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RESEARCH ARTICLE

Dalmanoğlu et al.: CRP in bacteriuria

C-reactive protein, rather than pyuria, may help differentiate asymptomatic bacteriuria from symptomatic urinary tract infection

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ABSTRACT

Distinguishing asymptomatic bacteriuria (ASB) from symptomatic urinary tract infection (UTI) may reduce unnecessary antibiotic use. We retrospectively compared admission C-reactive protein (CRP), urinary leukocyte count, and hematologic indices in 400 consecutive episodes of significant bacteriuria in 337 adults referred to an infectious diseases service between January 2021 and June 2026. Two investigators independently applied Infectious Diseases Society of America (IDSA) criteria to documented symptoms; bacteremia concordant with the urine isolate indicated infection. Analyses used areas under the receiver operating characteristic (ROC) curves (AUCs), patient-level cluster-bootstrap confidence intervals (CIs), and multivariable logistic regression. ASB accounted for 154 episodes (38.5%); baseline characteristics were broadly similar between groups. All ASB episodes received antibiotics (median 11 days; 1,778 antibiotic-days); 47 of 95 with bacterial isolates (49.5%) involved resistant organisms. CRP had an AUC of 0.892 (95% CI 0.858–0.923), outperforming the neutrophil-to-lymphocyte ratio (NLR; 0.714), procalcitonin (0.672), systemic immune-inflammation index (SII; 0.580), and platelet-to-lymphocyte ratio (PLR; 0.441; all comparisons $p < 0.001$). Urinary leukocyte count did not discriminate (AUC 0.482; 95% CI 0.429–0.539). CRP discrimination was lower against localized than systemic UTI (AUC 0.784 vs. 0.915). Below 5 mg/L, 3 of 46 episodes were symptomatic UTI (negative predictive value [NPV] 93.5%; 95% CI 82.5–97.8%). Among modeled inflammatory markers, only CRP was independently associated with symptomatic UTI (adjusted odds ratio [OR] 8.05 per log unit). Platelet counts were higher in ASB (272 vs. 243 $\times 10^3/\mu L$; $p = 0.003$), potentially explaining weaker performance of platelet-containing indices than NLR alone. In this retrospective cohort, admission CRP showed good discrimination between episodes classified as ASB and symptomatic UTI, whereas pyuria did not. The low-CRP threshold requires prospective validation before guiding antibiotic withholding.

Keywords: Bacteriuria, C-reactive protein, pyuria, urinary tract infections, antimicrobial stewardship, biomarkers, sensitivity and specificity.

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INTRODUCTION

Asymptomatic bacteriuria (ASB) is the growth of bacteria in urine at defined quantitative thresholds in the absence of signs or symptoms attributable to urinary tract infection (UTI). The 2019 Infectious Diseases Society of America (IDSA) guideline defines ASB explicitly as occurring irrespective of the presence of pyuria, and recommends screening and treatment only in pregnancy and before endoscopic urological procedures associated with mucosal trauma [1]. A systematic review and meta-analysis by the European Association of Urology (EAU) Urological Infection Guidelines Panel concluded that for most patients treatment is not beneficial and may be harmful, with benefit apparent only in pregnancy and before urological surgery [2].

These recommendations matter because antimicrobial resistance is among the leading global causes of death. Bacterial antimicrobial resistance was associated with an estimated 4.95 million deaths worldwide in 2019 [3], and modeled forecasts project a continued rise through 2050 [4]. Urinary tract infection is among the syndromes contributing to this burden [3], and antibiotic exposure for bacteriuria that does not require treatment adds to it directly.

Despite unambiguous guidance, treatment of ASB remains one of the most common forms of inappropriate antibiotic use in hospitals. In a study of 2,733 hospitalized patients across 46 hospitals, 83% of patients with ASB received antibiotics, and the factor most strongly associated with treatment was an abnormal urinalysis, a pattern the authors interpreted as misapplication of UTI diagnostic criteria [5]. Comparable rates have been documented across national health systems [6]. Large-scale quality improvement programs [7] and a stepped-wedge cluster randomized de-implementation trial [8] have reduced but not eliminated the practice.

The persistence of this pattern reflects a genuine clinical difficulty rather than simple unfamiliarity with guidelines. In older, catheterized, bedbound or cognitively impaired patients, symptoms attributable to the urinary tract are often unobtainable or non-specific, and the clinician facing a positive urine culture must decide whether bacteriuria explains the presentation. A systematic review and meta-analysis of adults aged 65 years and older found that asymptomatic bacteriuria was not significantly associated with delirium, even though it is routinely invoked as its cause, which leaves a large and vulnerable population in a diagnostic gray zone [9]. Because pyuria

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accompanies ASB as often as it accompanies UTI, urinalysis cannot resolve this question, yet it continues to be used as though it can [5]. An objective laboratory adjunct that helps to separate bacterial colonization from infection would address the decision point at which most inappropriate prescribing originates.

Hematologic inflammatory indices derived from the complete blood count have been proposed for problems of this kind. The systemic immune-inflammation index (SII), originally described in oncology and calculated as neutrophil count multiplied by platelet count divided by lymphocyte count, the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR) are inexpensive, universally available and have been reported as prognostic across many infectious and non-infectious conditions [10]. Whether they, or the more established C-reactive protein (CRP), can distinguish ASB from symptomatic UTI has not been directly examined.

The question has acquired additional relevance because UTI classification itself is being restructured. In 2025 the EAU abandoned the terms complicated and uncomplicated in favor of a distinction between localized and systemic UTI defined by clinical signs and symptoms, and explicitly called for validation studies of the new scheme against clinical outcomes [11, 12]. A classification anchored in symptoms raises the question of how well symptom-based categories correspond to measurable host inflammatory response.

We therefore conducted a retrospective cohort study in adults with bacteriuria managed by a hospital infectious diseases service, with three aims: to characterize the extent and duration of antibiotic exposure among episodes classified as ASB; to compare the ability of CRP, procalcitonin, pyuria, NLR, PLR and SII to distinguish ASB from symptomatic UTI; and, within symptomatic UTI, to explore the association of the same markers with severity and clinical outcomes, and the discriminative performance of the 2025 EAU classification.

MATERIALS AND METHODS

Study design and setting

This was a single-center retrospective observational cohort study conducted at the infectious diseases and clinical microbiology outpatient clinic and inpatient service of a university health application and research hospital serving as a tertiary referral center.

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Consecutive adults referred to the infectious diseases service between 1 January 2021 and 1 June 2026 because a urine culture had been reported by the clinical microbiology laboratory as showing significant growth were identified from the hospital information management system and from patient records; data were extracted between 20 July and 5 October 2026. No prospective intervention, questionnaire or additional biological sampling was undertaken.

The culture that prompted referral was the eligibility criterion. At the consultation the infectious diseases team routinely requested a repeat urine culture, and it is this repeat culture, obtained on the day of assessment, that is reported in the results; because empirical antibiotics had often been started by the referring team before the repeat specimen was collected, the repeat culture showed no growth or was reported as contaminated in a proportion of episodes. Consultation records were screened consecutively; the number of referrals that did not meet the eligibility criteria was not recorded, so the flow diagram reports only eligible episodes and the analysis subsets (Figure 1).

Participants

Eligible episodes were those in patients aged 18 years or older with a documented urine culture result, an admission complete blood count and C-reactive protein (CRP) measurement, and clinical follow-up data sufficient for outcome ascertainment. Episodes were excluded when the patient had a hematologic malignancy, was receiving active chemotherapy or immunosuppressive therapy, had known chronic liver disease or prior splenectomy, had a concurrent active infection at another site, or when admission laboratory or clinical records were incomplete. Because a minority of patients contributed more than one episode, patient identity was retained as a clustering variable. A new episode in the same patient was defined as a separate infectious diseases consultation prompted by a new positive urine culture obtained after completion of antibiotic treatment for the previous episode.

Definitions and group assignment

Significant bacteriuria was defined as growth of a single organism at $\geq 10^5$ colony-forming units (CFU)/mL in a voided midstream specimen, $\geq 10^4$ CFU/mL in a specimen from an indwelling catheter and $\geq 10^3$ CFU/mL in a specimen obtained by in-and-out catheterization. These thresholds are laboratory criteria for significant growth rather

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than the diagnostic criteria of the Infectious Diseases Society of America (IDSA) guideline. The clinical microbiology laboratory reports the quantitative colony count of a single isolate, performs identification and susceptibility testing according to the national clinical microbiology practice guideline [13], adds a comment that counts below 10^5 CFU/mL in voided specimens should be interpreted with the clinical findings, and reports growth of two or more organisms as contamination; the specimen-specific thresholds given above are those used by the infectious diseases service, in agreement with the laboratory, in routine practice and in this study. They are equal to or higher than the quantitative criteria of the IDSA definition ($\geq 10^5$ CFU/mL in a voided specimen or $\geq 10^2$ CFU/mL in a catheterized specimen), so every included episode also met the IDSA quantitative criterion; the IDSA recommendation that bacteriuria in asymptomatic women be confirmed in two consecutive voided specimens was not applied, because eligibility was determined by the single culture that prompted referral [1]. A repeat culture was considered positive when a single organism was isolated at these thresholds. The isolate was a recognized bacterial uropathogen (Enterobacterales, *Pseudomonas* species, *Enterococcus* species or *Staphylococcus saprophyticus*) in 246 episodes and *Candida albicans* in 18. Candiduria was reported by the laboratory at the same quantitative thresholds, and the 18 episodes were handled in the same way as the bacterial episodes: they were classified as asymptomatic bacteriuria or symptomatic infection on documented symptoms, were counted as culture-positive in the repeat-culture results and were included in the primary analysis; their exclusion was examined in a sensitivity analysis. Antibacterial resistance was assessed only among bacterial isolates.

