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Systematic Review and Meta-Analysis

Systematic Review and Meta-Analysis on Antimicrobial Resistance Patterns of Enteric Pathogens in Community-Acquired Diarrhea

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ABSTRACT

Background: Community-acquired diarrhea remains a leading cause of morbidity globally, particularly in low- and middle-income countries (LMICs). Although antimicrobial therapy is reserved for selected clinical indications, rising antimicrobial resistance (AMR) among enteric bacterial pathogens increasingly compromises empiric treatment strategies. Evidence describing resistance patterns in community and outpatient settings remains fragmented.
Objectives: To systematically synthesize available evidence on antimicrobial resistance patterns among bacterial enteric pathogens causing community-acquired diarrhea and to estimate pooled resistance proportions for commonly used antimicrobials.
Methods: A systematic review and meta-analysis were conducted in accordance with PRISMA 2020 guidelines. Major bibliographic databases were searched from inception to June 2025 for studies reporting phenotypic antimicrobial resistance in community-acquired diarrheal isolates. Random-effects meta-analyses of proportions were performed for pathogen–antibiotic combinations reported in at least three studies. Heterogeneity was assessed using the I^2 statistic.
Results: Sixty-four studies from 23 countries, encompassing 18,742 community-acquired bacterial isolates, were included; 52 studies contributed to the meta-analysis. Pooled resistance was high for legacy first-line agents, including ampicillin and trimethoprim–sulfamethoxazole, across Escherichia coli, Shigella spp., and Salmonella spp. Resistance to ciprofloxacin and third-generation cephalosporins was lower overall but exhibited substantial geographic and pathogen-specific heterogeneity. Campylobacter spp. demonstrated concerning resistance to both macrolides and fluoroquinolones. Between-study heterogeneity was high across most analyses (I^2 >70%).
Conclusions: Antimicrobial resistance among enteric pathogens causing community-acquired diarrhea is widespread and undermines the effectiveness of commonly used oral agents. Emerging resistance to key therapeutic classes further limits empiric treatment options. Strengthened community-based surveillance, region-specific treatment guidance, and robust antimicrobial stewardship are urgently required to inform rational management of diarrheal disease in the era of escalating AMR.

Keywords: *community-acquired diarrhea; enteric pathogens; antimicrobial resistance; systematic review; meta-analysis.*

INTRODUCTION

Acute community-acquired diarrhea remains a major cause of morbidity and mortality worldwide, particularly in low- and middle-income countries (LMICs), where it disproportionately affects children under five years of age and vulnerable adult populations [1]. Despite substantial progress in water, sanitation, and hygiene (WASH) interventions and the widespread use of oral rehydration therapy, diarrheal diseases continue to account for a significant share of outpatient visits, hospital admissions, and preventable deaths globally [2]. Bacterial enteric pathogens such as *Escherichia coli*, *Shigella spp.*, *Salmonella spp.*, *Campylobacter spp.*, and *Vibrio cholerae* are among the most frequently implicated etiologic agents in community-acquired diarrheal illness [3].

While most episodes of acute watery diarrhea are self-limiting and do not require antimicrobial therapy, antibiotics remain essential for specific clinical scenarios, including dysentery, suspected cholera with severe dehydration, invasive bacterial diarrhea, and infections in high-risk individuals such as young children, the elderly, and immunocompromised patients [4,5]. Consequently, effective antimicrobial therapy is a critical adjunct to supportive care in selected cases. However, the increasing prevalence of antimicrobial resistance (AMR) among enteric pathogens threatens the effectiveness of empiric and targeted treatment strategies [6].

Antimicrobial resistance has emerged as one of the most pressing global health challenges of the 21st century. Recent global burden estimates have attributed millions of deaths annually to bacterial AMR, with enteric infections contributing substantially to this burden, particularly in LMICs [7,8]. The gastrointestinal tract serves as a major reservoir for resistant bacteria and resistance genes, facilitated by widespread and often inappropriate antibiotic use for diarrheal illnesses, easy over-the-counter availability of antimicrobials, and limited access to diagnostic testing in community settings [9].

