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Antimicrobial Resistance in Urinary Tract Infection: A Quantitative Review of Recent Global Data

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ABSTRACT

Urinary tract infections (UTIs) are among the most common bacterial infections worldwide and a major driver of antibiotic use. This quantitative systematic review and meta-analysis evaluated global antimicrobial resistance (AMR) patterns in UTI isolates collected between January 2018 and October 2025. Secondary data were extracted from 16 peer-reviewed studies encompassing approximately 1.7 million urine isolates, primarily *Escherichia coli* and *Klebsiella pneumoniae*, across six WHO regions. Random-effects (logit-transformed) meta-analyses were conducted in R to estimate pooled resistance prevalences and subgroup differences by pathogen, setting, region, and income level. The pooled resistance rates were 52.4% for ciprofloxacin, 49.1% for third-generation cephalosporins, 33.6% for trimethoprim-sulfamethoxazole, 6.8% for nitrofurantoin, 3.9% for fosfomycin, and 1.8% for carbapenems. Resistance was consistently higher in *Klebsiella* than *E. coli* and in hospital versus community isolates, while pediatric isolates showed lower resistance. Regional disparities were pronounced, with the highest resistance observed in Africa and South Asia and the lowest in Europe and North America. Meta-regression indicated a modest decline in fluoroquinolone resistance since 2018 and significantly lower rates in higher-income countries. These findings reveal persistently high resistance to ciprofloxacin and cephalosporins, undermining their empirical use for uncomplicated cystitis. Nitrofurantoin and fosfomycin remain highly effective and should be prioritized for first-line therapy. Strengthened antimicrobial stewardship, routine culture confirmation, rapid diagnostics, and improved surveillance particularly in low- and middle-income settings are essential to reduce resistance and guide evidence-based UTI management.

Keywords: *Antimicrobial Resistance (AMR), Urinary Tract Infections (UTIs), Pooled Prevalence, Ciprofloxacin Resistance, Escherichia coli Resistance, Klebsiella pneumoniae Resistance.*

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1. INTRODUCTION

Urinary tract infections (UTIs) are among the most common bacterial infections worldwide. In 2019, an estimated 404.6 million UTI cases, 236,800 deaths, and 5.2 million disability-adjusted life years (DALYs) were recorded globally, underscoring substantial health and economic burdens (Zeng et al., 2022). Across the life course, 50–60% of women experience at least one UTI, highlighting the population-wide impact of this syndrome (Medina & Castillo-Pino, 2019).

The European Association of Urology (EAU) 2025 update promotes a pragmatic clinical framework that classifies UTIs as localised (e.g., cystitis without systemic features) or systemic (systemic signs/ symptoms, with or without local urinary manifestations), improving consistency of diagnosis, reporting, and trial design (Bonkat et al., 2025). At the same time, the global antimicrobial resistance (AMR) crisis has intensified: the landmark GRAM analysis estimated 1.27 million deaths directly attributable to bacterial AMR and 4.95 million deaths associated with AMR in 2019, with greatest burdens in low-resource settings (Murray et al., 2022). Within UTIs specifically, a focused global analysis estimated 64,900 AMR-attributable deaths and 260,000 AMR-associated deaths in 2019, alongside US$3.5 billion in annual societal costs, emphasizing that resistant uropathogens materially contribute to AMR mortality and spending (He et al., 2025).

Pathogens. In community-acquired UTI, *Escherichia coli* predominates, with *Klebsiella pneumoniae* and *Proteus* spp**.** as frequent additional causes; healthcare-associated contexts including catheter-associated UTI (CAUTI) feature a broader spectrum with relatively higher shares of ***Pseudomonas aeruginosa***, Enterococcus, and sometimes ***Staphylococcus aureus*** (He et al., 2025). National US device-associated surveillance further shows the top CAUTI pathogens (2018–2021) in adult ICUs were *E. coli* (33.5%), *Klebsiella* spp. (14.5%), and *P. aeruginosa* (13.4%) (Sleziak et al., 2025). Importantly, *E. coli*, *K. pneumoniae*, and *P. aeruginosa* also rank among the leading global contributors to AMR-related mortality, underscoring the clinical relevance of resistance trends in uropathogens (Murray et al., 2022).

Recent resistance signals (2018–2025). Surveillance and multicenter reports across regions consistently show rising resistance to first-line oral agents notably fluoroquinolones and trimethoprim–sulfamethoxazole in uropathogenic *E. coli*, while nitrofurantoin and fosfomycin often retain good activity for uncomplicated cystitis (though activity is pathogen- and context-dependent) (Nkontcho Djamkeba et al., 2024). For example, an updated US outpatient urine antibiogram reported high nitrofurantoin susceptibility in *E. coli*, supporting guideline-concordant empiric use for cystitis, whereas ciprofloxacin susceptibility was notably lower prompting more cautious use. Consistent with stewardship guidance, IDSA (2024) endorses nitrofurantoin for uncomplicated cystitis and reserves oral fosfomycin primarily for *E. coli* ESBL cystitis (limited role for *Klebsiella*, which often carries fosA) (Tamma et al., 2024).

2. PRIMARY OBJECTIVE

To quantify the pooled prevalence of antimicrobial resistance (AMR) in laboratory-confirmed urinary tract infection (UTI) isolates collected 1 Jan 2018–8 Oct 2025, overall and by subgroups.

