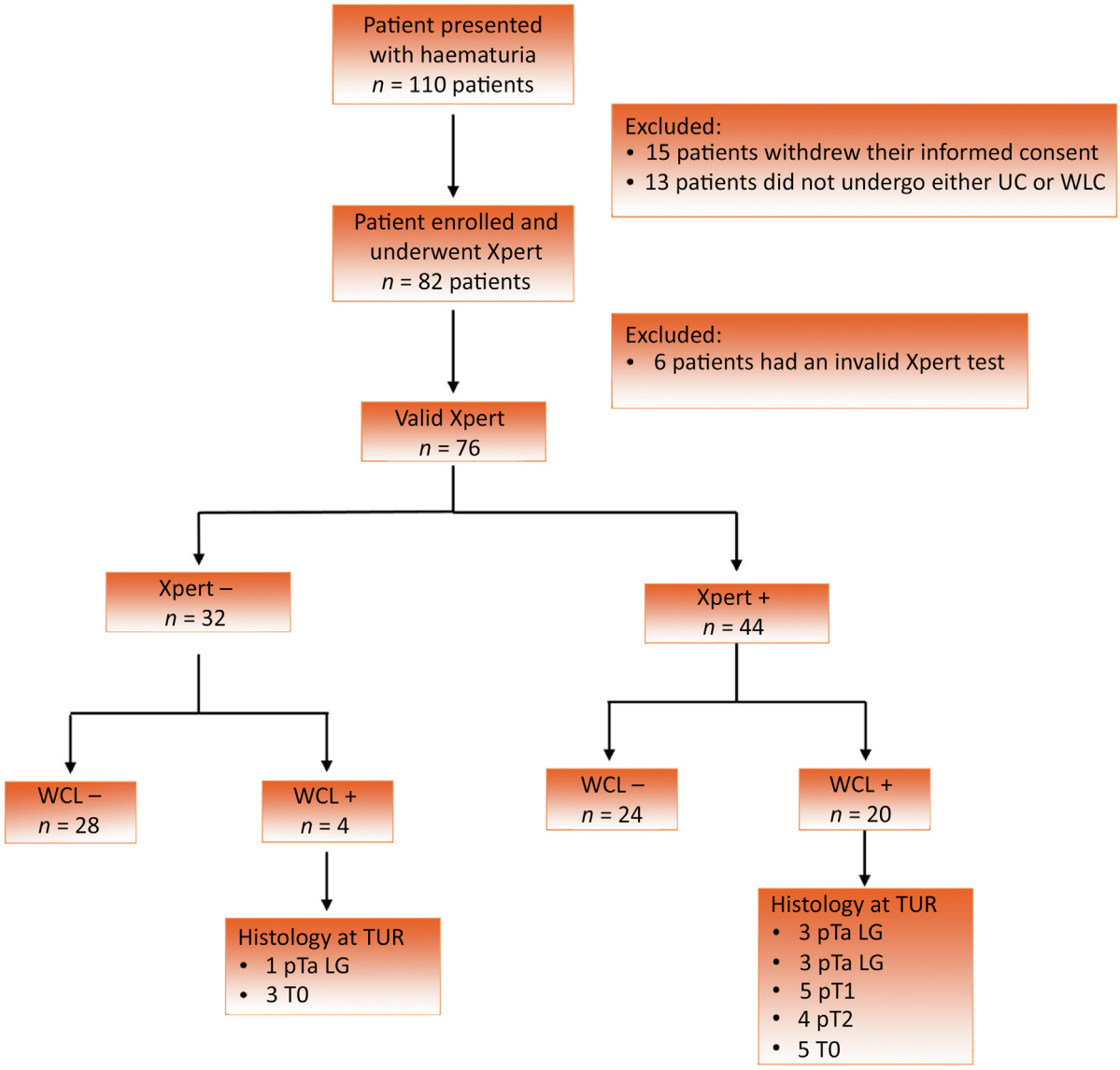

Fig. 1 – Flowchart of enrolment in the study. WLC = white-light cystoscopy; TUR = transurethral resection; UC = urine cytology; LG = low grade; HG = high grade.

Table 1 – Baseline characteristics of the overall study population

Parameter	Result
Median age, yr (IQR)	66 (22–89)
Male, *n*/*N* (%)	64/76 (84.2)
Median body mass index, kg/m^2 (range)	26.5 (18.7–38.5)
Family history of urothelial cancer, *n*/*N* (%)	2/76 (2.6)
Men with benign prostatic hyperplasia, *n*/*N* (%)	21/76 (27.6)
Hypertension, *n*/*N* (%)	44/76 (57.9)
Anticoagulant or antiplatelet therapy, *n*/*N* (%)	33/76 (43.4)
Smoking history, *n*/*N* (%)	
Current smoker	7/76 (9.2)
Former smoker	17/76 (22.4)

versus 44.4% for detection of ≥pT1 and/or HG BC. There was no significant difference in AUC between the Xpert BCD test and UC for detection of any BC (p = 0.78) or ≥pT1 BC (p = 0.40).

