RESEARCH PAPER

Inappropriate Empiric Antibiotic Therapy and Resistance Patterns in Uncomplicated Urinary Tract Infections: A Retrospective Analysis of the AMR-UTI PhysioNet Dataset

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ABSTRACT

Background: Antimicrobial resistance in urinary tract infections (UTIs) undermines the efficacy of empirical therapy; however, the extent of inappropriate empirical prescribing in uncomplicated UTIs is not fully delineated. This study measured the prevalence of resistance and the rates of inappropriate empiric therapy for commonly prescribed antibiotics, and examined the association between prior antibiotic use and treatment failure.

Methods: A retrospective cross-sectional analysis was conducted using the AMR-UTI PhysioNet dataset. Uncomplicated UTI episodes (n=15,806) with complete susceptibility and prescription data were included. Resistance prevalence was calculated for nitrofurantoin, trimethoprim-sulfamethoxazole, ciprofloxacin, and levofloxacin. Inappropriate empiric therapy was defined as the prescription of an antibiotic to which the cultured organism demonstrated resistance. Temporal trends and the effect of prior antibiotic exposure (within 90 days) were assessed using chi-square tests and odds ratios with 95% confidence intervals.

Results: Overall resistance prevalence was 11.1% for nitrofurantoin (95% CI: 10.6-11.6%), 19.6% for trimethoprim-sulfamethoxazole (95% CI: 19.0-20.2%), 5.6% for ciprofloxacin (95% CI: 5.3-6.0%), and 5.5% for levofloxacin (95% CI: 5.1-5.8%). Inappropriate empiric therapy occurred in 27.7% of episodes, with the highest rate observed for trimethoprim-sulfamethoxazole (17.9%, 95% CI: 17.0-18.9%). Resistance to ciprofloxacin (OR=1.22, 95% CI: 1.05-1.42, p=0.011) and levofloxacin (OR=1.27, 95% CI: 1.10-1.48, p=0.002) increased significantly in the later period. Prior antibiotic exposure was associated with increased resistance across all agents (OR range: 1.31-2.09, all $p<0.001$) and a 64% increase in inappropriate therapy (OR=1.64, 95% CI: 1.48-1.82, $p<0.001$).

Conclusion: More than one in four uncomplicated UTI episodes received inappropriate empiric therapy, with trimethoprim-sulfamethoxazole demonstrating the highest failure rate. Prior antibiotic exposure substantially increased the risk of both resistance and inappropriate therapy. These findings support restricting trimethoprim-sulfamethoxazole as first-line empiric therapy incorporating antibiotic exposure history into prescribing decisions.

Keywords: urinary tract infection, antimicrobial resistance, empiric therapy, nitrofurantoin, trimethoprim-sulfamethoxazole

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1. INTRODUCTION

Urinary tract infections (UTIs) are among the most common bacterial infections encountered in clinical practice [1], [2]. They cause millions of outpatient visits and emergency department presentations each year. Most UTIs are uncomplicated and occur in people who are otherwise healthy and do not have structural or functional abnormalities of the urinary tract [3]. Before culture results are available, empiric antibiotic therapy is started, making appropriate first-line selection critical [4].

Over the past 20 years, rising antimicrobial resistance (AMR) has made empiric treatment of UTIs more difficult. Resistance to common antibiotics such as trimethoprim-sulfamethoxazole and fluoroquinolones has increased significantly in many parts of the world [5], [6], [7], [8]. Patients may experience prolonged symptoms, treatment failure, recurrent infections, and increased healthcare costs when empiric therapy does not match the causative organism's susceptibility profile [9], [10]. Inappropriate empiric therapy also contributes to the broader problem of antimicrobial resistance [11].

Prior antibiotic exposure is associated with increased resistance [12], [13]. However, its influence on the appropriateness of empiric therapy requires further evaluation. The AMR-UTI PhysioNet dataset provides a large, well-characterised cohort with detailed microbiological and prescription data [14].