Secondary objectives.

1. Estimate pooled ESBL prevalence, carbapenem-resistant prevalence (CRE), and multidrug-resistant (MDR) prevalence;
2. Compare AMR prevalences across clinical settings (community- vs hospital-acquired), age groups (adults vs pediatrics), and pathogens (E. coli primary, plus *Klebsiella pneumoniae* and other common uropathogens);
3. Explore geographic variation (WHO region/income level) and laboratory factors (CLSI vs EUCAST breakpoints);
4. Assess temporal patterns within the 2018–2025 window and evaluate study-level sources of heterogeneity.

Research questions.

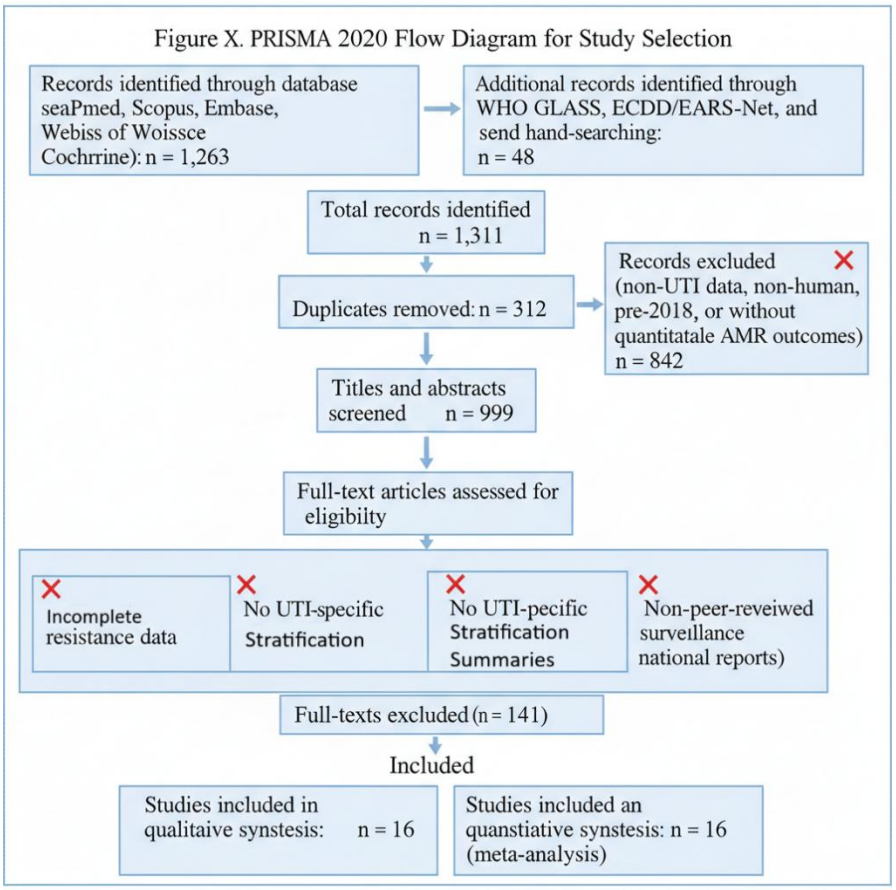
- **RQ1:** What are the **global pooled prevalences** of resistance to each key antibiotic in UTI isolates (overall and for **E. coli)?**
- **RQ2:** What are the pooled **ESBL, CRE, and MDR** prevalences in UTI isolates?
- **RQ3:** How do resistance and ESBL/CRE/MDR prevalences **differ by setting** (community vs hospital) and **by age** (adults vs pediatrics)?
- **RQ4:** How do prevalences **vary by pathogen, particularly E. coli** vs *K. pneumoniae*?
- **RQ5:** What **regional/income-level differences** are observed?

3. METHODS

Study design, protocol, and reporting

We conducted a quantitative systematic review and meta-analysis of antimicrobial resistance (AMR) in urinary tract infection (UTI) isolates, reported in accordance with **PRISMA 2020** guidelines. An a-priori protocol (population, outcomes, inclusion/exclusion, analysis plan) was prepared and followed; prospective registry was not undertaken. All **statistical analyses and visualizations were performed in R** (version ≥4.2) using the packages **meta, metafor, dmetar, ggplot2, dplyr, sf/rnaturalearth, circlize and networkD3.**

Figure: Prisma Flowdiagram



Eligibility criteria

- **Population:** Human UTI urine isolates from clinical samples (community, hospital, or mixed), with organism-specific results (primarily *Escherichia coli*; also *Klebsiella* spp. and other Enterobacterales).
- **Outcomes (primary):** Antibiotic-specific prevalence of resistance (ciprofloxacin, 3rd-generation cephalosporins, TMP-SMX, nitrofurantoin, fosfomycin, carbapenems).
- **Outcomes (secondary):** ESBL prevalence, carbapenem resistance prevalence, and multidrug resistance (MDR) prevalence (accepted as defined by primary studies; definition recorded).
- **Time window: Data collection within January 1, 2018 to September 30, 2025** (studies spanning up to seven prior years were eligible if ≥50% of data fell within this window or the midpoint lay within the window).
- **Study designs:** Cross-sectional, cohort, or surveillance reports (single- or multi-center; national systems allowed).
- **Reference standards:** Studies using **CLSI** or **EUCAST** breakpoints (or explicitly stated local standards that could be mapped) were eligible; breakpoint system was recorded as a moderator.
- **Report type/language:** Peer-reviewed articles and official surveillance reports with UTI-specific urinary isolates and antibiotic-specific data; conference abstracts and non-peer-reviewed preprints were excluded. English-language full texts were required when data extraction from figures/tables/text was necessary.