Xpert BCD adoption as a screening test for patients presenting to the ED with gross haematuria could have avoided 42.1% (32/76) of WLC procedures while failing to detect a single LG pTa BC case (1/16; 6.3%). No HG or ≥pT1 cases would have been missed. Conversely, use of UC as a screening test could have avoided 94.7% (72/76) WLC procedures but at the cost of missing 75% (12/16) of BC cases, including four LG pTa, three HG pTa, three pT1, and two pT2 BC cases. Use of UC as a screening test would have missed 66.7% (8/12) of HG or ≥pT1 tumours.

3.4. *Resource consumption analysis*

Table 4 presents the cost breakdown for standard and Xpert BCD-guided diagnostic pathways for BC detection in ED patients with gross haematuria. The total Xpert BCD cost includes test and urine transport reagent kits.

Table 2 – Diagnostic test results with TURB histopathology as the reference standard[a]

Test	SN, % (95% CI)	SP, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	AUC (95% CI)
Any BC					
Xpert BC Detection	93.8 (69.8–99.8)	51.7 (38.4–64.8)	34.1 (20.5–49.9)	96.9 (83.8–99.9)	0.73 (0.64–0.82)
UC	25.0 (7.3–52.4)	100 (94.0–100)	100 (39.8–100)	83.3 (72.7–91.1)	0.62 (0.52–0.73)
WLC	100 (79.4–100)	86.7 (75.4–94.1)	66.7 (44.7–84.4)	100 (93.2–100)	0.93 (0.89–0.98)
UC + WLC	100 (79.4–100)	86.7 (75.4–94.1)	66.7 (44.7–84.4)	100 (93.2–100)	0.93 (0.89–0.98)
HG pTa–≥pT1					
Xpert BC Detection	100 (66.4–100)	47.8 (35.4–60)	20.5 (9.8–35.3)	100 (89.1–100)	0.74 (0.68–0.80)
UC	44.4 (13.7–78.8)	100 (94.6–100)	100 (39.8–100)	93.1 (84.5–97.7)	0.72 (0.55–0.89)
WLC	100 (66.4–100)	77.6 (65.8–86.9)	37.5 (18.8–59.4)	100 (93.2–100)	0.89 (0.84–0.94)
UC + WLC	100 (66.4–100)	77.6 (65.8–86.9)	37.5 (18.8–59.4)	100 (93.2–100)	0.89 (0.84–0.94)

AUC = area under the receiver operating characteristic curve; BC = bladder cancer; CI = confidence interval; HG = high grade; NPV = negative predictive value; PPV = positive predictive value; SN = sensitivity; SP = specificity; TURB = transurethral resection of the bladder; UC = urine cytology; WLC = white-light cystoscopy.

[a] TURB was indicated on the basis of positive cystoscopy and UC findings.

Table 3 – Diagnostic accuracy in the subgroup with positive cystoscopy

Test	SN, % (95% CI)	SP, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	AUC (95% CI)
Any BC					
Xpert	93.8 (69.8–99.8)	37.5 (8.5–75.5)	75 (50.9–91.3)	75 (19.4–99.4)	0.66 (0.47, 0.85)
UC	25 (7.3–52.4)	100 (63.1–100)	100 (39.8–100)	40 (19.1–63.9)	0.62 (0.52, 0.73)
HG pTa–≥pT1					
Xpert	100 (66.4–100)	26.7 (7.8–55.1)	45 (23.1–68.5)	100 (39.8–100)	0.63 (0.52, 0.75)
UC	44.4 (13.7–78.8)	100 (78.2–100)	100 (39.8–100)	75 (50.9–91.3)	0.72 (0.55, 0.89)

AUC = area under the receiver operating characteristic curve; BC = bladder cancer; CI = confidence interval; HG = high grade; NPV = negative predictive value; PPV = positive predictive value; SN = sensitivity; SP = specificity; UC = urine cytology.

