Published in final edited form as:

Am J Emerg Med. 2015 December ; 33(12): 1838–1839. doi:10.1016/j.ajem.2015.09.026.

External validation of an ED protocol for reflex urine culture cancelation^{☆,☆☆}

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To the Editor

Excess use of urine cultures in the emergency department (ED) results in unnecessary costs and consumes limited human and laboratory resources [1–3]. In a prior single-center study, Jones et al [4] developed an ED reflex urine culture cancelation protocol based on low-risk findings for infection on urinalysis. They found that reflex cancelation of urine cultures for samples with low-risk urinalysis findings (negative for nitrites, leukocyte esterase, and bacteria and <10 leukocytes per high-power field [HPF]) would have reduced the total number of cultures performed by 39.1%, with only 1.8% of these cultures targeted for cancelation positive for a pathogen [4]. Using similar methods, we performed an external validation of the reflex urine culture cancelation protocol described by Jones et al [4] at a different institution.

A retrospective observational study was performed at a large academic ED in the United States with approximately 70000 adult ED visits per year. Emergency department visits meeting all of the following criteria were included: patient older than 18 years; visit date between January 1, 2013, and December 31, 2013; and both a urine culture and urinalysis performed for standard clinical care within 4 hours of each other.

A *positive urine culture* was defined as a culture that grew greater than or equal to 10000 CFU/mL of likely urinary pathogens, such as gram-negative rods, or a culture that grew greater than or equal to 50 000 CFU/mL of unlikely urinary pathogens, such as coagulase-negative staphylococci [4]. A *low-risk urinalysis* was defined as a urine sample meeting all of the following criteria according to the reflex culture cancelation protocol [4]: negative nitrites, negative leukocyte esterase, negative bacteria, and less than or equal to 10 leukocytes/HPF.

Positive predictive value was the proportion of patients with a high-risk urinalysis who had a positive urine culture. Negative predictive value (NPV) was the proportion of patients with a low-risk urinalysis who had a negative culture. The false omission rate, calculated as $1 -$

[☆]Reprints: Not available from the authors.

^{☆☆}Funding: Dr Self is partially supported by a grant from the National Institute of General Medical Sciences (K23GM110469). Dr Barrett is supported in part by a grant from the National Heart, Lung, and Blood Institute (K23KL102069). Dr Ward is supported by a grant from the National Heart, Lung, and Blood Institute (K12HL109019).

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NPV, was the proportion of patients with a low-risk urinalysis who had a positive culture. The false omission rate was considered a key statistic because it represented the proportion of positive cultures among cultures that would have been canceled if the reflex culture cancellation protocol had been used. Comparisons of the false omission rate between sexes and age groups were conducted with the χ^2 test.

A total of 4849 urine samples were included in the study, including 1137 (23.4%) with a positive urine culture. Median (range) patient age was 50 years (18–103 years); 3107 study patients (64.1%) were female. The most common pathogens isolated from positive urine cultures were *Escherichia coli* (48.4%), *Klebsiella pneumoniae* (12.7%), and *Enterococcus faecalis* (9.1%).

A total of 1676 urine samples were classified as low risk and targeted for cancellation based on the reflex urine culture cancellation protocol (Table 1). Thus, if urine cultures had been canceled based on the reflex protocol, 1676 fewer cultures (34.6%) would have been performed during the 1-year study period. Of the 1676 samples with low-risk urinalyses targeted for cancellation, 78 had positive urine cultures (false omission rate, 4.7%; 95% confidence interval [CI], 3.6%–5.7%) (Table 2).

After stratification of the study population by sex, the false omission rate was higher for females (6.9%; 95% CI, 5.2%–8.6%) than males (2.3%; 95% CI, 1.3%–3.3%) ($P < .01$). After age stratification at 50 years old, the false omission rate was similar in adults younger than 50 years (3.9%; 95% CI, 2.6%–5.3%) and those 50 years or older (5.3%; 95% CI, 3.8%–6.8%) ($P = .18$).

Thus, in conclusion, we found implementation of the reflex urine culture cancellation protocol derived by Jones et al [4] would have resulted in a 34.6% absolute reduction in the number of urine cultures completed in the study ED during a 1-year period and that 4.7% of these samples targeted for cancellation would have been positive for a pathogen. In our study population, the reflex cancellation protocol performed better in men (2.3% false omission rate) than women (6.9% false omission rate), suggesting that it might be particularly helpful for optimizing the use of urine cultures in men. Together, the results of the derivation study [4] and our external validation study suggest that a reflex urine culture cancellation protocol for samples with low-risk features on urinalysis could potentially result in a substantial reduction in the number of urine cultures performed while maintaining a relatively low rate of missed positive cultures.

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Table 1

Summary of urinalysis results for 4849 samples included in the study

Urinalysis findings	n (%)
Positive nitrites	522 (10.8)
Positive leukocyte esterase	2505 (51.7)
Positive bacteria	2272 (46.9)
>10 leukocytes/HPF	1675 (34.5)
1 of the above criteria (high-risk urinalysis)	3173 (65.4)
None of the above criteria (low-risk urinalysis)	1676 (34.6)

Diagnostic test characteristics of the low-risk urinalysis criteria compared to urine culture results (criterion standard) in the full study population and after stratification by sex and age group

Table 2

Population	n	Positive urine cultures, n (%)	Low-risk urinalysis, n (%)	Test characteristics of the low-risk urinalysis criteria				
				Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	False omission rate (95% CI)
Full population	4849	1137 (23.4)	1676 (34.6)	93.1 (91.7–94.6)	43.1 (41.5–44.6)	33.4 (31.7–35.0)	95.4 (94.3–96.4)	4.7 (3.6–5.7)
Female adults 18 years old	3107	811 (26.1)	853 (27.5)	92.7 (90.9–94.5)	34.6 (32.6–36.5)	33.4 (31.4–35.3)	93.1 (91.4–94.8)	6.9 (5.2–8.6)
Male adults 18 years old	1742	326 (18.7)	823 (47.2)	94.2 (91.6–96.7)	56.8 (54.2–59.4)	33.4 (30.4–36.5)	97.7 (96.7–98.7)	2.3 (1.3–3.3)
Age 18–49 (both sexes)	2382	530 (22.3)	790 (33.2)	94.2 (92.2–96.1)	41.0 (38.7–43.2)	31.3 (29.1–33.6)	96.1 (94.7–97.4)	3.9 (2.6–5.3)
Age 50 (both sexes)	2467	607 (24.6)	886 (35.9)	92.3 (90.1–94.4)	45.1 (42.8–47.4)	35.4 (33.1–37.8)	94.7 (93.2–96.2)	5.3 (3.8–6.8)

Abbreviation: PPV, positive predictive value.