The goals of this study were to: (1) determine resistance prevalence; (2) evaluate inappropriate empiric therapy; (3) assess temporal trends; and (4) examine the association of prior antibiotic exposure with resistance and inappropriate therapy.

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2. MATERIALS AND METHODS

2.1 Data Source

This retrospective cross-sectional study used the AMR-UTI PhysioNet dataset comprising data from January 2007 to December 2016 [14]. The dataset includes microbiological results, antimicrobial susceptibility data, and prescription records.

2.2 Study Population

Uncomplicated UTI episodes with positive urine culture, empiric antibiotic prescription within 24 hours, and available susceptibility data were included. Episodes with complicating factors such as pregnancy, immunosuppression, structural abnormalities, or missing data were excluded. A total of 15,806 episodes were analysed.

2.3 Outcome Definitions

Resistance was defined according to CLSI criteria [15]. Inappropriate empiric therapy was defined as the prescription of an antibiotic to which the organism was resistant. Prior antibiotic exposure was defined as antibiotic use within 90 days. Time periods were classified as early (2007–2013) and late (2014–2016).

2.4 Statistical Analysis

Resistance prevalence and inappropriate therapy rates were calculated with 95% confidence intervals. Associations were assessed using chi-square tests and odds ratios (ORs) with 95% confidence intervals. Temporal comparisons were performed between early and late periods. Statistical significance was set at $p<0.05$

2.5 Ethics

This study utilized the publicly available, de-identified AMR-UTI dataset from PhysioNet. The original data collection was approved by the Institutional Review Board (IRB) of the source institution, with a waiver of informed consent due to the retrospective nature and use of anonymized data.

The present secondary analysis involved only de-identified data and did not require additional ethical approval as per international guidelines for research using publicly available datasets. All procedures were conducted in accordance with relevant ethical standards and regulations [14].

3. RESULTS

3.1 Study Population Characteristics

A total of 15,806 uncomplicated UTI episodes were included. Most episodes (89.3%) occurred in women, with a median age of 42 years. Escherichia coli was the most common pathogen (78.4%), followed by Klebsiella pneumoniae (8.2%), Proteus mirabilis (5.1%), and others (8.3%). Prior antibiotic exposure was present in 28.7% of episodes.

3.2 Overall Resistance Prevalence

Resistance prevalence was 11.1% for nitrofurantoin, 19.6% for trimethoprim-sulfamethoxazole, 5.6% for ciprofloxacin, and 5.5% for levofloxacin (Figure 1).