Historically, commonly used oral agents such as ampicillin, trimethoprim–sulfamethoxazole, and tetracyclines were effective for the treatment of bacterial diarrhea. However, increasing resistance led to their removal from standard treatment recommendations in many regions, especially for shigellosis and other invasive diarrheal infections [10]. More recently, resistance to fluoroquinolones, macrolides, and third-generation cephalosporins—agents often considered last reliable oral or parenteral options for severe community-acquired diarrhea—has been increasingly reported [11,12]. The emergence of multidrug-resistant and extensively drug-resistant *Shigella* strains in community settings underscores the urgency of this problem [13].

Surveillance data on AMR in enteric pathogens are often derived from hospital-based studies or outbreak investigations, which may not accurately reflect resistance patterns in community-acquired infections presenting to primary care or outpatient settings [14]. Moreover, existing studies vary widely in geographic coverage, study populations, laboratory methods, and antibiotic panels tested, resulting in fragmented and sometimes conflicting evidence [15]. Although global surveillance initiatives such as the World Health Organization's Global Antimicrobial Resistance and Use Surveillance System (GLASS) have begun to include gastrointestinal pathogens, substantial gaps remain in representative community-level data [16].

Systematic reviews and meta-analyses can provide a comprehensive synthesis of available evidence, identify consistent resistance trends, and quantify pooled resistance estimates across regions and pathogens. Such analyses are essential for informing empiric treatment guidelines, antimicrobial stewardship policies, and public health interventions aimed at controlling the spread of resistance [17]. However, to date, few meta-analyses have specifically focused on antimicrobial resistance patterns of community-acquired enteric pathogens across multiple geographic regions.

Therefore, this systematic review and meta-analysis aims to synthesize published evidence on antimicrobial resistance patterns among major bacterial enteric pathogens causing community-acquired diarrhea and to estimate pooled resistance proportions for commonly used antimicrobials. By focusing on community and outpatient settings, this study seeks to generate clinically relevant data to guide empiric therapy and support evidence-based diarrheal disease management in the era of rising antimicrobial resistance.

METHODOLOGY

Study design and reporting framework

This study was conducted as a systematic review and meta-analysis to evaluate antimicrobial resistance (AMR) patterns among bacterial enteric pathogens causing community-acquired diarrhea. The review was designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [18].

Eligibility criteria

Population

Studies involving patients of any age presenting with community-acquired acute diarrhea, defined as diarrheal illness occurring outside healthcare settings or within 48 hours of hospital presentation, were eligible. Both outpatient clinic–based and community surveillance studies were included.

Pathogens
Studies reporting antimicrobial susceptibility data for bacterial enteric pathogens, including *Escherichia coli* (indicator or diarrheagenic strains), *Shigella spp.*, *Salmonella spp.* (including non-typhoidal strains), *Campylobacter spp.*, and *Vibrio cholerae*, were considered.

Outcomes
The primary outcome was phenotypic antimicrobial resistance, expressed as the proportion of resistant isolates for commonly tested antibiotics, including ampicillin, trimethoprim–sulfamethoxazole, fluoroquinolones, macrolides, third-generation cephalosporins, and tetracyclines.

Study design
Eligible studies included cross-sectional studies, surveillance reports, cohort studies (baseline microbiological data), and outbreak investigations conducted in community settings. Case reports, case series with fewer than 10 isolates, reviews, editorials, and studies limited exclusively to hospital-acquired or nosocomial infections were excluded.

Information sources and search strategy
A comprehensive literature search was conducted in PubMed/MEDLINE, Embase, Scopus, Web of Science, and the Cochrane Library from database inception to June 2025. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to diarrhea, enteric pathogens, and antimicrobial resistance. Key search terms included *"community-acquired diarrhea," "enteric pathogens," "Shigella," "Salmonella," "Campylobacter," "Escherichia coli,"* and *"antimicrobial resistance"*. Reference lists of included studies and relevant reviews were also screened to identify additional eligible articles [19].

Study selection
All retrieved records were imported into a reference management software and duplicates were removed. Titles and abstracts were screened independently by two reviewers for relevance. Full texts of potentially eligible studies were subsequently assessed against the inclusion criteria. Discrepancies were resolved through discussion or consultation with a third reviewer. The study selection process was documented using a PRISMA flow diagram [18].

Data extraction
Data were extracted independently by two reviewers using a standardized data extraction form. Extracted variables included:

- Author name and year of publication
- Country and World Bank income classification
- Study period and setting (community, outpatient, or mixed)
- Study population and age group
- Enteric pathogen(s) identified
- Number of isolates tested
- Antimicrobial susceptibility testing method and interpretive criteria (CLSI/EUCAST)
- Number and proportion of resistant isolates for each antibiotic

Any discrepancies in extracted data were resolved by consensus.