Group assignment was made retrospectively by the investigators during data extraction, independently of the treatment decision taken at the time of care. All episodes were classified independently by two infectious diseases physicians (E.D. and A.Y.) using a standard data form; disagreements were resolved by consensus with the third author (Y.Ç.). The number of episodes requiring consensus was not recorded. Classification was based only on documented symptoms and signs; CRP, urinalysis and other inflammatory markers were not part of the classification criteria, but the assessors were not formally blinded to laboratory results, which were visible in the record. Applying IDSA criteria to the symptoms and signs documented in the record, episodes were classified as asymptomatic bacteriuria (ASB) when significant bacteriuria was present

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without acute signs or symptoms attributable to the urinary tract and without bacteremia caused by the same organism as the urine isolate, and as symptomatic urinary tract infection (UTI) otherwise [1]. Delirium, acute mental status change and fatigue occurring without localizing genitourinary features or systemic signs were not counted as UTI symptoms; urinary incontinence and lower urinary tract symptoms were counted only where the record indicated a new or worsening complaint. A symptom was regarded as new or worsening when the patient or caregiver reported it as such and it was absent from earlier outpatient or inpatient notes; persistent symptoms documented in earlier records, such as chronic incontinence, long-standing catheter-related complaints or stable behavioral change in dementia, were not counted. Fever or rigors recorded in an episode that the treating team had not attributed to the urinary tract did not by themselves lead to classification as UTI, because the reference standard was the documented clinical assessment; the effect of reversing these judgments was examined in sensitivity analyses. For episodes with a positive blood culture, the blood isolate was compared with the urine isolate; episodes in which the two were concordant were classified as symptomatic (bacteremic) UTI even in the absence of documented symptoms, whereas discordant isolates consistent with skin flora were regarded as probable contaminants and did not alter the classification. Reporting follows the Standards for Reporting Diagnostic Accuracy (STARD) 2015 [14] and Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statements; both completed checklists are provided as online supplementary material. Symptomatic UTI was categorized as acute cystitis, acute pyelonephritis or complicated UTI, and for the secondary analysis reclassified by the 2025 European Association of Urology (EAU) scheme as localized or systemic, systemic being defined by fever, rigors, costovertebral angle tenderness, altered mental status, documented general deterioration or bacteremia [11].

Acute kidney injury (AKI) was defined according to the serum creatinine criteria of the Kidney Disease: Improving Global Outcomes (KDIGO) guideline as an admission serum creatinine at least 1.5 times the baseline value [15]. Because the comparison used the creatinine measured at presentation, AKI as defined here was present at the time the index tests were drawn and is treated as a marker of severity at presentation rather than as a subsequent outcome. Because only a single admission creatinine was available for outpatient episodes, neither the 0.3 mg/dL rise within 48 hours nor the urine output

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criterion could be applied and renal replacement therapy was not captured; AKI was therefore treated as a binary variable and severity staging is not reported. Baseline creatinine was the most recent pre-admission outpatient measurement where available (311 episodes, 77.8%), used regardless of interval rather than the seven-day window KDIGO specifies, which may underestimate AKI where kidney function had already declined. Where no measured baseline existed (89 episodes, 22.2%) it was estimated by back-calculation from the Modification of Diet in Renal Disease equation assuming a glomerular filtration rate of 75 mL/min/1.73 m², with clinical adjudication of each case. This approach may over- or underestimate mild AKI while rarely misclassifying severe stages [16]; consistent with this, AKI was identified in 21 of the 89 episodes with an estimated baseline creatinine (2 ASB and 19 symptomatic UTI episodes), and injury in these 21 episodes was predominantly mild (median admission creatinine 1.82 mg/dL). A prespecified sensitivity analysis restricted to measured-baseline episodes was performed.

A resistant organism was defined as extended-spectrum beta-lactamase production, AmpC production, or multidrug, carbapenem or extensively drug-resistant phenotype according to standard international definitions [17]. Bacteremia was defined as growth of an organism in blood culture; coagulase-negative staphylococci discordant with the urine isolate were regarded as probable contaminants and are reported as positive blood cultures rather than as bacteremia attributable to the urinary tract.

Timing of assessments and laboratory methods

Symptom assessment by the infectious diseases team, the complete blood count, CRP, procalcitonin where measured, urine microscopy and the repeat urine culture were all obtained at the index consultation, on the same day and before any antibiotic prescribed by the infectious diseases service; empirical antibiotics started by the referring team before consultation were recorded but could not always be timed relative to the referral culture. The index time for all analyses was this consultation.

Urine microscopy was performed on automated urine sediment analyzers (FUS-200 and MUS-3600, Dirui Industrial, Changchun, China) without manual centrifugation; counts are generated by the analyzer from automated imaging of the uncentrifuged specimen, so no manual field count applies, and leukocyte counts were reported as cells per high-power field (HPF) by the laboratory information system. Values were extracted exactly

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as reported, without rounding, recoding or unit conversion. For part of the study period the laboratory reported counts on a semi-quantitative scale (0, 1, 2, 3, 4, 5, 8, 10, 15, 20, 25, 30, 40, 50, 75, 100, 150, 200, 300, 500, 1,000 and 2,000 cells/HPF, the last being the highest reportable category), and for the remainder as continuous counts without an upper limit; the tiered distribution of values in Figure 3 reflects this reporting format. Because the area under the curve is rank-based, the format affects only the handling of ties. Serum CRP was measured by immunoturbidimetric assay on the Atellica CH analyzer and procalcitonin by chemiluminescent immunoassay on the Atellica IM analyzer (Atellica Solution, Siemens Healthineers, Erlangen, Germany); the upper reference limit for CRP was 5 mg/L. Complete blood counts were performed on a Sysmex XN-1000 hematology analyzer (Sysmex Corporation, Kobe, Japan). Urine was cultured with a calibrated 10 µL loop on a biplate of blood agar and eosin methylene blue agar and colony counts were read at 24 hours; blood cultures were incubated in the BD BACTEC FX system (Becton Dickinson, Sparks, MD, USA). Bacterial isolates were identified by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry (MALDI Biotyper, Bruker Daltonics, Bremen, Germany), and antimicrobial susceptibility testing was performed on the BD Phoenix M50 system (Becton Dickinson), supplemented by disc diffusion where automated results were unreliable, with European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints; yeasts were identified by MALDI-TOF mass spectrometry and confirmed on chromogenic agar.

Variables and outcomes

Admission laboratory variables comprised white blood cell count, absolute neutrophil and lymphocyte counts, platelet count, hemoglobin, CRP, erythrocyte sedimentation rate, procalcitonin, serum creatinine and urine microscopy. Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and systemic immune-inflammation index (SII) were computed from raw counts as neutrophils divided by lymphocytes, platelets divided by lymphocytes, and platelets multiplied by neutrophils divided by lymphocytes, respectively. Demographic, comorbidity, urological, symptom, microbiological and treatment variables were extracted as recorded. Procalcitonin was not part of a fixed admission panel and was requested at the discretion of the treating team, so it was available in a subset of episodes that is characterized in the results.

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The primary analytic target was group membership, that is, symptomatic UTI versus ASB. Secondary analyses, restricted to the symptomatic UTI stratum, examined the association of the markers with severity at presentation and with clinical course. AKI and bacteremia were ascertained from specimens obtained at presentation and are therefore markers of severity at the index time; hospitalization (admission at or after the index consultation), intensive care unit admission and in-hospital death occurred after the index time. A composite adverse outcome was defined as any of AKI, intensive care unit admission, bacteremia or in-hospital death. Because the index markers and two of the composite components were measured at the same time, these analyses describe associations with severity and outcome and are not presented as prognostic prediction. Antibiotic exposure was quantified as total treatment duration in days and as prescription of an oral antibiotic at discharge.

Ethical statement

The study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Balıkesir University (decision number 2026-12-1, 14 July 2026). Given the retrospective design and the use of anonymized routine clinical data, the requirement for written informed consent was waived by the committee. The study was conducted in accordance with the Declaration of Helsinki. Personal identifiers were removed before analysis.

Statistical analysis

Continuous variables are presented as median with interquartile range and compared by the Mann–Whitney U test; categorical variables are presented as number with percentage and compared by the chi-square or Fisher exact test. Discriminative performance was quantified by the area under the receiver operating characteristic (ROC) curve (AUC). Because 55 patients contributed more than one episode, all confidence intervals (CIs) for AUCs and all comparisons between markers were obtained by a patient-level cluster bootstrap: patients, with all their episodes, were resampled with replacement 2,000 times, the AUC of each marker and the difference between the AUCs of CRP and each comparator were recalculated in every resample, and percentile 95% CIs and two-sided bootstrap p values were derived from the resulting distributions. A prespecified analysis restricted to the first episode of each patient was also performed. Comparisons between CRP and procalcitonin were made

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within the subset of episodes in which both markers had been measured, so that the two AUCs and their difference were estimated in the same patients. Optimal thresholds were identified by the Youden index and are reported as descriptive quantities only, since thresholds derived in the same dataset are optimistically biased. Because the intended clinical use is to identify episodes in which antibiotics may be withheld, performance was additionally tabulated at two thresholds chosen before inspection of the data: 5 mg/L, the upper reference limit of the assay, and 10 mg/L, a conventional clinical cut-off. Sensitivity, specificity and predictive values at these thresholds are reported with Wilson 95% CIs, which treat episodes as independent; because 55 patients contributed more than one episode, patient-level cluster-bootstrap percentile intervals for the same quantities (2,000 resamples of patients with all their episodes) were also computed and are reported alongside, and the proportion of symptomatic UTI falling below each threshold is reported.

