From Static Tables to Smart Signals: Automating Hospital Antibiograms with Wastewater Genomics at Walter Reed National Military Medical Center

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INTRODUCTION

Hospital antibiograms are essential antimicrobial stewardship tools. However, at Walter Reed National Military Medical Center (WRNMMC), conventional antibiograms are typically only generated annually from clinical isolate antimicrobial susceptibility testing (AST) data. As a result, antibiograms may lag behind emerging resistance trends.

Wastewater-based genomic surveillance (WWGS) offers a complementary data stream for antimicrobial resistance (AMR) monitoring. Because wastewater integrates biological signal from the broader hospital population, including individuals without ordered cultures, it can provide near-real-time insight into changes in antimicrobial resistance gene (ARG) abundance. We evaluated whether WWGS could support more dynamic AMR situational awareness and help identify when clinical antibiograms may need targeted updates.

METHODS

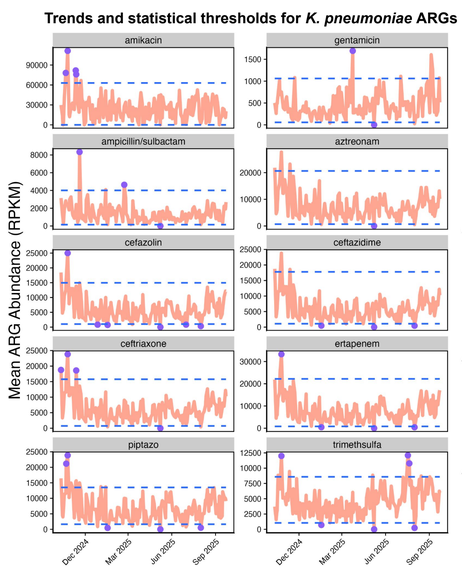
To evaluate WWGS as a complementary AMR surveillance tool, we paired de-identified clinical AST data with longitudinal wastewater sequencing data from WRNMMC. Hospital wastewater samples were analyzed using targeted metagenomic sequencing capable of detecting a broad set of pathogens and ARGs. For each bug-drug combination represented on the hospital antibiogram, we identified relevant ARGs and tracked the relative abundance of those ARGs when co-detected with the focal pathogen in a wastewater sample.

We then developed statistical thresholds to identify deviations from historical wastewater ARG abundance. Baseline levels were established from the first six months of wastewater surveillance data and modeled using a negative binomial framework. High and low thresholds were used to flag increases or decreases in ARG abundance, and results were summarized as a prototype “wastewater antibiogram” showing recent deviations from baseline by organism, drug, and collection site.

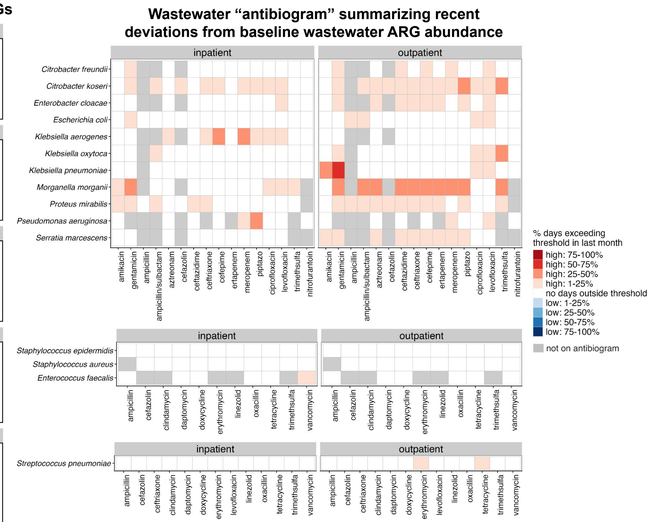
RESULTS

Wastewater surveillance detected clinically relevant AMR signals

Wastewater sequencing detected diverse ARGs, including carbapenemases and extended-spectrum β-lactamases. A prototype wastewater antibiogram was generated to summarize recent deviations from historical ARG baselines. Unlike a traditional antibiogram, which summarizes clinical isolate susceptibility across a calendar year, the wastewater antibiogram highlights recent changes in population-level AMR signal. Colored cells indicate bug-drug combinations where recent wastewater ARG abundance exceeded statistical thresholds, with stronger signals reflecting a greater fraction of recent samples above threshold.



Wastewater abundance of ARGs associated with *K. pneumoniae* at inpatient sites. Trend lines track ARG abundance averaged over inpatient collection sites by date. Blue dotted lines show statistical thresholds for deviations from baseline levels. Purple dots indicate dates flagged as significant deviations after applying a correction for multiple hypothesis testing.



Wastewater antibiogram for September 23, 2025. The antibiogram shows where the abundance of wastewater ARGs from the previous month (August 23 - September 23, 2025) deviates from baseline historical levels.

Wastewater ARG abundance correlated with clinical resistance trends

Wastewater ARG abundance was evaluated against clinical AST data for organisms with sufficient representation in both data streams. For *Escherichia coli* and *Klebsiella pneumoniae*, wastewater abundance of pathogen-specific ARGs was a statistically significant predictor of resistant-organism counts in clinical AST data (mixed effects poisson model; $p < 0.01$). For *E. coli*, wastewater ARG abundance with a one-week lag was significantly correlated with clinical counts of resistant isolates, suggesting that wastewater may provide an early warning signal for some resistance trends. For *K. pneumoniae*, wastewater ARG abundance was significantly associated with clinical resistance without a lag, indicating that wastewater captured resistance patterns concurrently with clinical testing.

DISCUSSION

These findings support a dual-surveillance model in which conventional clinical AST data remain the basis for patient-facing antibiograms, while WWGS provides a near-real-time population-level signal that can identify emerging resistance trends, support interim review, and guide targeted antibiogram updates. WWGS provides broader situational awareness, including signal from asymptomatic carriage and patients without cultures. Together, these approaches could help military treatment facilities move from static, annual antibiograms toward dynamic, genomics-informed AMR monitoring.

The wastewater antibiogram is intended to complement, not replace, conventional antimicrobial stewardship tools. Key limitations include:

- ARGs detected in metagenomic wastewater data cannot always be assigned to specific host organisms.
- Hybrid-capture metagenomic sequencing provides semi-quantitative abundance estimates that may be influenced by microbial community composition and assay bias.
- WWGS data can be noisy, particularly in outpatient settings, increasing the risk of false-positive anomaly detection.

Additional validation is needed across more organisms, facilities, and time periods before clinical integration.

CONCLUSION

These findings demonstrate the feasibility of a dynamic AMR surveillance framework in which wastewater signals help identify when clinical antibiograms may need targeted review or interim update. This approach could improve antimicrobial stewardship, infection prevention, and AMR situational awareness.

ACKNOWLEDGMENTS

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DISCLAIMER

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