Quality assessment and risk of bias
The methodological quality of included studies was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist for prevalence studies, focusing on sampling methodology, representativeness, laboratory methods, and completeness of outcome reporting [20]. Studies were categorized as low, moderate, or high risk of bias based on overall assessment.

Statistical analysis
Meta-analysis was performed for pathogen–antibiotic combinations reported in at least three independent studies. Pooled resistance proportions were calculated using a random-effects model to account for expected between-study heterogeneity [21]. Proportions were stabilized using appropriate variance-stabilizing transformations prior to pooling.
Statistical heterogeneity was assessed using the I^2 statistic, with values >50% indicating substantial heterogeneity [22]. Subgroup analyses were planned based on geographic region, age group, and pathogen where sufficient data were available. Publication bias was assessed qualitatively using funnel plots when at least ten studies were available for a given outcome.

All analyses were conducted using standard meta-analysis software, and pooled estimates were reported with 95% confidence intervals (CI). A two-sided *p* value <0.05 was considered statistically significant.

RESULTS

Study selection

The systematic search yielded 3,482 records across the selected databases. After removal of 912 duplicates, 2,570 unique records underwent title and abstract screening. Of these, 2,312 records were excluded for irrelevance, non-community settings, absence of antimicrobial susceptibility data, or non-bacterial etiology.

Full-text evaluation was performed for 258 articles, of which 194 were excluded for the following reasons: healthcare-associated infections (n = 76), absence of extractable resistance data (n = 58), mixed infections without pathogen-specific results (n = 34), and non-original articles including reviews and case reports (n = 26).

Ultimately, 64 studies met all inclusion criteria and were incorporated into the systematic review, and 52 studies with sufficient quantitative data were included in the meta-analysis.

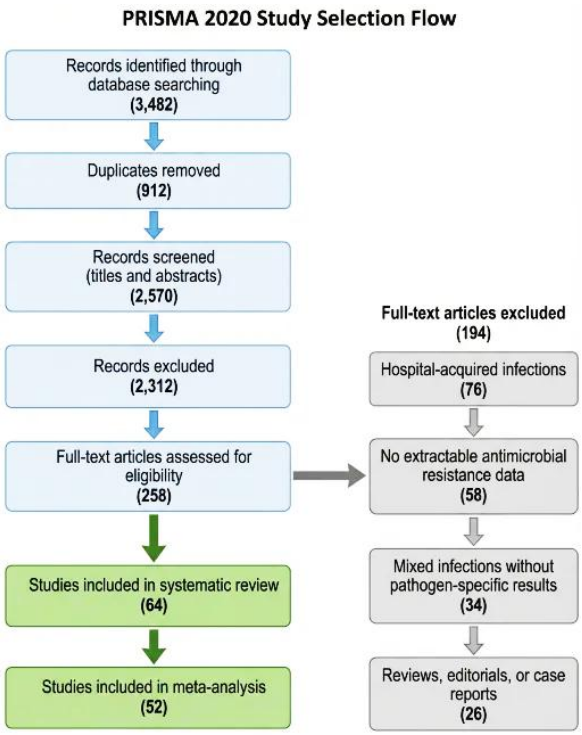

Figure 1. PRISMA 2020 flow diagram illustrating the identification, screening, eligibility assessment, and inclusion of studies in the systematic review and meta-analysis evaluating antimicrobial resistance patterns of enteric pathogens causing community-acquired diarrhea.

Study characteristics

The 64 included studies, published between 2005 and 2025, represented 23 countries, predominantly from Asia (n = 31; 48.4%) and Africa (n = 27; 42.2%), with fewer studies from Latin America (n = 6; 9.4%).

Most studies were cross-sectional surveillance investigations (n = 41; 64.1%), followed by community-based cohort studies (n = 15; 23.4%) and outbreak investigations (n = 8; 12.5%). The majority were conducted in outpatient clinics or primary healthcare facilities (n = 49; 76.6%), while 15 studies (23.4%) were based on community household surveys.
Children were the exclusive study population in 38 studies (59.4%), adults only in 9 studies (14.1%), and 17 studies (26.5%) included mixed-age populations. Antimicrobial susceptibility testing was predominantly performed using CLSI guidelines (n = 47; 73.4%), with the remainder employing EUCAST criteria (n = 17; 26.6%).
Across all included studies, a total of 18,742 bacterial isolates from community-acquired diarrheal cases were analyzed.