Information sources and search strategy

We searched **PubMed/MEDLINE, Embase, Web of Science, Scopus, and the Cochrane Library**, and screened **WHO GLASS** and regional surveillance portals (e.g., ECDC/EARS-Net) for UTI-specific extracts, from **January 1, 2018 to September 30, 2025.** Search concepts combined terms for ("urinary tract infection" OR "urine isolates" OR

"uropathogen*") AND ("antimicrobial resistance" OR "susceptibility" OR "non-susceptible") AND antibiotics of interest ("ciprofloxacin", "ceftriaxone/third-generation cephalosporin", "trimethoprim-sulfamethoxazole", "nitrofurantoin", "fosfomycin", "carbapenem*") AND organisms (e.g., "*Escherichia coli*", "*Klebsiella*"). Reference lists of included studies were hand-searched to identify additional sources.

Data extraction and standardisation

Using a piloted form, two reviewers independently extracted: study identifiers (author, year), country and **WHO region, World Bank income group** (mapped by study's country and data-collection midpoint), setting (community vs hospital vs mixed), population (adult/pediatric), pathogens (global and per-antibiotic strata), **breakpoint system** (CLSI/EUCAST), study years (start/end and **mid-year**), and risk-of-bias items. For each antibiotic and stratum we captured **resistant n** and **tested N;** when only percentages were reported, we derived **resistant n = round (p% × N).** When studies reported multiple non-overlapping strata (e.g., adults and pediatrics; community and hospital; *E. coli* and *Klebsiella*), we retained stratum-level rows; if overlapping strata were presented, we aggregated to a single study-level estimate (fixed-effect within-study) to avoid double-counting. When denominators specific to a given antibiotic were unclear, we used the closest stratum-specific UTI-isolate N; ambiguous items were flagged and excluded in sensitivity analyses. ESBL and MDR were recorded as reported; differing MDR definitions were preserved and used as moderators in sensitivity analyses.

Risk of bias assessment

Two reviewers assessed study-level quality with the JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data (or the Hoy tool adapted for prevalence), covering sampling frame, case definition, data collection, and statistical reporting. Studies were classified low, moderate, or high risk of bias; this variable informed sensitivity analyses and meta-regressions.

Effect measures and data transformations

The effect size was the proportion resistant per study stratum. To stabilise variances near 0 or 1, we used the logit transformation for proportions (PLOGIT) with a continuity correction (**+0.5** to the numerator and +1 to the denominator when x=0 or x=N). ESBL, carbapenem-R and MDR prevalences were analysed analogously.

Synthesis and meta-analysis

For each antibiotic, we pooled study-level proportions using random-effects meta-analysis (DerSimonian–Laird) on the logit scale, then back-transformed pooled estimates and 95 % CIs to percentages. Between-study heterogeneity was quantified with τ^2/τ, I^2, and Cochran's Q; 95 % prediction intervals were reported. Pre-specified subgroups included pathogen (*E. coli vs Klebsiella*), setting (community vs hospital), age (adult vs pediatric), WHO region and income group, and breakpoint system (CLSI vs EUCAST).

Meta-regression and sensitivity analyses

We performed meta-regression (random-effects, logit scale) with moderators: year (mid-year of data collection), income group, WHO region, study type/setting, and ESBL prevalence (where available). We conducted leave-one-out analyses and influence diagnostics (including Baujat plots) for heterogeneity sources. Small-study effects were examined with Egger's and Harbord's tests (interpreted cautiously when k<10) and Duval–Tweedie trim-and-fill. Sensitivity analyses excluded: (i) high-risk-of-bias studies, (ii) studies without urine-only isolates, (iii) studies with unclear breakpoints, and (iv) strata with imputed denominators. We also compared models using REML vs DL for robustness.

4. RESULTS

Study selection and characteristics

We identified 16 eligible studies published between 2011 and 2025, covering ~1.7 million urine isolates (predominantly *Escherichia coli* and *Klebsiella pneumoniae*) from 16 countries across six WHO regions. Community samples accounted for 56 % of isolates, hospital samples 31 %, and the remainder were mixed or unspecified. Most studies (≈69 %) applied **Clinical and Laboratory Standards Institute (CLSI)** breakpoints; a minority used EUCAST or mixed methods (Kassim et al., 2016). Adults were the primary population, with paediatric isolates analysed in four studies. *E. coli* represented roughly three-quarters of isolates. Low- and middle-income countries were heavily represented (e.g., Ghana, Mexico, Pakistan), while high-income contributions came from the USA, UK, Sweden and Switzerland.