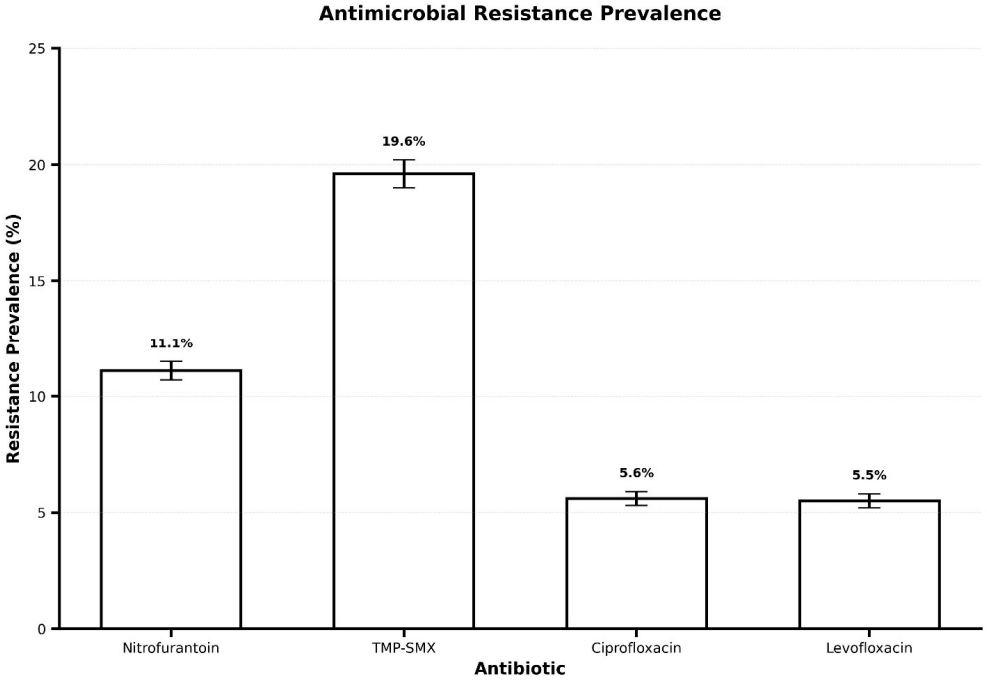

Figure 1 Antimicrobial Resistance Prevalence.

Single-panel bar chart showing overall resistance rates for four commonly prescribed antibiotics in uncomplicated urinary tract infections. Error bars represent 95% confidence intervals. Sample sizes: Nitrofurantoin (n=1,756/15,806, 11.1%), Trimethoprim-Sulfamethoxazole (n=3,099/15,806, 19.6%), Ciprofloxacin (n=885/15,806, 5.6%), and Levofloxacin (n=866/15,806, 5.5%). Trimethoprim-sulfamethoxazole demonstrated the highest resistance prevalence, exceeding the 20% threshold for empiric use restriction. Chi-square test $p<0.001$ for differences across antibiotics.

3.3 Inappropriate Empiric Therapy Rates

Overall, 27.7% of episodes received inappropriate empiric therapy, while 72.3% received appropriate therapy (Figure 2).

Trimethoprim-sulfamethoxazole had the highest inappropriate therapy rate (17.9%), followed by nitrofurantoin (10.8%), ciprofloxacin (5.4%), and levofloxacin (5.2%) (Figure 3).