A multivariable logistic regression model for group membership included log-transformed CRP, NLR and SII together with age, sex, urinary catheter, diabetes mellitus and urological pathology, with standard errors clustered by patient to account for repeated episodes. Prespecified sensitivity analyses comprised restriction to the first episode per patient; reclassification of ASB episodes accompanied by bacteremia, intensive care admission or death as symptomatic UTI; restriction to patients without a urinary catheter; restriction to patients aged 65 years or older; restriction to repeat-culture-positive episodes; and restriction to episodes with a measured baseline creatinine. Following peer review, four further analyses were added: repetition of the primary analysis under the original classification, in which the eight episodes with bacteremia concordant with the urine isolate had been retained as ASB; exclusion of episodes in which *Candida albicans* was the urine isolate; reclassification as UTI, and separately exclusion, of ASB episodes with recorded fever or rigors; and separate comparison of ASB with localized and with systemic UTI as defined by the 2025 EAU scheme. Two further post hoc analyses reclassified as symptomatic UTI those ASB episodes in which a lower urinary tract symptom, or a lower urinary tract symptom together with fever or costovertebral angle tenderness, had nonetheless been recorded. Post hoc subgroup analyses examined discrimination in patients with and without comorbidity, with and without a urinary catheter, with diabetes mellitus, and with a modified Charlson index of 2 or more.

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For the secondary outcome aim, the minimum sample size required to develop a multivariable model was calculated using the criteria of Riley and colleagues, deriving the anticipated Cox-Snell R^2 from an assumed C-statistic of 0.80 and the observed outcome proportion [18, 19]. The AKI analysis was repeated in the subset of symptomatic episodes with a measured baseline creatinine. Analyses were performed in Python (scipy, scikit-learn, statsmodels) and R. Two-sided *p* values below 0.05 were considered statistically significant.

RESULTS

Cohort composition

Four hundred episodes of significant bacteriuria in 337 adults met the eligibility criteria (Figure 1); 282 patients contributed one episode, 48 contributed two, six contributed three and one contributed four. Review of blood culture isolates identified 14 episodes without documented urinary symptoms in which blood cultures were positive. In eight, the blood isolate was *Escherichia coli* and concordant with the urine isolate; these were classified as bacteremic symptomatic urinary tract infection (UTI). In the remaining six the blood isolate was *Staphylococcus epidermidis*, discordant with the urine isolate and consistent with skin contamination; these episodes retained their classification as asymptomatic bacteriuria (ASB). After this step, 154 episodes (38.5%) in 146 patients were classified as ASB and 246 (61.5%) in 216 patients as symptomatic UTI. Among symptomatic episodes, 53 were acute cystitis, 138 acute pyelonephritis, 47 complicated UTI and eight bacteremic UTI without localizing symptoms.

The repeat urine culture obtained at consultation grew a single organism at a significant count in 264 episodes (66.0%), a bacterial uropathogen in 246 and *Candida albicans* in 18 (eight ASB, ten UTI), showed no growth in 107 (26.8%) and was reported as contaminated in 29 (7.3%). Repeat-culture positivity did not differ between groups (103 of 154, 66.9% versus 161 of 246, 65.4%; $p = 0.768$).

Of the 154 ASB episodes, 74 (48.1%) had no recorded symptom. In the remainder the findings were predominantly non-specific: urinary incontinence in 41 (26.6%), fatigue in 38 (24.7%) and altered mental status in 21 (13.6%). Fever was documented in two (1.3%) compared with 154 (62.6%) of symptomatic UTI episodes. In five ASB episodes fever or rigors had been recorded but had not been attributed to the urinary tract by the treating team; the repeat urine culture was negative in three, and C-reactive protein

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(CRP) ranged from 4.9 to 12.6 mg/L. These episodes retained their classification, and the effect of reclassifying or excluding them is shown in Table 4. Eighteen ASB episodes (11.7%) nonetheless had a lower urinary tract symptom recorded (dysuria 9, suprapubic tenderness 5, frequency 4) and 21 (13.6%) costovertebral angle tenderness; in these the finding had not been judged a new or worsening complaint at data extraction. Because that judgment cannot be verified with certainty, the effect of reversing it was quantified in two post hoc analyses.

The two groups were broadly similar on baseline characteristics (Table 1). Age, sex distribution, modified Charlson comorbidity index, diabetes mellitus, hypertension, dementia, chronic kidney disease, urological pathology, urinary catheter use, bedbound status, recent antibiotic exposure and previous UTI history did not differ significantly; malignancy was more frequent in ASB (22.1% versus 13.4%, $p = 0.024$). The groups otherwise differed only in symptoms, inflammatory markers and clinical outcomes.

Antibiotic exposure in asymptomatic bacteriuria

All 154 episodes retrospectively classified as ASB had received antibiotic therapy at the time of care. Because the cohort comprised patients referred to and managed by the infectious diseases service, this proportion reflects the composition of a consultation cohort and is not an institutional treatment rate. The median treatment duration was 11 days (interquartile range 7 to 15), amounting to 1,778 antibiotic-days, or 11.5 days per episode. Treatment duration in ASB did not differ significantly from that in symptomatic UTI (median 12 days, $p = 0.139$). One hundred and four ASB episodes (67.5%) were additionally prescribed an oral antibiotic at discharge, and 43 (27.9%) were managed as inpatients.

Among repeat-culture-positive episodes, the leading pathogen distribution was similar in ASB and symptomatic UTI. *Escherichia coli* was isolated in 47 ASB and 79 UTI episodes, and *Klebsiella pneumoniae* in 20 and 22 respectively. A resistant organism was recovered in 47 of the 95 ASB episodes with a bacterial isolate (49.5%), of which 39 were extended-spectrum beta-lactamase producers, compared with 63 of the 151 UTI episodes with a bacterial isolate (41.7%; $p = 0.234$).

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Discrimination of asymptomatic bacteriuria from symptomatic urinary tract infection

CRP was markedly higher in symptomatic UTI than in ASB (median 31.0 versus 7.4 mg/L, $p < 0.001$) and discriminated the two groups well, with an area under the receiver operating characteristic curve (AUC) of 0.892 (95% CI 0.858 to 0.923). All other markers performed significantly worse (Table 2, Figure 2). Neutrophil-to-lymphocyte ratio (NLR) achieved an AUC of 0.714, neutrophil count 0.654, procalcitonin 0.672, white blood cell count 0.634, systemic immune-inflammation index (SII) 0.580 and platelet-to-lymphocyte ratio (PLR) 0.441; every cluster-bootstrap comparison against CRP yielded $p < 0.001$, and the first-episode analysis gave an AUC of 0.899 (0.862 to 0.933) for CRP, 0.474 for urinary leukocyte count and 0.707 for NLR.

Urinary leukocyte count did not discriminate at all (AUC 0.482, 95% CI 0.429 to 0.539), with medians of 62 and 75 cells per high-power field (HPF) in ASB and symptomatic UTI respectively ($p = 0.540$).

Procalcitonin had been measured in 229 episodes (74 ASB, 155 UTI). Compared with episodes without a procalcitonin result, those with one were more often hospitalized (49.3% versus 24.0%), more often had systemic features (55.5% versus 39.2%) and had a higher median CRP (23.3 versus 13.6 mg/L), consistent with selective testing of sicker patients. Within this subset the AUC of CRP was 0.896 (0.851 to 0.936) and that of procalcitonin 0.672 (0.601 to 0.747); the paired difference was 0.223 (0.151 to 0.298, $p < 0.001$).

Discrimination by CRP depended on the type of symptomatic infection. Against the 43 localized UTI episodes of the European Association of Urology (EAU) scheme, in which the median CRP was 20.3 mg/L, the AUC was 0.784 (0.700 to 0.857); against the 203 systemic episodes, median CRP 34.6 mg/L, it was 0.915 (0.880 to 0.944). Median CRP was 18.0 mg/L in acute cystitis, 36.4 mg/L in acute pyelonephritis and 33.7 mg/L in complicated UTI. Urinary leukocyte count did not discriminate in either comparison (0.474 and 0.483), and NLR discriminated only against systemic infection (0.476 versus 0.764) (Table 4).

Platelet count was higher in ASB than in symptomatic UTI (median 272 versus 243 $\times 10^3/\mu L$, $p = 0.003$), in the opposite direction to neutrophil count (5.3 versus 6.8 $\times 10^3/\mu L$, $p < 0.001$). PLR was accordingly higher in ASB (158.4 versus 147.8, $p =$

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0.048) and discriminated inversely, while SII, which multiplies the neutrophil signal by the platelet count, differed only modestly between groups (880.0 versus 971.5, p = 0.007) (Figure 3).