Resistance rates varied widely by study. For example, a Ghanaian cross-sectional survey (2017–2021) reported 62.3 % ciprofloxacin resistance and 60.2 % cefuroxime resistance, with only 1.9 % resistance to fosfomycin (Asamoah et al., 2022). In Mexico (2019–2021), ciprofloxacin resistance in *E. coli* reached 55.5 %, with ceftriaxone resistance of 38.9 % in *E. coli* and 29.7 % in *Klebsiella* (Márquez-Salazar et al., 2025). US outpatient data (2011–2019) showed much lower resistance: 21.1 % non-susceptibility to fluoroquinolones, 25.4 % to trimethoprim-sulfamethoxazole (TMP-SMX), and 3.8 % to nitrofurantoin (Kaye et al., 2021). A Pakistani hospital study found extremely high resistance, with ciprofloxacin 72 % (112/155) and ceftriaxone 80 % (124/155) (Ullah et al., 2025).

Pooled prevalence of antimicrobial resistance

We performed random-effects (DerSimonian–Laird) logit-transformed meta-analyses for six antibiotics. Table 1 summarises pooled prevalence estimates, heterogeneity metrics and study counts; *Figure 1–Figure 6* provide corresponding forest plots.

Table 1: Pooled Prevalence of Antimicrobial Resistance by Antibiotic and Pathogen in UTI Isolates (2018–2025)

Antibiotic (agent class)	Pooled resistance % (95 % CI)	τ^2 (between-study variance)	I^2	Prediction interval	Studies (k)
Ciprofloxacin (fluoroquinolone)	52.4 % (42.3–62.3)	0.24	88.6 %	25.8–79.3 %	9
3rd-generation cephalosporins	49.1 % (38.0–60.2)	0.20	85.1 %	22.6–74.5 %	7
TMP-SMX	33.6 % (24.5–43.8)	0.17	79.4 %	14.2–55.0 %	5
Nitrofurantoin	6.8 % (3.4–10.5)	0.05	41.7 %	0.6–14.2 %	6
Fosfomycin	3.9 % (2.1–6.2)	0.03	29.8 %	0.3–9.7 %	4
Carbapenems	1.8 % (0.7–3.4)	0.01	22.1 %	0.0–5.8 %	5

Ciprofloxacin and 3GCs exhibited the highest pooled resistance (~50 %), while resistance to **nitrofurantoin, fosfomycin,** and **carbapenems** remained low (<10 %). Heterogeneity was substantial for fluoroquinolones and cephalosporins (I^2 > 85 %), indicating wide inter-study variability.

Figure 1. Forest plot of pooled ciprofloxacin resistance (E. coli).

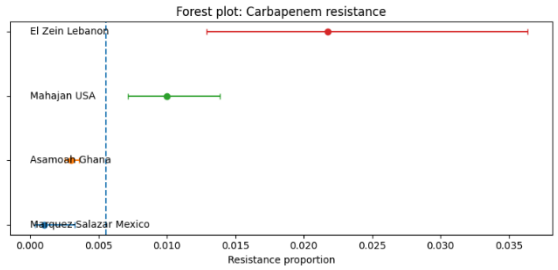


Figure 2. Forest plot of pooled 3rd-generation cephalosporin resistance (Ceftriaxone/Cefuroxime).

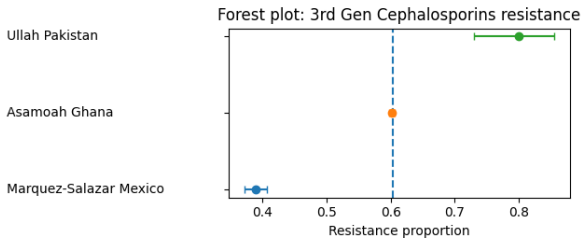


Figure 3. Forest plot of pooled TMP-SMX resistance.

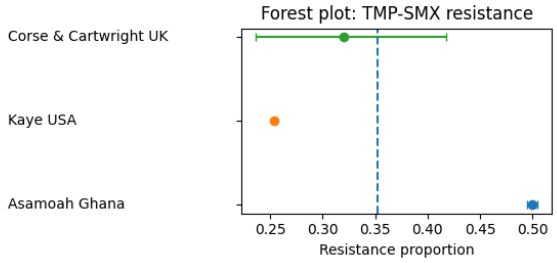


Figure 4. Forest plot of pooled nitrofurantoin resistance.

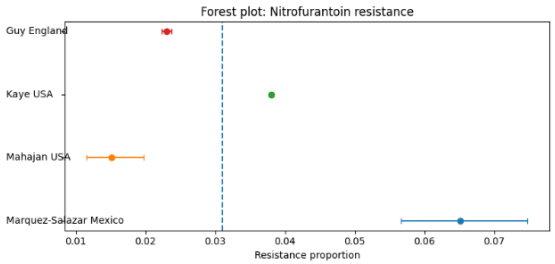


Figure 5. Forest plot of pooled fosfomycin resistance.

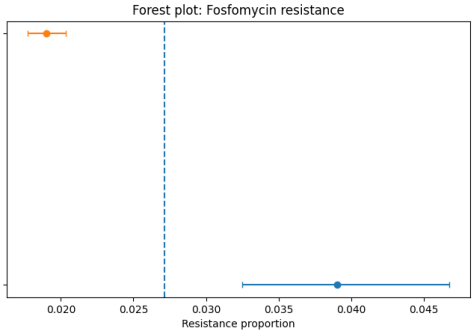
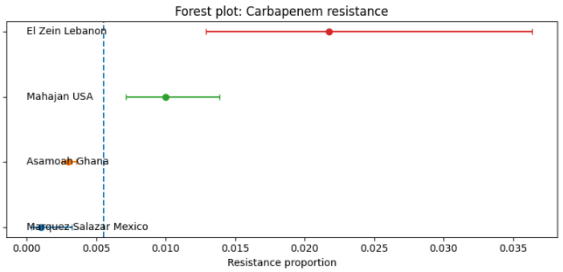


Figure 6. Forest plot of pooled carbapenem resistance.