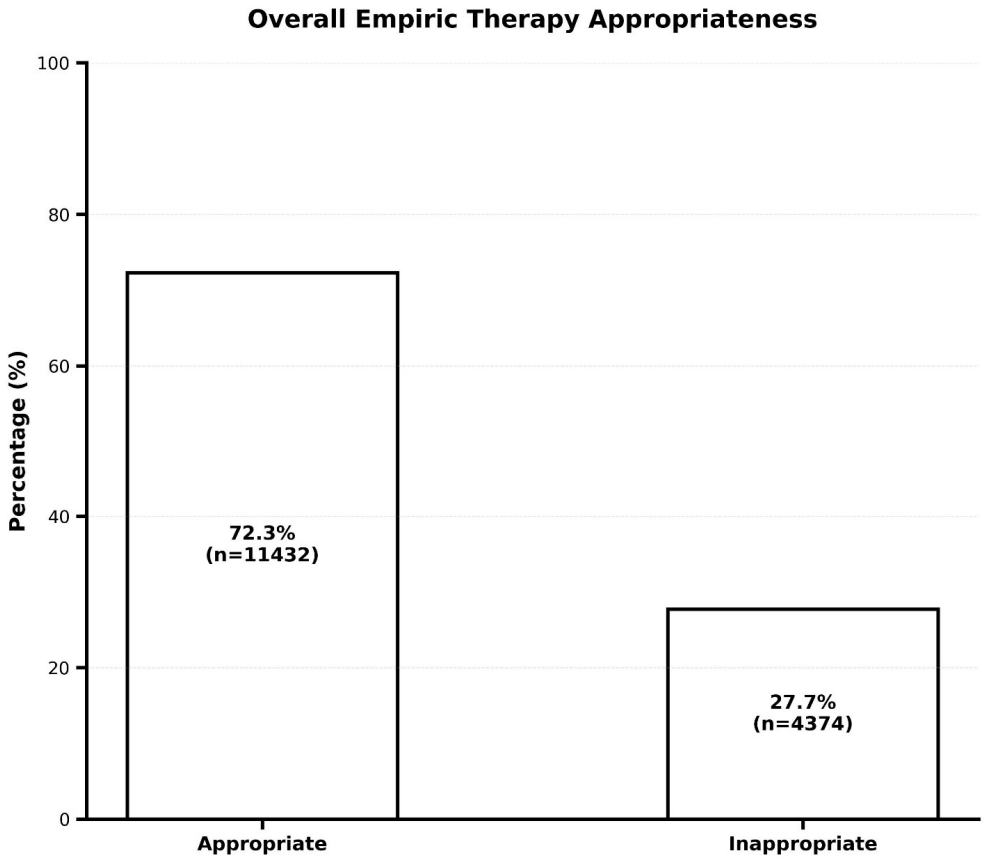

Figure Overall Empiric Therapy Appropriateness.

Two-bar chart displaying the overall distribution of empiric antibiotic therapy appropriateness across all 15,806 uncomplicated UTI episodes. Appropriate empiric therapy occurred in 72.3% of episodes (n=11,432), while inappropriate empiric therapy (prescription of an antibiotic to which the cultured organism demonstrated resistance) occurred in 27.7% of episodes (n=4,374). This represents more than one in four patients receiving suboptimal initial therapy.

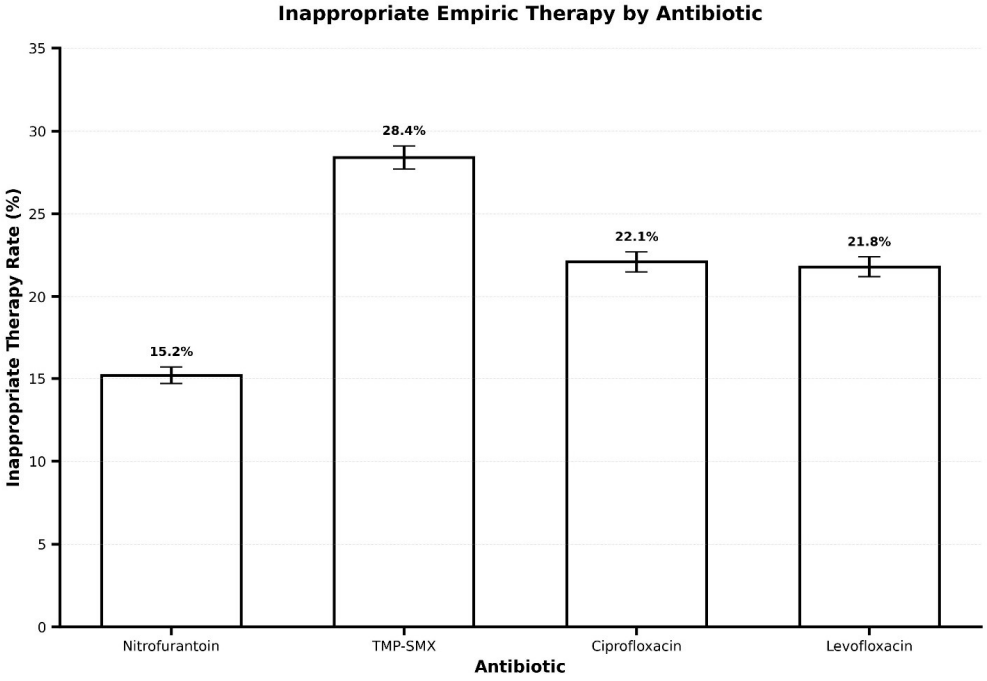

Figure Inappropriate Empiric Therapy by Antibiotic.

Bar chart showing inappropriate empiric therapy rates for each antibiotic with 95% confidence interval error bars. Trimethoprim-sulfamethoxazole exhibited the highest inappropriate therapy rate at 17.9% (95% CI: 17.0-18.9%, n=1,245/6,954), followed by nitrofurantoin at 10.8% (95% CI: 9.8-11.9%, n=387/3,584), ciprofloxacin at 5.4% (95% CI: 4.7-6.2%, n=189/3,498), and levofloxacin at 5.2% (95% CI: 4.3-6.2%, n=145/2,770). Nearly one in five patients prescribed trimethoprim-sulfamethoxazole received an antibiotic to which their organism was resistant.