A CRP threshold of 13.0 mg/L, identified by the Youden index, yielded 84.6% sensitivity, 83.8% specificity, 89.3% positive predictive value and 77.2% negative predictive value. The corresponding NLR threshold of 3.22 gave 76.8% sensitivity but only 57.8% specificity, and a procalcitonin threshold of 0.25 ng/mL gave 43.2% sensitivity and 82.4% specificity.

Because the clinical purpose of such a test is to identify episodes in which antibiotics might be withheld, performance was additionally examined at the two prespecified thresholds favoring exclusion rather than at the Youden point. At the Youden threshold, 38 of the 167 episodes below the cut-off (22.8%) were symptomatic UTI, too high a proportion to support withholding treatment. At a threshold of 5 mg/L, only 3 of 46 episodes below the cut-off (6.5%) were symptomatic UTI, corresponding to a sensitivity of 98.8% (95% CI 96.5 to 99.6), a specificity of 27.9% (21.4 to 35.5) and a negative predictive value of 93.5% (82.5 to 97.8); at 10 mg/L the corresponding figures were 21 of 127 (16.5%), sensitivity 91.5% (87.3 to 94.3), specificity 68.8% (61.1 to 75.6) and negative predictive value 83.5% (76.0 to 88.9). Patient-level cluster-bootstrap intervals, which account for repeated episodes, were similar: at 5 mg/L, 97.2 to 100 for sensitivity, 20.9 to 34.9 for specificity and 85.3 to 100 for negative predictive value; at 10 mg/L, 87.9 to 94.8, 61.4 to 76.2 and 76.7 to 89.6 respectively. All three symptomatic episodes below 5 mg/L were acute cystitis managed as outpatients: a 52-year-old woman with dysuria and frequency (CRP 4.5 mg/L, 150 leukocytes/HPF, *E. coli*), a 67-year-old catheterized man with diabetes, frequency and suprapubic tenderness (CRP 4.5 mg/L, 2 leukocytes/HPF, repeat culture contaminated), and a 68-year-old woman with frequency (CRP 4.7 mg/L, 500 leukocytes/HPF, *E. coli*). No systemic UTI episode had a CRP below 5 mg/L. No threshold of urinary leukocyte count leaving at least 10 episodes below the cut-off achieved a negative predictive value above 39.1%.

In multivariable analysis (Table 3, Figure 4), CRP was the only inflammatory marker among those entered into the model that was independently associated with symptomatic UTI (adjusted odds ratio 8.05 per log unit, 95% CI 4.26 to 15.21, p < 0.001). Neither NLR (adjusted odds ratio 3.98, 95% CI 0.82 to 19.21, p = 0.085) nor SII (adjusted odds ratio 0.81, 95% CI 0.35 to 1.87, p = 0.613) retained significance.

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Female sex was associated with symptomatic presentation (adjusted odds ratio 1.80, $p = 0.042$) and diabetes mellitus with asymptomatic presentation (adjusted odds ratio 0.39, $p = 0.010$). The full model achieved an AUC of 0.907, only marginally above CRP alone (0.892).

Discrimination by CRP was stable across the prespecified sensitivity analyses, with AUCs ranging from 0.879 in repeat-culture-positive episodes to 0.904 when bacteremic, intensive care and fatal ASB episodes were reclassified as symptomatic UTI; under the original classification, with the eight concordant bacteremic episodes retained as ASB, the AUC was 0.884 (0.846 to 0.921); exclusion of the 18 *Candida* episodes gave 0.890; and reclassifying the five ASB episodes with recorded fever or rigors as UTI gave 0.884, excluding them 0.891. In the post hoc analyses, reclassifying the 18 ASB episodes with a recorded lower urinary tract symptom changed the AUC from 0.892 to 0.881, and additionally reclassifying the 19 episodes with recorded fever or costovertebral angle tenderness changed it to 0.851 (Table 4).

Discrimination in clinical subgroups

Because most patients with bacteriuria seen by this service carried comorbidity, discrimination was examined in clinically relevant subgroups. CRP performed comparably in patients with any comorbidity (AUC 0.876) and without (0.933), in those with a urinary catheter (0.901) and without (0.887), in patients with diabetes mellitus (0.885), and in those with a modified Charlson index of 2 or more (0.883) (Table 4). The exclusion threshold of 5 mg/L behaved similarly: among patients with comorbidity, 2 of the 29 episodes below the cut-off were symptomatic UTI, and among catheterized patients, 1 of 17.

Association with severity and clinical outcomes within symptomatic urinary tract infection

Within the 246 symptomatic UTI episodes, 111 (45.1%) required hospitalization, 81 (32.9%) had acute kidney injury (AKI) at presentation, 21 (8.5%) were admitted to intensive care, 24 (9.8%) were bacteremic and nine (3.7%) died in hospital; 102 (41.5%) met the composite adverse outcome.

The ranking of markers reversed relative to the diagnostic analysis. NLR was the marker most strongly associated with each outcome, with AUCs of 0.871 for

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hospitalization, 0.801 for AKI and 0.783 for the composite outcome, exceeding procalcitonin (0.745, 0.746, 0.780; n = 155) and CRP (0.704, 0.770, 0.724). SII again performed poorly (0.605, 0.576, 0.582) and PLR was inversely associated (0.434, 0.459, 0.473) (Figure 5). In the 184 symptomatic episodes with a measured baseline creatinine, of which 62 had AKI (the remaining 19 of the 81 AKI episodes had an estimated baseline), the pattern was unchanged: NLR 0.805 (0.739 to 0.869), procalcitonin 0.793 (n = 112), CRP 0.777, SII 0.564 and PLR 0.442.

Applying the 2025 EAU classification, 203 episodes (82.5%) were systemic and 43 (17.5%) localized. Systemic episodes had higher rates of hospitalization (51.2% versus 16.3%), AKI (36.5% versus 16.3%), intensive care admission (10.3% versus 0%) and composite adverse outcome (46.8% versus 16.3%). Discrimination by the EAU classification exceeded that of the former complicated versus uncomplicated dichotomy for every outcome (hospitalization AUC 0.602 versus 0.526; AKI 0.566 versus 0.536; composite 0.591 versus 0.544), although absolute discrimination by either classification alone remained modest.

Sample size adequacy for a prognostic model was formally inadequate. Applying the criteria of Riley and colleagues with 12 candidate predictor parameters and an assumed C-statistic of 0.80, the minimum required sample size was 381 episodes for hospitalization, 395 for AKI and 373 for the composite outcome, against 246 available. These findings are therefore reported as exploratory associations and no multivariable prognostic model was developed.

DISCUSSION

In this cohort of 400 episodes of significant bacteriuria managed by a hospital infectious diseases service, two findings stand out. First, asymptomatic bacteriuria (ASB) accounted for close to two-fifths of all episodes and was treated as intensively as symptomatic infection, accumulating 1,778 antibiotic-days in a group for whom guidelines recommend treatment only in narrowly defined circumstances. Second, the single laboratory finding most often invoked to justify such treatment, pyuria, carried no discriminative information, while a routinely available C-reactive protein (CRP) measurement separated episodes retrospectively classified as ASB from symptomatic urinary tract infection (UTI) with an area under the receiver operating characteristic curve (AUC) of 0.892.

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The juxtaposition of these observations is the central message. Petty and colleagues found that abnormal urinalysis was the strongest factor associated with antibiotic treatment of ASB in 2,733 hospitalized patients [5]. Our data indicate why this is a diagnostic dead end: urinary leukocyte counts were similar in ASB and symptomatic UTI, and the confidence interval for their area under the curve (0.429 to 0.539) includes chance. This is consistent with the Infectious Diseases Society of America (IDSA) guideline, which defines ASB irrespective of pyuria, states that neutrophil-driven responses including pyuria do not reliably discriminate the two conditions, and identifies the evaluation of biomarkers that could make this distinction as an explicit research need [1]. Diagnostic stewardship, that is, using the laboratory itself to steer appropriate antimicrobial use [20], requires such an alternative, and CRP is a candidate already measured in most of these patients.

The strength of the CRP signal depended on what it was asked to distinguish. Most symptomatic episodes in this consultation cohort were systemic, and against these CRP performed very well (AUC 0.915). Against localized infection, which is the distinction a clinician is more likely to find difficult, discrimination was lower (0.784) and the median CRP in acute cystitis (18.0 mg/L) was closer to that of ASB (7.4 mg/L). A substantial part of the overall AUC therefore reflects the separation of ASB from pyelonephritis and other systemic infection, and the overall estimate should not be read as the performance expected in a population dominated by cystitis. Even in the localized comparison, however, CRP remained informative and pyuria did not, and the exclusion threshold behaved consistently: no systemic episode and only three cystitis episodes had a CRP below 5 mg/L.

A question that follows directly from these data is why episodes meeting the definition of ASB were treated at all. These episodes were not labeled as ASB at the point of care; the label was applied retrospectively against strict criteria. What the clinician saw was an older, frequently catheterized or bedbound patient with a positive urine culture, pyuria, and one or more non-specific findings: urinary incontinence in 26.6%, fatigue in 24.7% and altered mental status in 13.6%. For delirium the IDSA guideline is explicit, recommending assessment for other causes and observation when localizing genitourinary features and systemic signs are absent [1]; for incontinence and fatigue it offers no comparable statement, and in an inpatient consultation they are readily interpreted as infection. Surveys confirm the gap: only 33.7% of resident physicians

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could distinguish ASB from UTI and 46.3% acknowledged prescribing antibiotics for ASB knowing they were not indicated [21, 22]. Our cohort therefore quantifies, in a single service, the antibiotic consequence of a diagnostic ambiguity that guidelines define away but do not resolve at the bedside [5, 7].