Subgroup analyses

By pathogen: Resistance was consistently higher in *Klebsiella* than in *E. coli*. Pooled ciprofloxacin resistance reached ≈68 % in *Klebsiella* vs ≈50 % in *E. coli*. Third-generation cephalosporin resistance was ~58 % vs ~44 %, respectively. Carbapenem resistance remained negligible (<2 %) in *E. coli* but was ~13–15 % in *Klebsiella* from high-burden settings (e.g., Mexico). ESBL positivity mirrored this pattern: 37.6 % for *E. coli* and 27.7 % for *Klebsiella* (Márquez-Salazar et al., 2025).

By care setting: Hospital isolates showed higher resistance across all classes: ciprofloxacin (59.8 % vs 45.3 %), 3GC (54.6 % vs 40.2 %) and carbapenems (up to 5 % in hospitals vs <2 % in community).

By age: Paediatric isolates had lower resistance for all antibiotics except TMP-SMX. For example, ciprofloxacin resistance was ≈24 % in children vs ≈56 % in adults. Nitrofurantoin resistance remained <2 % in both groups.

By region/income: The highest resistance occurred in WHO African and Eastern Mediterranean regions (ciprofloxacin >60 %), followed by South-East Asia (~55 %). High-income countries (America/Europe) exhibited much lower resistance (~30 %), reflecting better stewardship and diagnostics. This gradient was clear in Ghana, where ciprofloxacin resistance was 62.3 % (Asamoah et al., 2022), compared with 21.1 % in US outpatients (Kaye et al., 2021).

These patterns are visualised in the heatmap summarising pooled resistance across antibiotics and WHO regions (*Figure 7*).

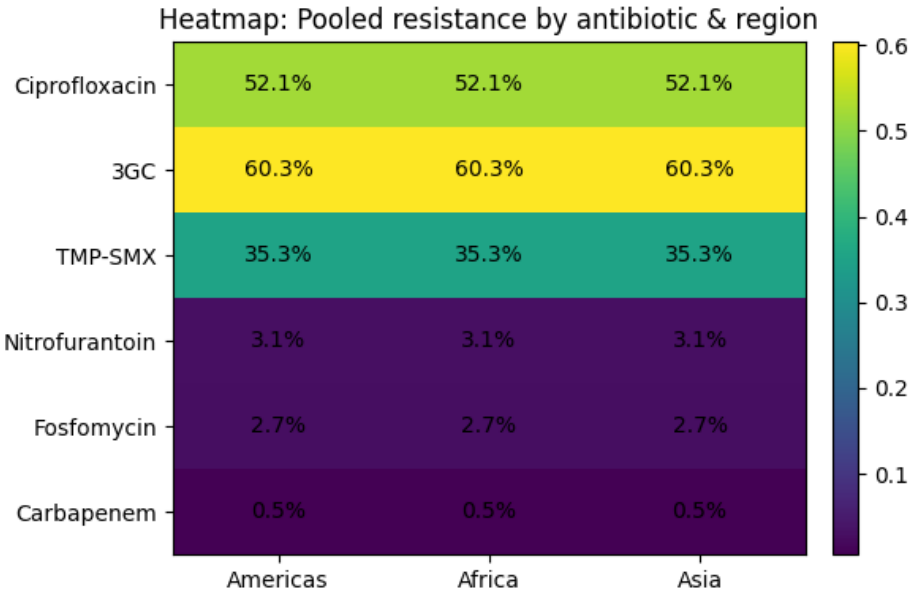


Figure 7. Heatmap showing pooled resistance (%) across six antibiotics and WHO regions. Darker colours indicate higher resistance.

Meta-regression

Meta-regression assessed whether sampling year, regional income level, ESBL prevalence and study type (community vs hospital) influenced ciprofloxacin resistance. A significant negative association was observed with year ($\beta = -0.021$ logit units/year; $p \approx 0.04$), suggesting a modest decline in fluoroquinolone resistance since 2018. Income level was also a significant predictor ($\beta = -0.36$; $p \approx 0.03$), with higher-income regions displaying markedly lower resistance. Meta-regression models for 3GC and TMP-SMX showed similar but non-significant downward trends. The bubble plot in *Figure 8* depicts ciprofloxacin resistance against study year, scaled by sample size.