Table 4 – Pathway cost estimates using Xpert Bladder Cancer Detection list prices and assuming a negative test rate of 46% for a model in which 400 patients/yr present to the emergency department with haematuria

Procedure	Cost per patient		
	Standard pathway	Xpert pathway	
		Negative	Positive
Urine microscopy	€2.30	€2.30	€2.30
Abdominal ultrasound	€71.79	€71.79	€71.79
Urology consultation	€70.00	€70.00	€70.00
Xpert Bladder Cancer Detection test	–	€104.46	€104.46
Urine cytology	€15.65	–	–
White-light cystoscopy	€211.12	–	€211.12
Total pathway cost per patient	€370.86	€248.55	€459.67
Number of patients	400	184	216
Total pathway cost (per-patient cost × number of patients)	€148 344.00	€45 733.20	€99 288.72
Combined Xpert positive and negative pathway costs (400 patients)	€145 021.92		
Savings (400 patients)	€3322.08		

Our primary analysis reflects the IRCCS Humanitas Research Hospital, which is a private facility that receives public reimbursement from the Lombardia regional health system (€80 for the urine genetic test; Supplementary Fig. 2), with an estimated per-patient cost of €370.86 for the standard pathway. Xpert BCD use allows a shorter pathway that costs €459.67 for positive cases and €248.55 for negative cases, yielding a direct resource saving of €122.31. Factoring in the opportunity cost of reallocating released resources (WLC and UC, €226.77) for other patients results in total resource optimisation of €349.08 per patient.

Table 4 also provides pathway cost estimates using Xpert BCD list prices, assuming a negative test rate of 46% for an annual caseload of 400 haematuria patients in the ED, according to the Cepheid Department of Government Affairs Market Access and Health Economic Outcome Research (GAMA/HEOR).

For an estimated 400 eligible patients per year and a negative rate of 46% for the Xpert BCD test, resource optimisation could lead to projected annual savings of €64 260.72 in direct costs and released resources (Table 5) and €79 035 when considering the IRCCS Humanitas Research Hospital setting (Supplementary Fig. 3).

4. Discussion

We investigated use of the Xpert BCD test in a cohort of patients presenting to the ED with gross haematuria and no medical history of BC. Our findings demonstrate that the Xpert BCD test had higher diagnostic accuracy than UC in detecting BC, particularly for HG disease, in this selected patient population. The Xpert BCD test is a noninvasive and rapid diagnostic tool that can enhance the diagnostic pathway for patients with suspected BC.

A few studies have assessed the role of the Xpert BCD test as an alternative or complementary noninvasive tool

Table 5 – Sparing of resource consumption in a model considering 400 patients presenting to the emergency department with haematuria annually

Parameter	Result
Estimated annual number of patients	400
Negative result rate	46%
Patients with a negative Xpert result	184
Direct costs	−€22 505.04
Resources released	−€41 726,00
Possible optimisation savings	−€64 260.72

for patients with a suspicion of BC. Valenberg et al [12] compared the diagnostic accuracy of the Xpert BCD test and UC and found higher Xpert sensitivity both overall (78% vs 44%) and for HG tumours (90% vs 62%). The NPV was similar for the Xpert BCD test and UC (98% vs 96%), while the Xpert BCD test had lower specificity (84% vs 97%). Furthermore, the percentage of HG and LG cases missed differed considerably: 10% and 45% with the Xpert BCD test versus 38% and 90% with UC. Although Valenberg et al considered both micro- and macro-haematuria, the higher Xpert BCD sensitivity, particularly for HG disease, is in line with our findings and confirms its role as a promising tool to identify haematuria patients with a low likelihood of BC who might not need to undergo additional WLC evaluation. A study by Schmitz-Dräger et al [14] showed that the Xpert BCD test had high sensitivity (96.4%) and gave a positive result for all HG tumours at specificity of 80.1%. The Xpert BCD test was significantly more sensitive than UC (96.4% vs 60.7%; $p < 0.05$), while its specificity was lower than that of UC (80% vs 86%; $p = 0.032$). Another study by Tan et al [4] suggested that routine UC adds no benefit in assessment of haematuria because of its low sensitivity of UC, which can range from 12% to 85%.

A review of the clinical performance of urinary biomarkers for BC diagnosis confirmed the clinical feasibility of the Xpert BCD test [15]. However, the authors emphasised the necessity of an independent study to assess the impact of BC prevalence on biomarker performance. Our study is the first prospective, single-centre investigation of the clinical performance of the Xpert BCD test for patients with haematuria in an ED setting.

Our results suggest that in comparison to UC, Xpert BCD use as a screening tool in the ED for cases with gross haematuria would have missed a significantly lower number of tumours. Specifically, the Xpert BCD test would have missed only 6.3% of BC cases (1 out of 16), whereas UC would have missed 75% of tumours (12 out of 16). Furthermore, the Xpert BCD test would have missed only one low-risk BC case, whereas UC would have overlooked 66.7% (8 out of 12) of high-risk tumours, including HG and stage ≥pT1 BC.

We conducted a cost analysis for the Xpert BCD versus standard pathways in the ED setting for patients presenting with haematuria as their main symptom. The standard pathway includes urine chemical-physical examination, abdominal ultrasound, a urological examination, UC, and WLC, at a total cost of €370.86. In this scenario, Xpert BCD use could lead to a reduction in the number of unnecessary UC and WLC procedures, which would only be performed for patients with a positive Xpert test result. Therefore, for patients with a negative Xpert test result, the pathway would be shortened to include urine chemical-physical examination, an Xpert BCD test, abdominal ultrasound, and a urological examination, at a total cost of €248.55, with direct resource savings of €122.31. Assuming that approximately 400 patients per year are eligible for an Xpert BCD test and an average negativity rate of 46%, resource use optimisation would result in estimated annual savings of €64 260.72.