Interventions targeting this reasoning gap have been evaluated directly. Cognitive biases favoring treatment improve after a stewardship intervention [23], and algorithms that distinguish UTI from ASB have reduced inappropriate treatment: in catheter-associated bacteriuria overtreatment fell from 1.6 to 0.6 episodes per 1,000 bed-days with gains sustained after the intervention ended [24], and across an integrated health system the proportion of ASB episodes treated fell from 23.5% to 15.3% [25]. The largest program is the most instructive. Across 14,572 patients with a positive urine culture at 46 hospitals, ASB-related antibiotic use fell from 29.1% to 17.1%, but that gain came almost entirely from ordering fewer unnecessary cultures: among patients in whom ASB had already been identified, the proportion treated did not change significantly, from 82.0% to 76.3% [7]. Once a positive culture is in front of the clinician, education and audit have not been sufficient to change the treatment decision, and that decision is precisely where an objective discriminator would act.

The counterargument to withholding antibiotics is fear of missed bacteremic infection. This concern has been quantified: among hospitalized adults with ASB and altered mental status, bacteremia from a presumed urinary source occurred in 1.8% overall and 0.7% once patients with systemic signs were excluded [26]. A systematic review of antibiotic treatment for delirium in older adults with pyuria or bacteriuria identified only four studies in 652 patients and found no evidence of benefit, with two reporting worse outcomes after treatment [27]. Our own data illustrate the concern from the other side: eight episodes initially classified as ASB on symptom criteria proved, on review of blood isolates, to be bacteremic with the urine organism, and their CRP values ranged from 5.0 to 81.1 mg/L (median 14.8 mg/L), none below the 5 mg/L threshold. Together with the observation that CRP was low in the great majority of ASB episodes, these data are compatible with observation and objective monitoring rather than reflexive treatment in patients without systemic features, but they do not demonstrate that such a strategy is safe.

The direction in which the test is used matters more than its overall discrimination. For a stewardship decision the relevant question is not which threshold maximizes the

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Youden index but which threshold would make it reasonable to withhold antibiotics, and these are not the same. In our data the Youden threshold left more than a fifth of episodes below the cut-off with symptomatic infection, whereas a threshold of 5 mg/L reduced this to 6.5%, and the three symptomatic episodes below it were all cystitis managed as outpatients. The threshold analysis must nonetheless remain exploratory. Only 46 episodes fell below 5 mg/L, the confidence interval for the negative predictive value extends down to 82.5%, and the study included no group in which antibiotics were withheld on the basis of CRP, so it cannot show that doing so is safe. What the data support is that a bacteriuric patient without localizing urinary symptoms and with a CRP below 5 mg/L is unlikely to have systemic infection, and that this threshold deserves prospective validation in a study in which outcomes of observation are measured.

It is also worth stating how far these episodes were from the textbook picture of asymptomatic bacteriuria. Thirty-five (22.7%) had a localizing urinary sign, 20 (13.0%) had fever, rigors, a positive blood culture with a skin organism, an intensive care admission or died, and 29 (18.8%) had altered mental status or general deterioration; 65 (42.2%) had at least one of these. More than two-fifths therefore carried a finding that would prompt most clinicians to treat, even though none met the criteria for symptomatic infection. The remaining 89 episodes had none of these features and their treatment is not defensible on clinical grounds; this is precisely the practice the study documents. Even here the patients were not straightforward: 71 (79.8%) had urological pathology, 70 (78.7%) a comorbidity and 31 (34.8%) a catheter. The clinical value of any marker depends on whether it works in such patients, and a marker that discriminated only in otherwise healthy patients would be of little practical use. CRP discriminated comparably across these subgroups, which is the condition it must meet before prospective evaluation is worthwhile.

The median CRP in ASB, 7.4 mg/L, was above the assay reference limit, and 72.1% of ASB episodes had a value of 5 mg/L or more. Part of this is explained by comorbid illness: ASB episodes in patients with comorbidity had a median CRP of 8.6 mg/L compared with 6.1 mg/L in those without. CRP is a non-specific marker of systemic inflammation, and chronic illness, malignancy, which was more frequent in the ASB group, and non-infectious inflammatory conditions all raise it. This non-specificity works against rather than for the main finding, since it narrows the gap between the

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groups, but it also means that an elevated CRP in a bacteriuric patient cannot be attributed to the urinary tract without clinical assessment.

The comparative behavior of the composite indices is instructive and, we believe, generalizable beyond urinary infection. Systemic immune-inflammation index (SII) and platelet-to-lymphocyte ratio (PLR) both incorporate platelet count in a manner that assumes platelets rise with inflammation. In our cohort the opposite occurred: platelet counts were higher in ASB than in symptomatic UTI, a pattern that could reflect consumption, sequestration and early marrow effects during established infection, although our data cannot establish the mechanism. Multiplying a valid neutrophil-lymphocyte signal by a counter-directional platelet term degraded rather than enhanced discrimination, so that SII performed worse than its own neutrophil-to-lymphocyte ratio (NLR) component in both the diagnostic (0.580 versus 0.714) and outcome (0.605 versus 0.871 for hospitalization) analyses. Given the volume of literature reporting SII as a positive prognostic marker across conditions since its original description in hepatocellular carcinoma [10], a negative result in bacterial infection is worth recording, and suggests that composite indices should not be adopted without demonstrating superiority over their simpler components.

The reversal of marker ranking between the diagnostic and outcome analyses has a plausible interpretation. CRP, a hepatic acute-phase reactant driven by interleukin-6, may chiefly reflect whether an inflammatory response to infection is present at all and therefore help to separate colonization from infection. NLR reflects the magnitude of stress-induced neutrophilia and lymphopenia and may therefore track severity once infection is established. On this reading the two markers answer different questions and should be used for different purposes rather than treated as interchangeable inflammatory surrogates; the interpretation is offered as a hypothesis consistent with the data rather than as a demonstrated mechanism.

Our secondary analysis provides early empirical support for the 2025 European Association of Urology (EAU) reclassification. The EAU panel replaced the complicated and uncomplicated categories with a localized and systemic distinction and explicitly noted that validation against clinical outcomes was required [11]. In our cohort the new classification discriminated adverse outcomes better than the classification it replaces for every outcome examined, which is reassuring, but absolute discrimination remained modest for both. This supports the panel's framing of the new

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scheme as a communication and decision-structuring tool rather than a risk score, and suggests that combining it with an objective inflammatory measure would be more useful than either alone.

Diabetes mellitus was associated with asymptomatic rather than symptomatic presentation, consistent with the recognized high prevalence of ASB in diabetic patients and with the specific IDSA recommendation against screening this group [1].

The stakes extend beyond the individual patient. Resistant organisms were recovered from 49.5% of ASB episodes with a bacterial isolate in our cohort, and urinary tract infection is a major contributor to the global burden of antimicrobial resistance [28]. Every avoidable antibiotic course in this group therefore carries both individual and ecological cost. Interventions using clinical decision support at the point of urine culture ordering [29] and broader urine culture stewardship programs [30] provide the implementation framework into which an objective marker such as CRP could be embedded.

Limitations

First, design and classification. This is a retrospective, single-center study based on symptom documentation recorded for clinical rather than research purposes, and symptom ascertainment in patients with dementia, delirium or indwelling catheters is inherently unreliable. The number of referrals screened and excluded was not recorded, so selection into the cohort cannot be fully described. There is no independent reference standard for ASB; the classification rests on the same clinical record that the treating physicians generated, and although it was applied independently by two assessors using guideline criteria, the assessors were not blinded to laboratory results. A prespecified sensitivity analysis reclassifying bacteremic, intensive care and fatal ASB episodes strengthened rather than weakened the CRP finding, and review of blood isolates led to the reclassification of eight concordant bacteremic episodes, which likewise did not alter the conclusions, but neither can substitute for prospective blinded adjudication. Pregnancy and planned invasive urological procedures were not systematically recorded, so a small number of ASB episodes may have been treated appropriately. Significant bacteriuria was defined by the specimen-specific laboratory thresholds for significant growth applied to the single culture that prompted referral; the IDSA recommendation that bacteriuria in asymptomatic women be confirmed in two

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consecutive specimens was not applied, so some episodes classified as ASB in women may have represented transient bacteriuria.

Second, cohort selection. Every episode received antibiotics, because the cohort was assembled from patients referred to the infectious diseases service; bacteriuric patients who were appropriately not treated are absent, and referral itself may have been influenced by clinical severity, urinalysis or inflammatory markers. We therefore cannot estimate how much unnecessary antibiotic use occurs in asymptomatic bacteriuria, and our data characterize the duration of treatment among treated episodes rather than the proportion of ASB that is treated. Because the repeat culture at consultation was frequently obtained after empirical antibiotics, it was negative or contaminated in a third of episodes; restriction to repeat-culture-positive episodes did not change the findings.

