

Diagnostics Needs for Urinary Tract Infections in the Era of Antimicrobial Resistance

Lorenz Leitner^{1,2}, Shawna McCallin^{1,2}, Thomas M. Kessler^{1,2}

¹ Department of Neuro-Urology, Balgrist University Hospital, University of Zürich, Zürich, CH;

² Spinal Cord Injury Center, Balgrist University Hospital, University of Zürich, Zürich, CH
Lorenz.leitner@balgrist.ch

Summary:

Urinary tract infections (UTIs) are among the leading indications for antibiotic prescription worldwide and are increasingly complicated by antimicrobial resistance (AMR). Current diagnostic workflows remain slow and insufficiently precise for modern anti-infective strategies. Here, we present our hospital's experience with UTI microbiology, AMR, and development of novel urine-based diagnostics, including companion diagnostics for phage therapy. Our findings highlight the urgent need for rapid, functionally informative diagnostics capable of supporting antimicrobial stewardship and future precision therapies.

Keywords: antimicrobial resistance, urine, diagnostics, urinary tract infections, phage therapy, antibiotic susceptibility testing

Background, Motivation and Objective

Urinary tract infections (UTIs) affect hundreds of millions of patients annually and represent one of the largest drivers of empirical antibiotic use. Increasing antimicrobial resistance (AMR), particularly among *Escherichia coli* and other uropathogens, has substantially complicated antibiotic treatment selection and contributed to recurrent infection, treatment failure, and healthcare burden.

Current diagnostic workflows rely primarily on symptom assessment, urinalysis, and urine culture. While urinalysis provides rapid but indirect information, urine cultures typically require 24–72 h, with additional time needed for antimicrobial susceptibility testing (AST). In polymicrobial or recurrent infections, clinically actionable results may require several days. Consequently, antibiotic therapy is frequently initiated empirically before microbiological confirmation.

These workflows were developed in an era of broadly effective antibiotics and are increasingly strained by AMR. Furthermore, emerging precision anti-infective strategies, including bacteriophage therapy, require greater diagnostic resolution, including rapid pathogen identification and strain-level susceptibility testing.

The objective of this work was to evaluate limitations in current UTI diagnostic pathways and to investigate new urine-based diagnostic

approaches capable of supporting future precision therapies.

Description of the New Method or System

In clinical practice, we adhere to the current guidelines from the European Association of Urology (EAU). Our research is focused on developing and testing new therapies and diagnostics for UTIs, with a specific focus on recurrent and catheter-associated UTIs.

A prospective epidemiological study was conducted to characterize microbiology and AMR patterns within our patient population [1], while the ongoing MiLUT observational study longitudinally collects urine samples and clinical metadata for metabolomic, transcriptomic, proteomic, microbiome, and immunological analyses. These studies provide urine samples with associated clinical metadata and bacterial isolates for evaluation of next-generation therapies and diagnostics.

Using patient-derived urine and bacterial isolates, we validated a nano-luciferase-based companion diagnostic assay capable of simultaneously detecting *E. coli* and phage susceptibility directly in urine samples [2]. The assay is being developed to support patient enrollment and treatment selection in an upcoming phage therapy RCT.

Results

During a one-year prospective observation period, 2615 urine samples from 1820 patients underwent routine microbiological analysis and

AST. Culture-based diagnostic workflows required approximately 48–72 h to obtain susceptibility results, and resistance rates against commonly used antibiotics ranged from 1–38%. Within this cohort, standard urinalysis was a poor discriminator between asymptomatic bacteriuria and UTI, particularly in patients exposed to urinary catheters, the population in whom rapid, reliable diagnosis is most urgently needed. Catheter-stratified receiver-operating-characteristic curves (ROC) analysis (Fig. 1) showed only modest performance of leukocyte counts (AUC 0.59, 95 % CI 0.54 to 0.65) and essentially no discrimination of bacterial sediment counts (AUC 0.52, 95 % CI 0.45 to 0.58) in catheter-exposed patients, whereas in non-catheterized patients leukocytes performed substantially better (AUC 0.75, 95 % CI 0.64 to 0.86; bacteria AUC 0.63, 95 % CI 0.50 to 0.76). These findings indicate that conventional urinalysis cannot reliably guide antibiotic prescribing or trial enrolment decisions, motivating the development of rapid, pathogen-specific point-of-care diagnostics.

Using isolates and urine samples obtained through these studies, we validated a nano-luciferase-based assay for direct urine testing of phage susceptibility. Preliminary findings demonstrate the feasibility of simultaneous pathogen detection and functional susceptibility assessment directly in patient urine, with greatly reduced time-to-result compared to conventional microbiology. Ongoing work focuses on assay stabilization, integration of internal controls, and selection of clinically actionable readouts.

As therapeutic strategies become increasingly personalized, diagnostic systems must evolve from simple presence/absence testing toward adaptive platforms capable of supporting individualized treatment decisions directly from patient-derived samples. Further thought should be given to distribution and implementation in

high AMR burden, low resource settings, such as in hospitals in low- and middle- income countries (LMICs).

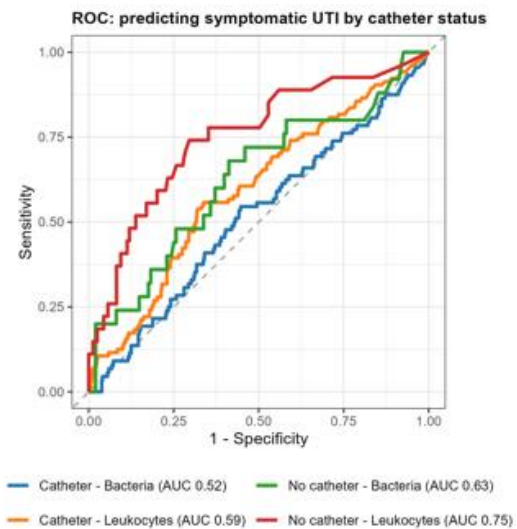


Fig. 1. Urinalysis as a discriminator between asymptomatic bacteriuria and UTI, stratified by catheter status. Top: leukocyte counts (Leu/ μ L, log10) in urine sediment. Middle: bacterial counts (Bact/ μ L, log10). Bottom: receiver-operating-characteristic curves for predicting UTI $n = 1271$ catheter-exposed and $n = 244$ non-catheter visits with paired urinalysis and clinical assessment.

References

- [1] V. Neumeier, F.P. Stangl, et al. Indwelling catheter vs intermittent catheterization: is there a difference in UTI susceptibility? *BMC Infect Dis.* 23(1):507. doi: 10.1186/s12879-023-08475-7
- [2] S. Meile, J. Du, et al. Engineered reporter phages for detection of *Escherichia coli*, *Enterococcus*, and *Klebsiella* in urine. *Nat Comm.* 14(1):4336. doi: 10.1038/s41467-023-39863-x