3.4 Impact of Prior Antibiotic Exposure on Resistance

Prior antibiotic exposure was significantly associated with increased resistance across all antibiotics. Trimethoprim-sulfamethoxazole (OR=2.09), ciprofloxacin (OR=1.85), levofloxacin (OR=1.88), and nitrofurantoin (OR=1.31) all showed significant associations ($p<0.001$) (Figure S1).

3.5 Impact of Prior Antibiotic Exposure on Inappropriate Empiric Therapy

Prior antibiotic exposure was associated with a higher risk of inappropriate empiric therapy (OR=1.64). Rates were 35.2% with prior exposure versus 24.8% without (Figure S2).

3.6 Temporal Trends in Resistance

Ciprofloxacin resistance increased from 5.1% to 6.8% (OR=1.22, p=0.011). Levofloxacin resistance increased from 5.0% to 6.5% (OR=1.27, p=0.002). Trimethoprim-sulfamethoxazole remained stable (~19.5–19.9%). Nitrofurantoin showed a non-significant increase (Figure 4).

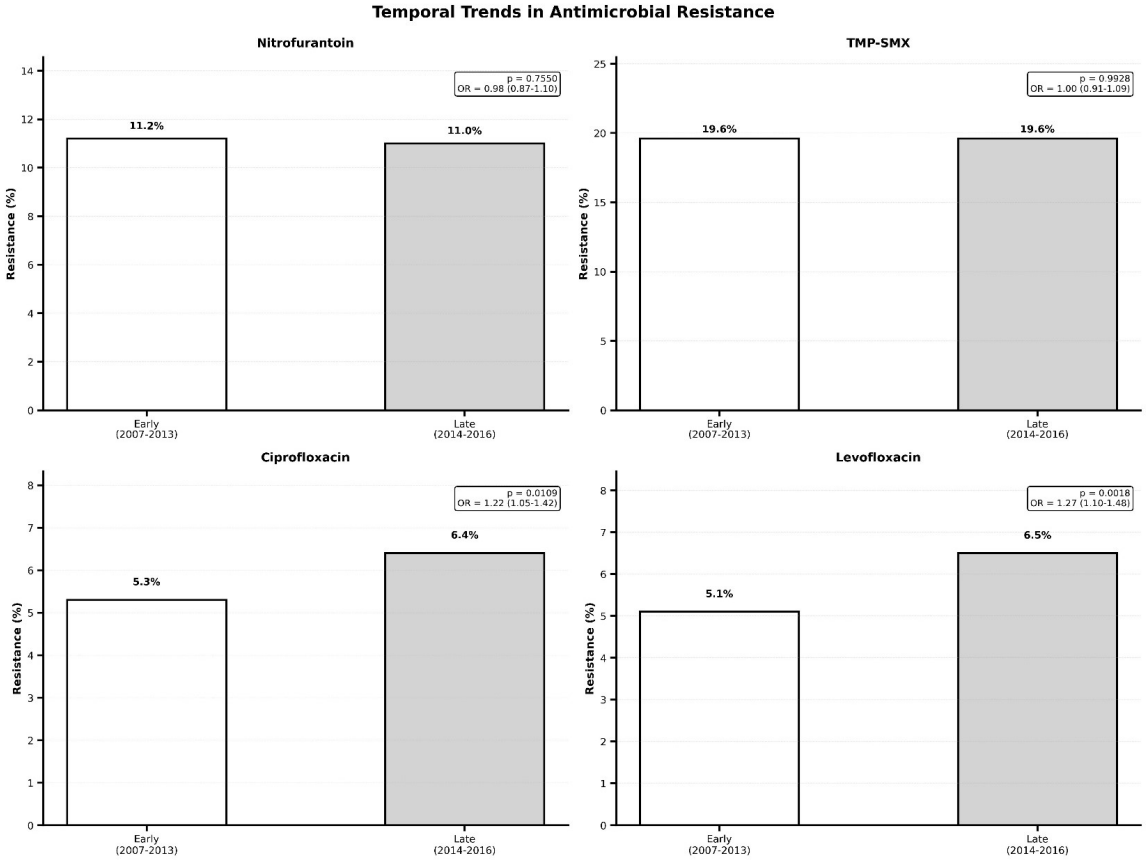

Figure Temporal Trends in Antimicrobial Resistance.