Third, incorporation bias and confounding. Group assignment was made retrospectively from documented symptoms alone, but those notes were written by physicians who had already seen the CRP and urinalysis results, so differential thoroughness of documentation cannot be excluded and would inflate the apparent performance of CRP. CRP is also non-specific: comorbid and malignant disease raise it independently of infection, malignancy was more frequent in the ASB group, and the markers and the classification were drawn from the same presentation, so residual confounding by illness severity cannot be excluded. Prospective evaluation with symptom adjudication blinded to inflammatory markers is required before CRP can be recommended for this purpose.

Fourth, measurement and power. Procalcitonin was available in only 57.2% of episodes, and selectively in sicker patients, so its comparative performance is provisional and a cohort in which it is measured systematically would be needed to establish its place alongside CRP. Urinary leukocyte counts were reported on a semi-quantitative scale for part of the study period, which limits resolution at high counts, although rank-based analyses are unaffected. The outcome analysis within symptomatic UTI did not meet minimum sample size criteria and is exploratory, acute kidney injury (AKI) and bacteremia were ascertained at the same time as the markers and therefore describe severity at presentation rather than subsequent events, and all thresholds were evaluated in the same dataset and require external validation. The Wilson confidence intervals for sensitivity, specificity and predictive values at the CRP thresholds treat the 400

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episodes as independent; the cluster-bootstrap intervals that account for the 55 patients with repeated episodes were similar but slightly wider, and both are reported.

CONCLUSION

Among adults with bacteriuria managed by an infectious diseases service, episodes classified as asymptomatic bacteriuria constituted 38.5% of the caseload and received antibiotic courses of similar duration to symptomatic infection. Pyuria, the test most commonly used to justify such treatment, provided no discriminative information, whereas admission C-reactive protein showed good discrimination between episodes retrospectively classified as asymptomatic bacteriuria and symptomatic urinary tract infection in this single-center retrospective cohort, with consistent results across sensitivity analyses and weaker, though still present, discrimination against localized infection. Composite hematologic indices incorporating platelet count performed worse than the neutrophil-to-lymphocyte ratio alone, and should not be assumed superior to their components. These findings are hypothesis-generating. C-reactive protein, and in particular a low C-reactive protein threshold for withholding treatment, merits prospective, externally validated evaluation with blinded adjudication before it is used as an objective adjunct to symptom assessment within antimicrobial stewardship programs targeting asymptomatic bacteriuria.

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TABLES AND FIGURES WITH LEGENDS

Table 1. Baseline characteristics, laboratory findings, and outcomes in asymptomatic bacteriuria versus symptomatic urinary tract infection.

Variable	ASB (*n* = 154)	UTI (*n* = 246)	*p*
Age, years, median (IQR)	63.5 (48.0–72.0)	64.5 (51.0–76.0)	0.077
Female sex, *n* (%)	84 (54.5)	154 (62.6)	0.110
Age ≥65 years, *n* (%)	72 (46.8)	123 (50.0)	0.527
Modified Charlson index, median (IQR)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	0.937
Diabetes mellitus, *n* (%)	45 (29.2)	64 (26.0)	0.484
Hypertension, *n* (%)	37 (24.0)	74 (30.1)	0.188
Malignancy, *n* (%)	34 (22.1)	33 (13.4)	0.024
Dementia, *n* (%)	15 (9.7)	18 (7.3)	0.391
Chronic kidney disease, *n* (%)	6 (3.9)	18 (7.3)	0.161
Urological pathology, *n* (%)	128 (83.1)	212 (86.2)	0.404
Urinary catheter, *n* (%)	57 (37.0)	86 (35.0)	0.677
Bedbound, *n* (%)	22 (14.3)	25 (10.2)	0.213
Antibiotic use in past month, *n* (%)	72 (46.8)	128 (52.0)	0.304
Previous UTI, *n* (%)	55 (35.7)	103 (41.9)	0.220
White blood cells, ×10³/µL	8.0 (6.0–10.5)	9.5 (7.2–12.7)	<0.001
Neutrophils, ×10³/µL	5.3 (4.2–7.0)	6.8 (4.9–8.9)	<0.001
Lymphocytes, ×10³/µL	1.6 (1.3–2.1)	1.7 (1.3–2.3)	0.302
Platelets, ×10³/µL	272.0 (222.0–323.8)	243.0 (197.2–315.5)	0.003
CRP, mg/L	7.4 (4.9–11.8)	31.0 (19.7–55.9)	<0.001
Procalcitonin, ng/mL (ASB *n* = 74; UTI *n* = 155)	0.11 (0.05–0.21)	0.21 (0.09–0.50)	<0.001
NLR	3.1 (2.7–3.7)	3.9 (3.3–5.0)	<0.001
PLR	158.4 (111.4–243.2)	147.8 (101.2–208.9)	0.048
SII	880.0 (681.8–1,116.6)	971.5 (715.3–1,299.2)	0.007

Urinary leukocytes, cells/HPF	62 (20–150)	75 (15–150)	0.540
Repeat culture positive, *n* (%)	103 (66.9)	161 (65.4)	0.768
Resistant organism, *n* (% of bacterial isolates)	47/95 (49.5)	63/151 (41.7)	0.234
Positive blood culture, *n* (%)	6 (3.9)	24 (9.8)	0.030
Hospitalization, *n* (%)	43 (27.9)	111 (45.1)	<0.001
Acute kidney injury at presentation, *n* (%)	17 (11.0)	81 (32.9)	<0.001
Intensive care admission, *n* (%)	11 (7.1)	21 (8.5)	0.617
In-hospital death, *n* (%)	1 (0.6)	9 (3.7)	0.096
Antibiotic duration, days	11 (7–15)	12 (8–17)	0.139

Continuous variables are presented as median (IQR) and categorical variables as *n* (%), unless otherwise specified. Continuous variables were compared using the Mann–Whitney U test and categorical variables using the chi-square or Fisher exact test. Procalcitonin was measured in 74 ASB and 155 UTI episodes. Repeat-culture-positive counts include 18 episodes with *Candida albicans* isolates (eight ASB and ten UTI); resistant-organism denominators are the numbers of episodes with bacterial isolates in each group. Acute kidney injury was ascertained from creatinine measured at presentation. All six positive blood cultures in the ASB group grew *Staphylococcus epidermidis* discordant with the urine isolate and were regarded as probable contaminants. **Abbreviations:** ASB, asymptomatic bacteriuria; CRP, C-reactive protein; HPF, high-power field; IQR, interquartile range; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; UTI, urinary tract infection.

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Table 2. Discrimination of symptomatic urinary tract infection from asymptomatic bacteriuria by admission markers.

Marker	*n*	AUC	95% CI	Difference from CRP (95% CI)	*p* vs CRP
CRP	400	0.892	0.858–0.923	—	reference
NLR	400	0.714	0.661–0.765	0.178 (0.124–0.230)	<0.001
Neutrophil count	400	0.654	0.598–0.707	0.238 (0.182–0.294)	<0.001
Procalcitonin	229	0.672	0.601–0.747	0.223 (0.151–0.298)	<0.001
White blood cell count	400	0.634	0.575–0.690	0.258 (0.200–0.316)	<0.001
SII	400	0.580	0.523–0.634	0.312 (0.248–0.376)	<0.001
Urinary leukocyte count	400	0.482	0.429–0.539	0.410 (0.348–0.476)	<0.001
PLR	400	0.441	0.386–0.501	0.451 (0.377–0.522)	<0.001

Confidence intervals and *p* values were obtained using a patient-level cluster bootstrap with 2,000 resamples. Differences are the AUC of CRP minus the AUC of each comparator, estimated among episodes with both markers available (n = 229 for procalcitonin). —, not applicable; CRP is the reference marker. **Abbreviations:** AUC, area under the receiver operating characteristic curve; CI, confidence interval; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index.

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Table 3. Multivariable logistic regression for symptomatic urinary tract infection versus asymptomatic bacteriuria with standard errors clustered by patient.

Variable	Adjusted OR	95% CI	*p*
CRP, per log unit	8.05	4.26–15.21	<0.001
NLR, per log unit	3.98	0.82–19.21	0.085
SII, per log unit	0.81	0.35–1.87	0.613
Age, per year	0.99	0.97–1.00	0.070
Female sex	1.80	1.02–3.18	0.042
Urinary catheter	0.69	0.39–1.22	0.205
Diabetes mellitus	0.39	0.19–0.80	0.010
Urological pathology	0.99	0.48–2.02	0.977

CRP, NLR, and SII were log-transformed, and standard errors were clustered by patient. The model AUC was 0.907, compared with 0.892 for CRP alone. **Abbreviations:** AUC, area under the receiver operating characteristic curve; CI, confidence interval; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; OR, odds ratio; SII, systemic immune-inflammation index.

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Table 4. Prespecified, post-review, and post hoc sensitivity and subgroup analyses of C-reactive protein discrimination.