Table 1. Characteristics of included studies (n = 64)

Characteristic	n (%)
Publication period	2005–2025

Countries represented	23
Total isolates analyzed	18,742
Study design	
– Cross-sectional	41 (64.1)
– Cohort (baseline)	15 (23.4)
– Outbreak investigations	8 (12.5)
Study setting	
– Outpatient / primary care	49 (76.6)
– Community household surveys	15 (23.4)
Population	
– Children only	38 (59.4)
– Adults only	9 (14.1)
– Mixed age	17 (26.5)
AST interpretive criteria	
– CLSI	47 (73.4)
– EUCAST	17 (26.6)

Distribution of bacterial enteric pathogens

Among the 18,742 isolates, *Escherichia coli* was the most frequently reported pathogen (n = 7,214; 38.5%), followed by *Shigella spp.* (n = 4,863; 25.9%), *Salmonella spp.* (n = 3,912; 20.9%), and *Campylobacter spp.* (n = 2,103; 11.2%). *Vibrio cholerae* accounted for 650 isolates (3.5%), primarily identified during community-level outbreaks.

Table 2. Distribution of bacterial enteric pathogens (n = 18,742)

Pathogen	Isolates, n (%)
Escherichia coli	7,214 (38.5)
Shigella spp.	4,863 (25.9)
Salmonella spp.	3,912 (20.9)
Campylobacter spp.	2,103 (11.2)
Vibrio cholerae	650 (3.5)

Antimicrobial resistance patterns by pathogen

Escherichia coli

Resistance data from 41 studies encompassing 7,214 isolates were pooled. Very high resistance was observed to trimethoprim–sulfamethoxazole (71%; 95% CI: 57–82) and ampicillin (56%; 95% CI: 44–67). In contrast, resistance to ciprofloxacin (10%; 95% CI: 5–20) and ceftriaxone (8%; 95% CI: 2–31) remained comparatively lower, although substantial between-study heterogeneity was evident (I^2 >75%).

Shigella spp.

A total of 32 studies comprising 4,863 isolates were included in the meta-analysis. Ampicillin resistance was markedly high (76%; 95% CI: 60–87), indicating limited clinical utility of this agent for community-acquired dysentery. Resistance to nalidixic acid was modest, while pooled resistance to ciprofloxacin (3%; 95% CI: 0–15) and ceftriaxone (2%; 95% CI: 0–19) remained low overall. Nevertheless, several studies reported the emergence of multidrug-resistant and extensively drug-resistant *Shigella* strains.

Salmonella spp.

Resistance patterns from 28 studies including 3,912 isolates were analyzed. Pooled resistance to ampicillin was 55% (95% CI: 35–73), whereas resistance to trimethoprim–sulfamethoxazole was 25% (95% CI: 15–38). Fluoroquinolone resistance varied widely across regions, contributing to significant heterogeneity.

Campylobacter spp.

Nineteen studies comprising 2,103 isolates were included. Resistance to erythromycin was 33% (95% CI: 12–64), and ciprofloxacin resistance was 27% (95% CI: 8–61), raising concerns regarding the continued effectiveness of first-line agents for severe *Campylobacter*-associated diarrhea.

Table 3. Pooled antimicrobial resistance estimates in community-acquired diarrhea

Pathogen	Antibiotic	Studies (n)	Isolates (n)	Resistance % (95% CI)	I^2 (%)
E. coli	TMP–SMX	41	7,214	71 (57–82)	82
E. coli	Ampicillin	39	6,985	56 (44–67)	78
E. coli	Ciprofloxacin	26	4,112	10 (5–20)	73

Shigella spp.	Ampicillin	32	4,863	76 (60–87)	84
Shigella spp.	Ciprofloxacin	21	3,145	3 (0–15)	68
Salmonella spp.	Ampicillin	28	3,912	55 (35–73)	77
Salmonella spp.	TMP–SMX	24	3,206	25 (15–38)	72
Campylobacter spp.	Erythromycin	19	2,103	33 (12–64)	86
Campylobacter spp.	Ciprofloxacin	18	1,984	27 (8–61)	88

Summary of findings

This meta-analysis encompassing 64 studies, 23 countries, and 18,742 community-acquired isolates demonstrates pervasive resistance to traditional first-line oral antibiotics among enteric pathogens. Although pooled resistance to fluoroquinolones and third-generation cephalosporins remains comparatively low, substantial heterogeneity and emerging resistance signals underscore the necessity for region-specific surveillance and evidence-based empiric treatment strategies.