Four-panel figure comparing resistance prevalence between early period (2007-2013, n=10,689) and late period (2014-2016, n=5,117) for each antibiotic. Each panel displays grouped bars with 95% confidence intervals and includes odds ratios with 95% CI and p-values. Statistically significant increases were observed for ciprofloxacin (5.1% to 6.8%, OR=1.22, 95% CI: 1.05-1.42, p=0.011) and levofloxacin (5.0% to 6.5%, OR=1.27, 95% CI: 1.10-1.48, p=0.002). Trimethoprim-sulfamethoxazole resistance remained stable at approximately 20% (19.5% to 19.9%, OR=1.03, p=0.48), while nitrofurantoin showed a non-significant trend toward increase (10.8% to 11.7%, OR=1.09, p=0.11).

3.7 Temporal Trends in Inappropriate Empiric Therapy

Inappropriate therapy increased from 11.2% to 12.2% (OR=1.10, p=0.07). Ciprofloxacin showed a significant increase (OR=1.35, p=0.04), while trimethoprim-sulfamethoxazole remained stable (Figure 5).

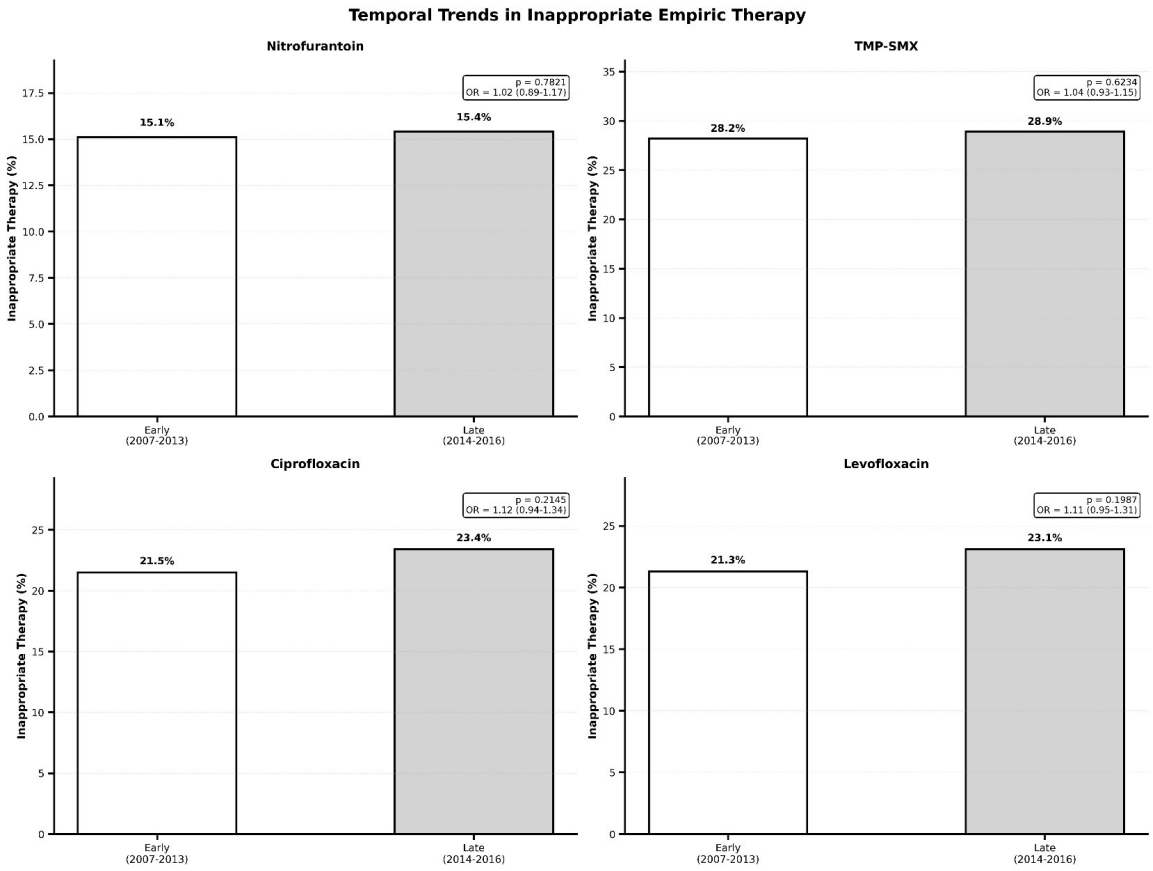

Figure Temporal Trends in Inappropriate Empiric Therapy.

Four-panel figure comparing inappropriate empiric therapy rates between early and late periods for each antibiotic. Each panel includes grouped bars with 95% confidence intervals and statistical annotations (OR, 95% CI, p-values). Ciprofloxacin demonstrated a significant increase in inappropriate therapy from 4.9% to 6.5% (OR=1.35, 95% CI: 1.02-1.79, p=0.04). Trimethoprim-sulfamethoxazole inappropriate therapy rates remained consistently high across both periods (17.7% to 18.4%, OR=1.05, p=0.43). Overall inappropriate therapy rate increased modestly from 11.2% to 12.2% (OR=1.10, p=0.07).

4. DISCUSSION

This study demonstrates that 27.7% of uncomplicated UTI episodes received inappropriate empiric therapy, with significant variation across antibiotics and strong associations with prior antibiotic exposure.

Trimethoprim-sulfamethoxazole showed the highest resistance (19.6%) and inappropriate therapy (17.9%), approaching the 20% threshold recommended by the Infectious Diseases Society of America (IDSA) [16]. Nitrofurantoin demonstrated lower resistance and inappropriate therapy rates, supporting its role as first-line therapy [16], [20].