Analysis	*n*	ASB	UTI	AUC	95% CI
Primary analysis, all episodes	400	154	246	0.892	0.858–0.923
First episode per patient only	337	134	203	0.899	0.862–0.933
Bacteremic, ICU or fatal ASB reclassified as UTI	400	136	264	0.904	0.867–0.937
Patients without a urinary catheter	257	97	160	0.887	0.839–0.931
Patients aged ≥65 years	195	72	123	0.881	0.826–0.929
Repeat-culture-positive episodes only	264	103	161	0.879	0.831–0.921
Episodes with a measured baseline creatinine	311	127	184	0.883	0.846–0.919
Original classification, eight concordant bacteremic episodes retained as ASB	400	162	238	0.884	0.846–0.921
Episodes with *Candida* excluded	382	146	236	0.890	0.852–0.923
ASB episodes with recorded fever or rigors reclassified as UTI	400	149	251	0.884	0.846–0.917
ASB episodes with recorded fever or rigors excluded	395	149	246	0.891	0.854–0.925
ASB versus localized UTI (EAU 2025)	197	154	43	0.784	0.700–0.857
ASB versus systemic UTI (EAU 2025)	357	154	203	0.915	0.880–0.944
ASB episodes with any lower urinary tract symptom reclassified as UTI (post hoc)	400	136	264	0.881	0.843–0.915
Lower urinary tract symptom, fever or costovertebral tenderness reclassified as UTI (post hoc)	400	117	283	0.851	0.809–0.891
Patients with any comorbidity (post hoc)	278	112	166	0.876	0.829–0.917
Patients without comorbidity (post hoc)	122	42	80	0.933	0.879–0.978
Patients with a urinary catheter (post hoc)	143	57	86	0.901	0.843–0.948
Patients with a modified Charlson index ≥2 (post hoc)	170	70	100	0.883	0.822–0.935
Patients with diabetes mellitus (post hoc)	109	45	64	0.885	0.818–0.939

The primary analysis and the next six sensitivity analyses were prespecified; the following six analyses were added after peer review. Analyses marked post hoc were added after inspection of the data. Confidence intervals were obtained using a patient-level cluster bootstrap with 2,000 resamples. Sample sizes refer to episodes; the first-episode analysis includes one episode per patient. Comorbidity was defined as any of diabetes mellitus, hypertension, coronary artery disease, asthma or chronic obstructive pulmonary disease, malignancy, dementia, cerebrovascular disease, or chronic kidney disease. **Abbreviations:** ASB, asymptomatic bacteriuria; AUC, area under the receiver operating characteristic curve; CI, confidence interval; EAU, European Association of Urology; ICU, intensive care unit; UTI, urinary tract infection.

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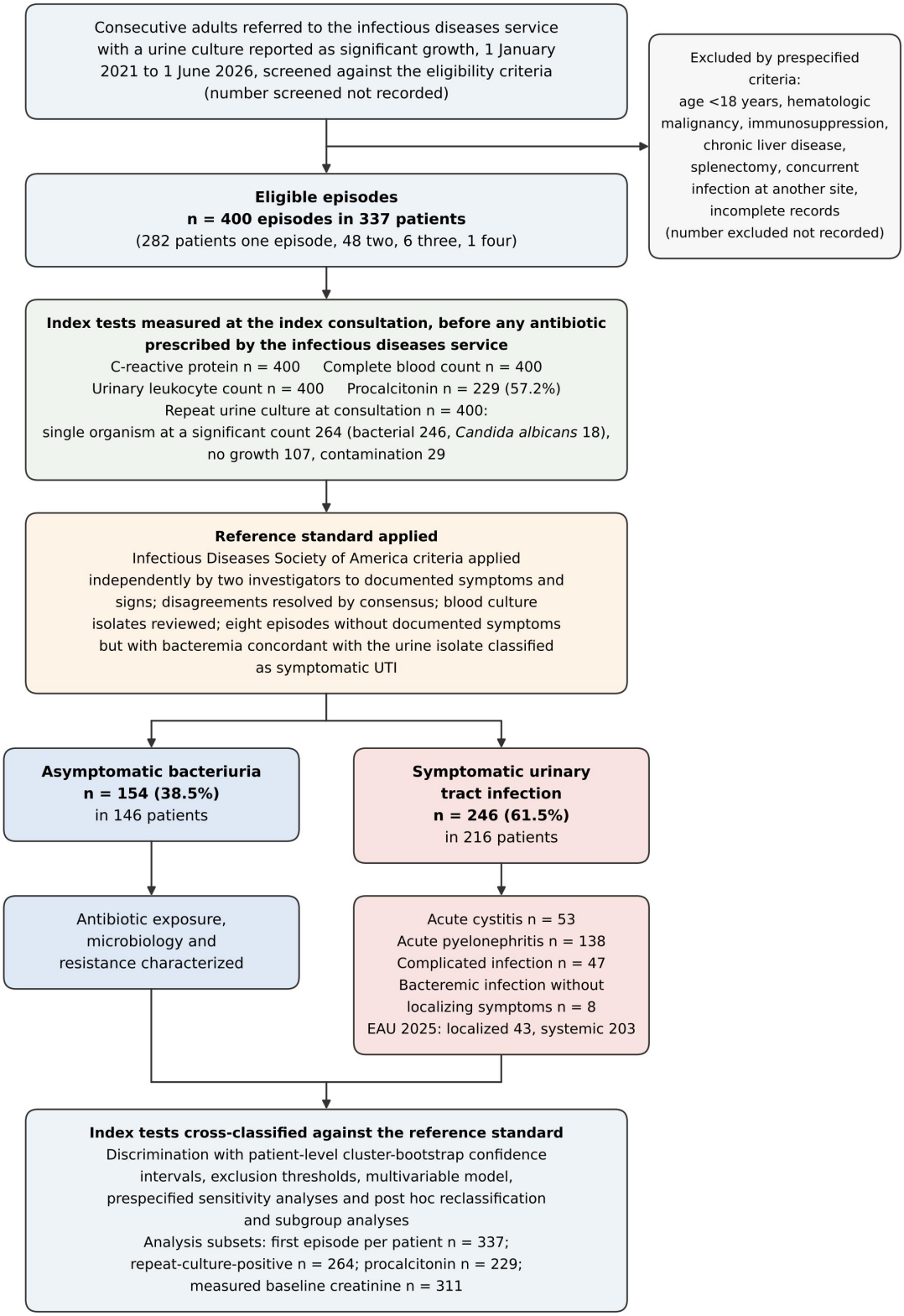


Figure 1. Study flow and classification of eligible episodes. The flow diagram summarizes eligibility, availability of admission tests and repeat urine cultures, application of the reference standard, and analysis subsets. The cohort comprised 400 episodes in 337 patients. Eight episodes with bacteremia concordant with the urine

isolate were classified as symptomatic urinary tract infection despite the absence of documented urinary symptoms. The final groups comprised 154 episodes of asymptomatic bacteriuria and 246 episodes of symptomatic urinary tract infection. The numbers screened and excluded were not recorded. The diagram was prepared according to the Standards for Reporting Diagnostic Accuracy 2015 statement. **Abbreviations:** EAU, European Association of Urology; UTI, urinary tract infection.

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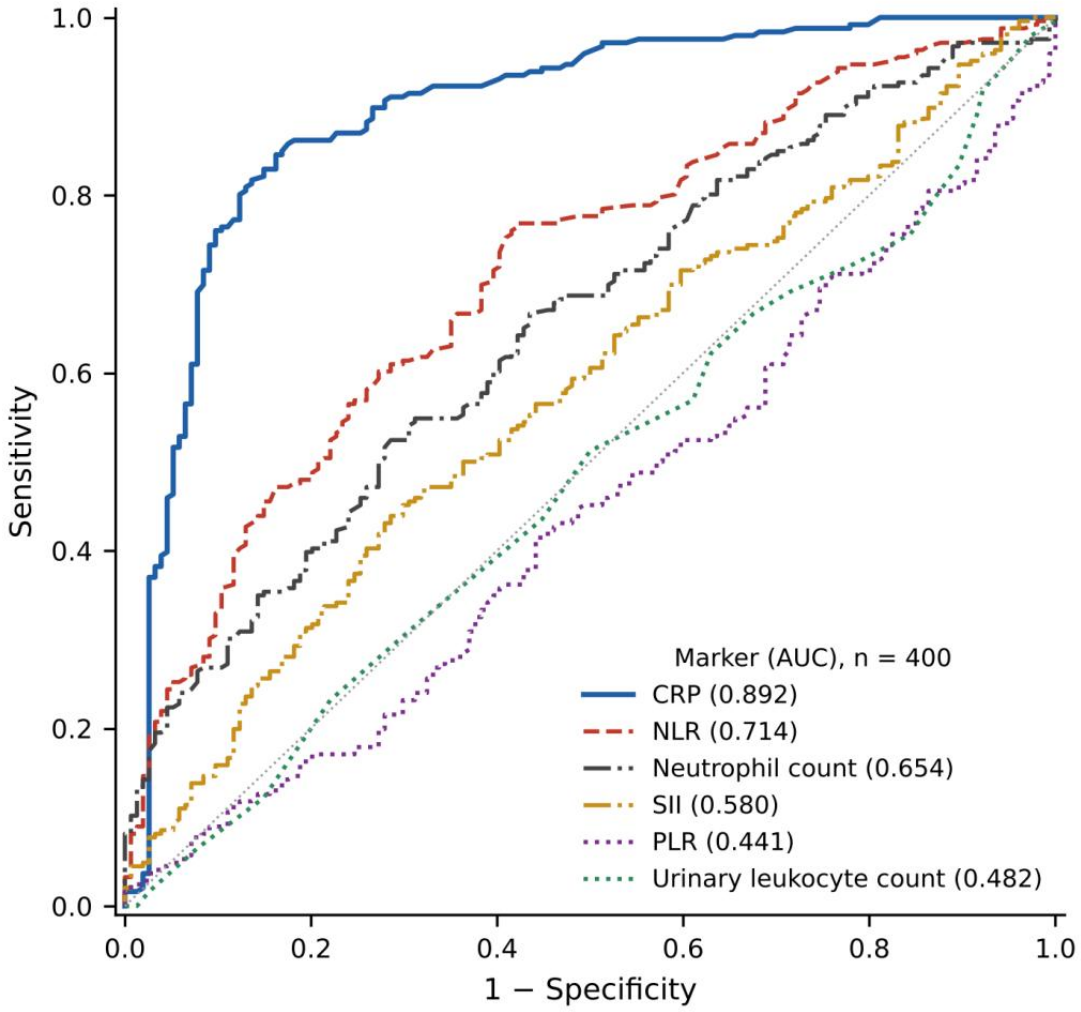


Figure 2. Discrimination of symptomatic urinary tract infection from asymptomatic bacteriuria by admission markers. Receiver operating characteristic curves are shown for C-reactive protein, neutrophil-to-lymphocyte ratio, neutrophil count, systemic immune-inflammation index, platelet-to-lymphocyte ratio, and urinary leukocyte count in all 400 episodes. The plot legend gives the area under each curve. Confidence intervals are reported in Table 2. The gray diagonal indicates chance-level discrimination. **Abbreviations:** AUC, area under the receiver operating characteristic curve; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index.