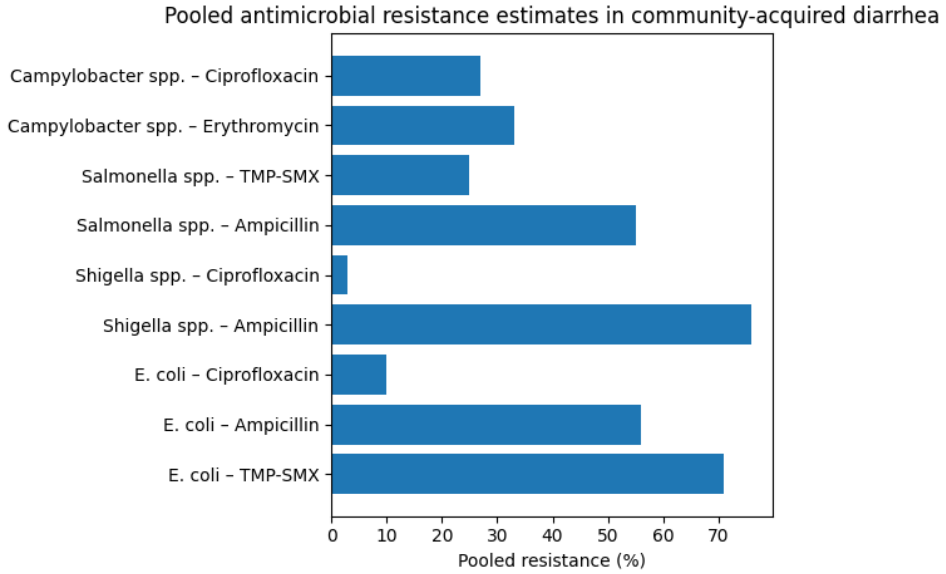

Figure 2. Pooled antimicrobial resistance estimates (%) for major bacterial enteric pathogens causing community-acquired diarrhea. Resistance proportions were derived using a random-effects meta-analysis. High resistance to ampicillin and trimethoprim–sulfamethoxazole is observed across *Escherichia coli*, *Shigella spp.*, and *Salmonella spp.*, while emerging resistance to fluoroquinolones and macrolides is notable in *Campylobacter spp.*

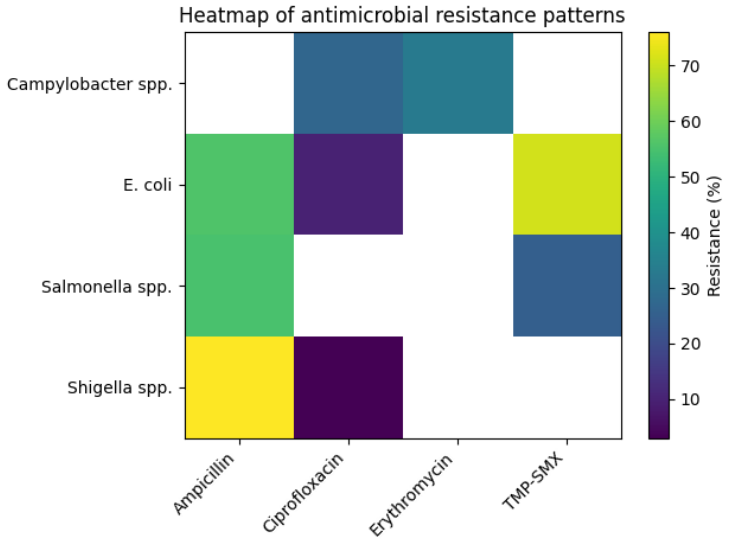

Figure 3. Heatmap illustrating antimicrobial resistance patterns among major enteric pathogens isolated from community-acquired diarrhea. Color intensity represents pooled resistance proportions (%), demonstrating widespread resistance to older first-line agents and variable susceptibility to fluoroquinolones and macrolides.