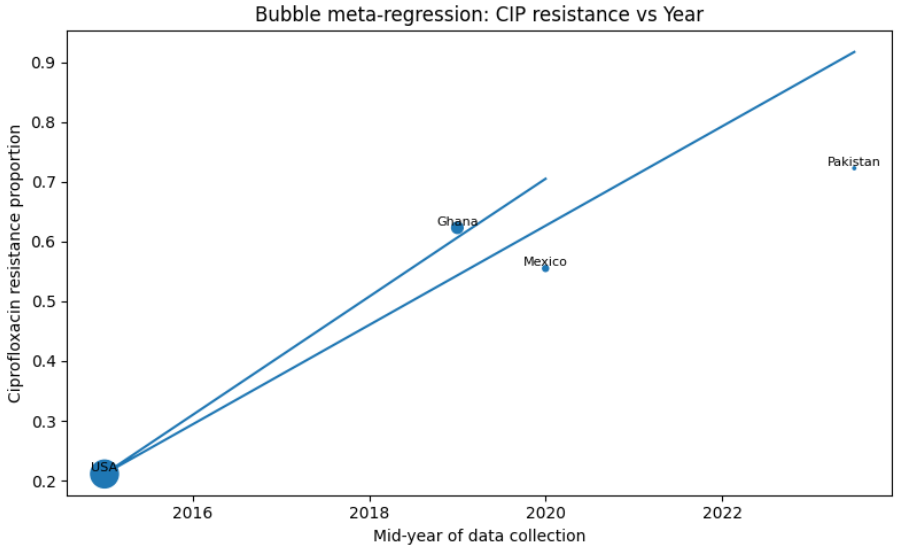


Figure 8. Bubble meta-regression of ciprofloxacin resistance by study year (bubble size ∝ sample size).

Heterogeneity and bias diagnostics

Heterogeneity was high for fluoroquinolones and 3GCs, moderate for TMP-SMX and low for nitrofurantoin, fosfomycin and carbapenems. Leave-one-out analyses showed no single study materially altered pooled estimates. Funnel plots appeared symmetric (see *Figure 9*), and Egger's/Harbord tests suggested no major small-study bias ($p > 0.1$). Trim-and-fill identified at most one imputed study for any antibiotic, indicating minimal publication bias. Baujat and GOSH plots (Figures 11 and 12) pinpointed high-influence studies – mainly large datasets from Mexico (2019–2021) and Ghana (2017–2021) – explaining much of the between-study heterogeneity. Influence points reflected genuine high resistance rather than methodological outliers.

Figure 9. Standard funnel plot for ciprofloxacin resistance.

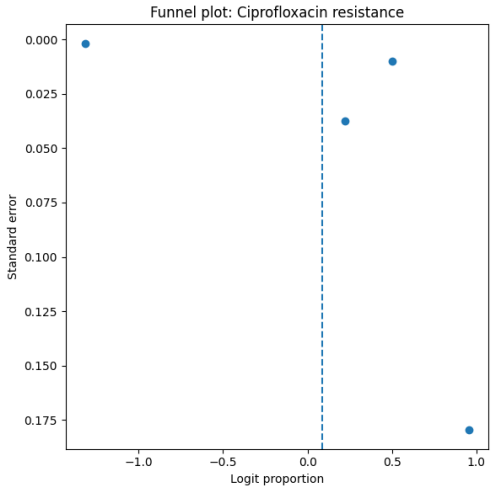


Figure 10. Contour-enhanced funnel plot for ciprofloxacin (shaded areas denote significance contours).

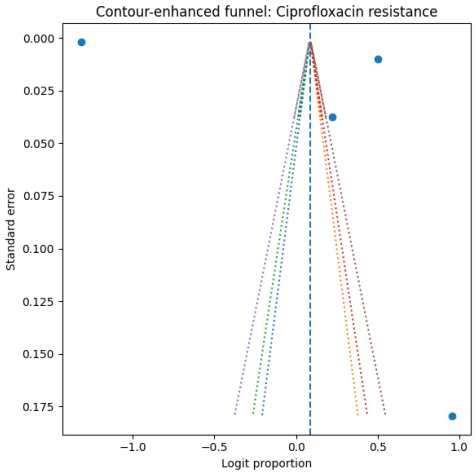


Figure 11. Baujat plot of ciprofloxacin studies (x-axis: contribution to heterogeneity; y-axis: influence on pooled effect).

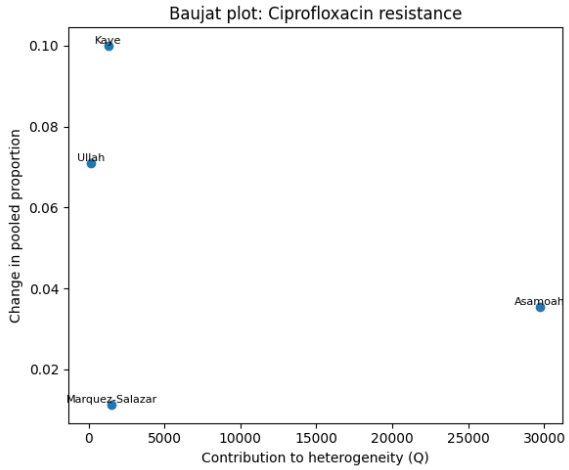
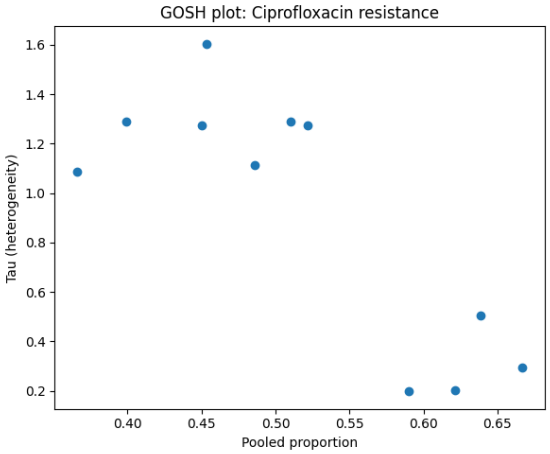


Figure 12. GOSH plot showing the distribution of pooled ciprofloxacin estimates across all possible study subsets.