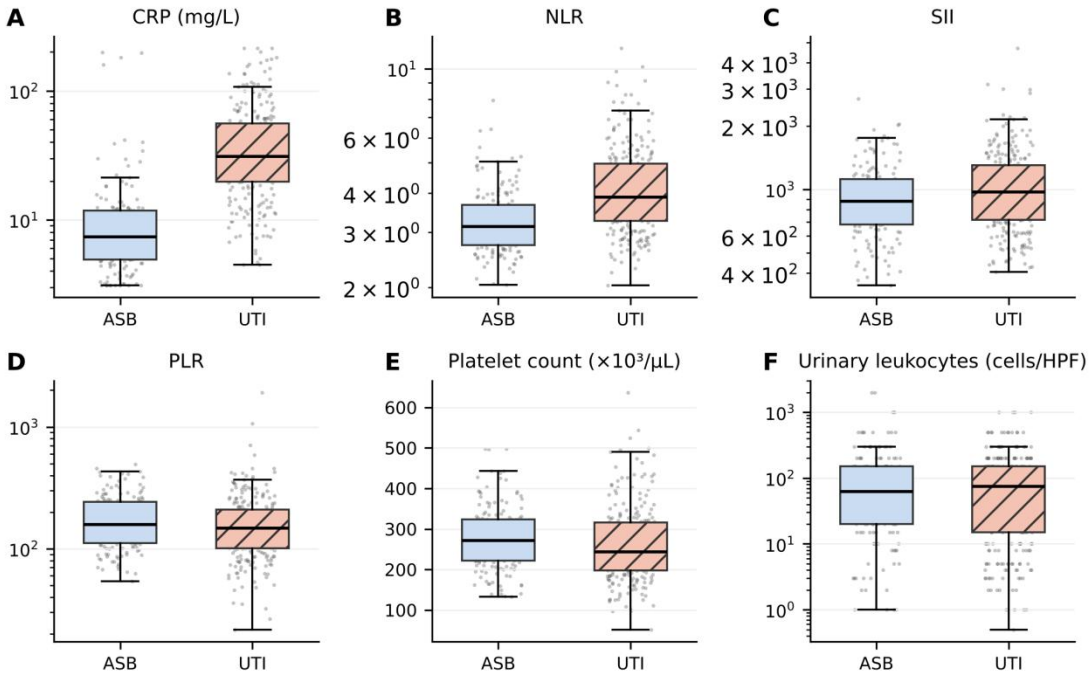


Figure 3. Distributions of admission markers in asymptomatic bacteriuria and symptomatic urinary tract infection. (A) C-reactive protein; **(B)** neutrophil-to-lymphocyte ratio; **(C)** systemic immune-inflammation index; **(D)** platelet-to-lymphocyte ratio; **(E)** platelet count; and **(F)** urinary leukocyte count. Boxes represent the interquartile range, central horizontal lines indicate the median, whiskers extend to the most extreme values within 1.5 times the interquartile range of the box (Tukey rule), and gray points represent individual episodes, including those beyond the whiskers. Blue boxes indicate asymptomatic bacteriuria, and hatched pink boxes indicate symptomatic urinary tract infection. Panels A–D and F use logarithmic vertical axes; panel E uses a linear vertical axis. The tiered urinary leukocyte values reflect the semiquantitative reporting scale used by the laboratory during part of the study period. **Abbreviations**: ASB, asymptomatic bacteriuria; CRP, C-reactive protein; HPF, high-power field; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; UTI, urinary tract infection.

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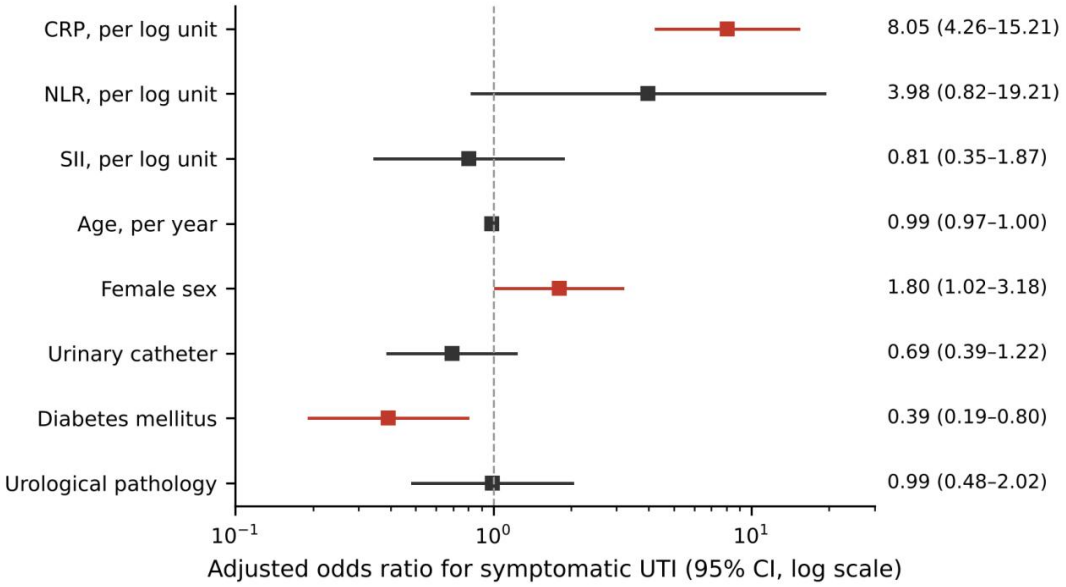


Figure 4. Adjusted associations with symptomatic urinary tract infection. Squares show adjusted odds ratios, and horizontal lines show 95% confidence intervals from the multivariable logistic regression model comparing symptomatic urinary tract infection with asymptomatic bacteriuria. Standard errors were clustered by patient. Red indicates $p < 0.05$. The vertical dashed line marks an odds ratio of 1; the horizontal axis is logarithmic. **Abbreviations:** CI, confidence interval; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; UTI, urinary tract infection.

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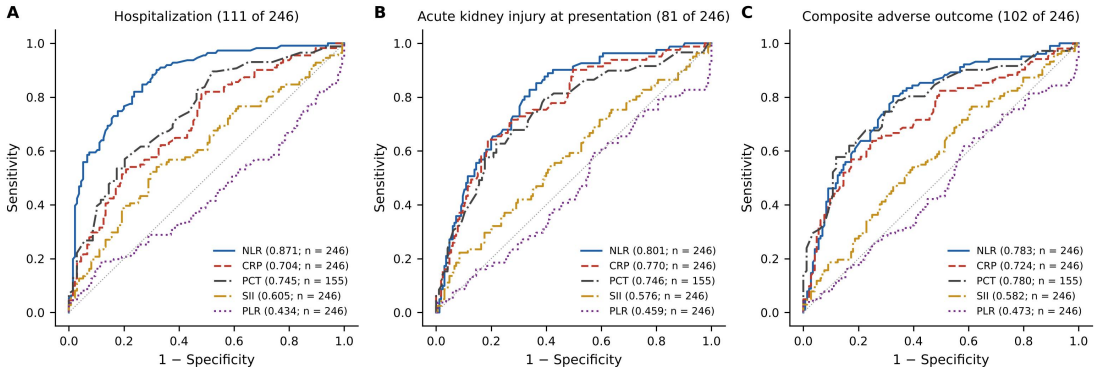


Figure 5. Admission markers in relation to severity and clinical outcomes within symptomatic urinary tract infection. Receiver operating characteristic curves are shown for **(A)** hospitalization, **(B)** acute kidney injury at presentation, and **(C)** the composite adverse outcome of acute kidney injury, intensive care unit admission, bacteremia, or in-hospital death. The analysis included 246 symptomatic urinary tract infection episodes, with 111 hospitalizations, 81 episodes of acute kidney injury, and 102 composite events. Plot legends give the area under the curve and the number of episodes available for each marker; procalcitonin was available in 155 episodes. Gray diagonals indicate chance-level discrimination. **Abbreviations:** CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; PCT, procalcitonin; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index.

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SUPPLEMENTAL DATA

Supplemental data are available at the following link:

www.bjbms.org/ojs/index.php/bjbms/article/download/15190/5483

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