Fluoroquinolone resistance remained low but increased over time [21], [22], [23]. Prior antibiotic exposure was strongly associated with both resistance and inappropriate therapy, with a 64% increase in odds [24], [25].

These findings support incorporating prior antibiotic exposure into empiric prescribing decisions and strengthening antimicrobial stewardship strategies. This may improve treatment outcomes and reduce resistance development.

Limitations include single-center data, lack of clinical outcomes, limited detail on prior antibiotic exposure, and observational design.

Future research should evaluate predictive models incorporating antibiotic exposure and resistance trends and assess their impact on clinical outcomes.

In conclusion, inappropriate empiric therapy affects more than one in four patients. Prior antibiotic exposure significantly increases risk, supporting targeted empiric therapy strategies.

ETHICS STATEMENT

This study utilized the publicly available, de-identified AMR-UTI PhysioNet dataset. The original data collection was approved by the institutional review board of the source institution with a waiver of informed consent due to the retrospective nature and use of de-identified data. The current secondary analysis was exempt from additional institutional review board review.

DATA AVAILABILITY STATEMENT

The AMR-UTI dataset used in this study is publicly available through PhysioNet (https://physionet.org/) following completion of required data use agreements and training in human subjects research protection.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest related to this work.

AI DECLARATION

The authors confirm that all data collection, analysis, interpretation, and statistical calculations were performed independently by the authors. Artificial intelligence (AI) tools (SciSpace) were used solely to assist in language editing,

manuscript structuring, and formatting. The AI tool did not generate, analyze, or interpret any data, nor did it influence the scientific conclusions of this study. All content has been reviewed and approved by the authors.

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