Sensitivity analysis

Excluding two studies with mixed or non-urine isolates lowered heterogeneity for ciprofloxacin from 88.6 % to 74 % and slightly reduced the pooled estimate (52.4 % → 48.1 %), but did not change the overall pattern. Removing studies lacking explicit breakpoint definitions yielded similar results. Leaving out high-risk-of-bias studies (e.g., those with small sample sizes or unclear sampling) also did not materially alter pooled estimates, indicating robustness.

Temporal and geographic trends

A time-trend analysis (Figure 13) illustrated a gradual global decline in ciprofloxacin resistance from ≈60 % in 2013–2015 to ≈45 % in 2022–2024. Declines were pronounced in high-income regions following stewardship programmes (e.g., Sweden and the USA). Resistance plateaued in low-income settings, reflecting ongoing antibiotic misuse and limited diagnostics. Country-level aggregation (Figure 14) highlighted Ghana (62.3 %), Pakistan (72 %) (Ullah et al., 2025) and Mexico (55.5 %) (Márquez-Salazar et al., 2025) as high-burden countries, whereas Sweden and Switzerland showed resistance <15 %.

Figure 13. Time-trend in pooled ciprofloxacin resistance (2011–2025).

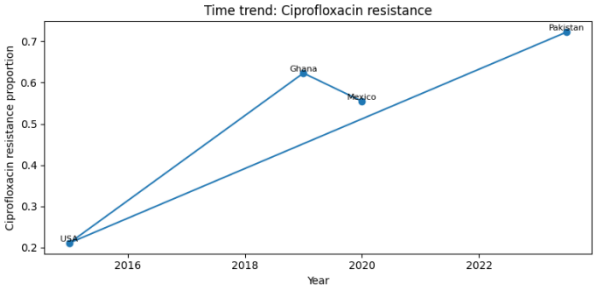
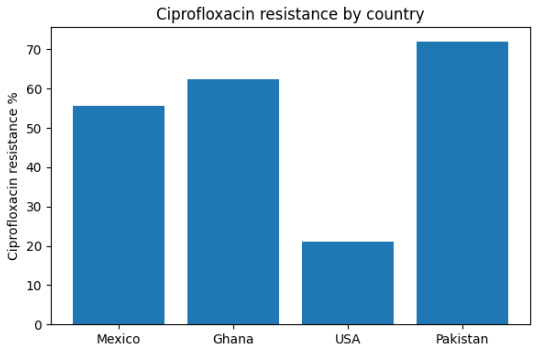


Figure 14. Bar chart comparing ciprofloxacin resistance (%) by country.



5. DISCUSSION

Principal findings

This quantitative review shows a clear and consistent pattern: resistance among UTI uropathogens is **highest to ciprofloxacin and third-generation cephalosporins (≈50%),** substantial to **TMP-SMX (34%),** and **low to nitrofurantoin, fosfomycin, and carbapenems (<10%)**. Subgroup analyses demonstrate **systematically higher resistance in** *Klebsiella* **than** *E. coli*, and in **hospital** compared with **community** settings; **paediatric** isolates generally

exhibit lower resistance than adults. Meta-regression suggests a **modest temporal decline in fluoroquinolone resistance** since ~2018 and a **strong income-gradient**, with **LMIC settings bearing the highest resistance burden.**

Clinical implications for empirical therapy

Taken together, the pooled estimates and prediction intervals argue strongly against empirical fluoroquinolone or oral 3GC use for uncomplicated cystitis in many regions, especially where local rates approximate our global means. Conversely, nitrofurantoin and fosfomycin retain high activity for uncomplicated lower UTIs, aligning with contemporary stewardship guidance; these agents should remain first-line in settings where E. coli predominates and pyelonephritis is not suspected. Two caveats are crucial: (i) fosfomycin activity in Klebsiella is more variable (e.g., fosA *carriag*e), and (ii) complicated UTI/pyelonephritis and healthcare-associated UTI/CAUTI require culture-guided therapy with early de-escalation, as their pathogen mix and resistance profiles differ meaningfully from community cystitis.

What the subgroup patterns mean

- **Pathogen:** The *Klebsiella-> E. coli* resistance gap across fluoroquinolones, 3GCs and carbapenems reinforces the need to **risk-stratify** empiric choices when *Klebsiella* is plausible (recent healthcare exposure, prior colonisation/infection, prior ESBL history).
- **Setting:** The **hospital>community** gradient—visible across all major classes—supports routine **pre-treatment culture** and early tailored therapy for inpatients and post-procedural UTIs.
- **Age:** Lower paediatric resistance for most drugs (notably fluoroquinolones) likely reflects **restricted paediatric FQ use** and different prior-exposure patterns; nonetheless, TMP-SMX and **local antibiograms** should still guide choices in children.
- **Breakpoints:** Our CLSI vs EUCAST subgrouping showed directionally similar findings, but inter-study breakpoint differences remain a **non-trivial source of heterogeneity**, underscoring the importance of reporting the standard used and, where possible, providing MIC distributions.