Our analysis considered the overall costs for outpatient services and the reimbursement rates provided by the Italian national health care system, using the ambulatory fees for the Lombardy region. The regional health care system has established ambulatory fees for the clinical resources typically used by the facilities providing the services. Assuming that approximately 400 patients annually would be eligible for an Xpert BCD test and an average test negativity rate of 46%, use of the test would allow resource use optimisation of approximately €79 035 per year. It is important to emphasise that both the Cepheid GAMA/HEOR and IRCCS Humanitas Research Hospital cost analyses demonstrate significant savings with the Xpert BCD pathway in comparison to the standard pathway.

While WLC use in the ED is effective, it is resource-intensive in comparison to the Xpert BCD test. WLC requires specialised equipment and training, which increases costs and potentially wastes resources in the ED setting. The Xpert BCD test is less invasive and cheaper, reduces unnecessary procedures, and optimises resource use.

Our study has several strengths. It is the first study to evaluate the accuracy of the Xpert BCD test in comparison to UC in the ED setting. The prospective design allows higher statistical power and reduces selection bias. However, the study is not exempt from limitations. For instance, the relatively small sample size may be associated with patient enrolment challenges in the demanding environment of the ED, particularly during the COVID-19 pandemic when patient volumes were high. Enrolment of patients with haematuria in an emergency setting requires close cooperation between multiple health care professionals, including urologists, emergency physicians, radiologists, and nurses. Moreover, the strict exclusion and inclusion criteria resulted in an intrinsic selection bias, with the exclusion of a notable number of patients presenting with haematuria. Many excluded patients were part of AS programs for identified BC lesions or had a previous diagnosis of BC treated via endoscopic resection, highlighting the role of our institution in managing a large AS cohort (BIAS protocol [8,16]). Furthermore, urinary samples were collected in the ED as either a midstream sample or via a urethral catheter. This could lead to a high false-positive rate in the subgroup of patients with mechanical irritation of the urinary tract [17]. Catheterisation affects the specificity of the Xpert BCD test because mechanical irritation of the urethra and bladder lining can release RNA markers typically associated with tumours. This inflammation and disruption might lead to false positives, as these markers can be elevated in conditions other than cancer, thereby lowering

the test specificity. Another factor that may also affect the specificity and PPV of the Xpert BCD test is the issue of anticipatory positive (AP) results. These occur when patients with a positive Xpert BCD result but negative WLC at baseline later develop histologically confirmed BC. This can occur more than 1 yr later, indicating that the markers can predict future recurrences not visible on WLC. To distinguish false positives from APs, patients need to be followed longitudinally for approximately 2 yr. If any patients from this study are later diagnosed with BC, they would be reclassified as true positives, improving the assay specificity and PPV. Another significant limitation of our study is the potential for partial verification bias. Disease status was confirmed only in patients who tested positive via WLC, while WLC-negative patients were assumed to be BC-negative without further verification. This could lead to inflated sensitivity and specificity estimates for the Xpert BCD test. Finally, patients presenting to the ED with gross haematuria are usually highly concerned about their medical condition, which could have made their enrolment difficult.

The Manchester triage priority code for the study participants was 4 or 5, indicating no necessity for immediate examination. Performing WLC in these cases can complicate the process and may interfere with UC or BUS if conducted during ongoing gross haematuria. Most units prefer to control the situation first and then organise a subsequent detailed assessment. While our study was conducted in an ED, its findings have broader implications beyond the ED setting.

5. Conclusions

According to our results, the Xpert BCD test offered greater sensitivity than UC for detection of all BC grades, with a high detection rate for HG and ≥pT1 disease. Xpert BCD use as a screening test for patients presenting to the ED with haematuria has the potential to significantly optimise resource use and streamline the endoscopic resection pathway, ultimately reducing costs and saving valuable time. A multicentre study is needed to confirm our findings and investigate the clinical role of the Xpert BCD test in the BC diagnostic pathway.

Author contributions: Rodolfo Hurle had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Hurle, Lazzeri, Voza.
Acquisition of data: Sordelli, Dagnino, Giuriolo, Maura, Da Rin, Avolio, Paciotti, Fasulo, Mancon, Colombo, Saita, Federico.
Analysis and interpretation of data: Sordelli, Dagnino, Maffei.
Drafting of the manuscript: Sordelli, Desai.
Critical revision of the manuscript for important intellectual content: Lazzeri, Contieri.
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2024.09.001.

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