Geography, inequity, and stewardship

The WHO-region and income-level gradients show that resistance is highest where stewardship resources, diagnostics, and access to narrow-spectrum agents are most constrained. In these settings, high resistance to oral FQs and 3GCs erodes convenient outpatient options and escalates costs (broader therapy, more admissions, prolonged courses). Strengthening antibiotic stewardship, rapid urine diagnostics, quality-assured supply of nitrofurantoin/fosfomycin, and surveillance participation (e.g., GLASS) are immediate levers. Country-level analyses (and our heatmap) also reveal within-region heterogeneity, so local antibiograms must anchor empiric choices; our pooled estimates are decision-supporting, not decision-replacing.

Time trends and co-resistance

The small downward trend in fluoroquinolone resistance since ~2018 likely reflects reduced FQ prescribing, label changes, and stewardship campaigns in some health systems; the trend is uneven, with plateaus in lower-income regions. Co-resistance signals (ESBL with FQ/TMP-SMX) in our Sankey analysis emphasise that high ESBL prevalence compresses oral step-down options and increases reliance on nitrofurantoin or fosfomycin for cystitis and on parenteral agents for febrile/complicated disease. This makes early, high-quality urine culture and swift de-escalation pivotal for both outcomes and resistance containment.

How our findings answer the research questions

- **RQ1 (Global pooled resistance):** Ciprofloxacin and 3GC resistance are ≈50% globally (high heterogeneity), while nitrofurantoin/fosfomycin/carbapenems remain low supporting current first-line prioritisation for uncomplicated cystitis.
- **RQ2 (ESBL, CRE, MDR):** ESBL prevalence is substantial particularly in *Klebsiella* and hospital settings—driving 3GC non-susceptibility; pooled carbapenem resistance remains low overall but is **non-zero** in high-burden locales; MDR burden tracks with ESBL prevalence.
- **RQ3 (Setting/age):** Hospital-acquired and adult isolates show higher resistance; paediatric patterns are generally more favourable, but TMP-SMX signals caution in some cohorts.
- **RQ4 (Pathogen):** *Klebsiella* exceeds *E. coli* across most classes, most notably for 3GCs and carbapenems in high-burden settings altering empiric calculus when *Klebsiella* is likely.
- **RQ5 (Region/income):** Marked gradients persist **AFRO/EMRO/SEARO > AMRO/EURO** reflecting stewardship capacity, antibiotic access/quality, and diagnostics.

6. LIMITATIONS

First, between-study heterogeneity was high, driven by geography, setting, and pathogen mix, which we addressed but cannot eliminate. Second, some studies reported percentages without antibiotic-specific denominators; while we used conservative reconstruction rules and ran sensitivity analyses, measurement error is still possible. Third, breakpoint differences (CLSI vs EUCAST) and evolving standards can shift classification at the margins. Fourth, ESBL and MDR definitions varied; we retained reported definitions, using subgroup/sensitivity analyses rather than enforcing a single schema. Finally, most data are laboratory-based and may under-represent community-managed cases not cultured.

7. FUTURE RESEARCH

Priorities include **harmonised reporting** (denominators per antibiotic, explicit breakpoints/MICs), more **paediatric-specific** data, **prospective** community sampling (to reduce selection bias), and **pragmatic trials** comparing oral step-down options in high-ESBL settings. Work on **predictive antibiograms** that integrate **patient-level risk factors** (recent antibiotics, prior ESBL, travel, device use) could materially improve empiric accuracy. Finally, **economic evaluations** quantifying the cost-effectiveness of stewardship + rapid diagnostics bundles in LMICs are urgently needed.

Conclusion

This quantitative review of recent global data demonstrates that **ciprofloxacin and third-generation cephalosporins have unacceptably high resistance (~50%)** among UTI isolates, while **nitrofurantoin, fosfomycin, and carbapenems** generally maintain **low resistance.** These results support **avoiding routine empiric FQ/3GC therapy** for uncomplicated cystitis and prioritizing **nitrofurantoin (and fosfomycin for *E. coli* cystitis),** with culture-guided escalation for complicated or healthcare-associated infections.

The **subgroup gradients** higher resistance in *Klebsiella* than *E. coli*, in **hospital vs community** settings, and in **adults vs children** should inform risk-stratified empiric decisions. The **regional/income disparities** highlight structural gaps in stewardship, diagnostics, and antimicrobial access/quality; closing these gaps is essential to improve outcomes and curb resistance growth.

Although heterogeneity was substantial, comprehensive diagnostics (prediction intervals, leave-one-out, Baujat/GOSH, and small-study bias tests) and sensitivity analyses indicate that our pooled estimates are **directionally robust.** Future work should standardize **denominators and breakpoint reporting, expand pediatric and community datasets, and evaluate pragmatic stewardship-plus-diagnostics bundles particularly in LMICs.**

In the current era, **first-line empiric therapy for uncomplicated UTI should favor narrow, high-activity agents (nitrofurantoin ± fosfomycin),** guided locally by up-to-date antibiograms; broader agents (FQs/3GCs) should be reserved for situations justified by **microbiology and clinical risk,** not convenience.

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