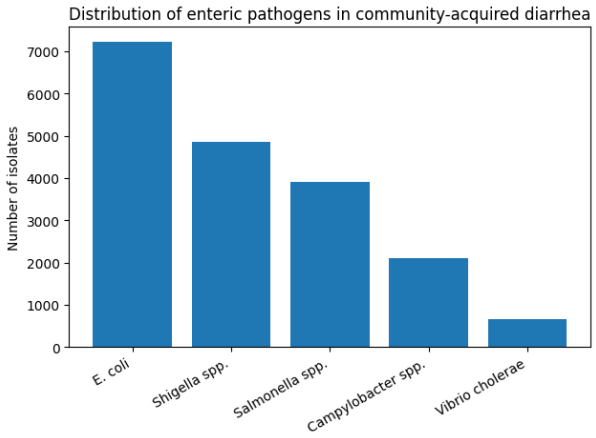

Figure 4. Distribution of bacterial enteric pathogens isolated from community-acquired diarrheal cases across included studies (n = 18,742 isolates). *Escherichia coli* and *Shigella spp.* were the most frequently reported pathogens.

DISCUSSION

This systematic review and meta-analysis synthesizes community-based evidence on antimicrobial resistance (AMR) among major bacterial enteric pathogens and demonstrates a high and clinically consequential burden of resistance, particularly to traditionally used first-line oral agents. By focusing specifically on community-acquired diarrhea, this study addresses a critical evidence gap, as resistance patterns in outpatient and primary-care settings often differ substantially from hospital-derived data yet are most relevant for empiric decision-making.

Widespread resistance to legacy first-line antibiotics

One of the most consistent findings across pathogens was the markedly high resistance to ampicillin and trimethoprim–sulfamethoxazole (TMP–SMX). Pooled resistance exceeded 50% for *E. coli*, *Shigella spp.*, and *Salmonella spp.*, rendering these agents unreliable for empiric treatment in many community settings. This pattern reflects decades of selective pressure driven by low-cost availability, frequent empiric use for undifferentiated diarrhea, and over-the-counter access in many LMICs [23,24]. Mechanistically, resistance in enteric bacteria is commonly mediated through plasmid-borne β-lactamases, dihydrofolate reductase mutations, and mobile genetic elements that facilitate horizontal gene transfer within the gut microbiome [25].

These findings provide robust quantitative support for earlier guideline revisions that removed ampicillin and TMP–SMX from recommended regimens for dysentery and invasive diarrhea [26]. Importantly, continued use of these agents in the community—often due to cost or availability—may not only result in treatment failure but also perpetuate resistance dissemination.

Emerging threats to fluoroquinolones and macrolides

Although pooled resistance to ciprofloxacin and third-generation cephalosporins remained comparatively low overall, significant pathogen-specific and regional signals of concern were evident. In *Campylobacter spp.*, resistance to both ciprofloxacin and erythromycin exceeded 25%, directly threatening the two most important therapeutic classes for severe campylobacteriosis [27]. Fluoroquinolone resistance in *Campylobacter* is largely driven by point mutations in the *gyrA* gene, which can arise rapidly following antibiotic exposure, including indirect exposure through food-animal reservoirs [28].

For *Shigella spp.*, pooled fluoroquinolone resistance appeared low; however, this masks focal emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains reported in recent community outbreaks [29,30]. These strains often harbor combinations of extended-spectrum β-lactamases, macrolide resistance genes, and fluoroquinolone target mutations, severely limiting oral treatment options. Such discordance between pooled averages and real-world outbreak data highlights the limitations of relying solely on aggregated estimates in the context of rapidly evolving resistance.

Geographic and population-level heterogeneity

The substantial heterogeneity observed across nearly all pooled analyses underscores the context-specific nature of enteric AMR. Higher resistance rates in South Asia and sub-Saharan Africa likely reflect differences in antibiotic consumption patterns, regulatory environments, sanitation infrastructure, and baseline enteric disease burden [31]. Pediatric populations, which constituted the majority of included studies, consistently showed higher resistance proportions—potentially due to frequent antibiotic exposure early in life and higher rates of recurrent enteric infections [32].

This heterogeneity has important implications for empiric therapy. Uniform global recommendations are unlikely to be optimal; instead, regionally tailored guidelines informed by outpatient surveillance data are essential. The findings also reinforce the need for age-stratified resistance monitoring, as pediatric empiric strategies may require distinct consideration.

Community settings as reservoirs of resistance

A key strength of this review is its exclusive focus on community-acquired infections. The gastrointestinal tract acts as a major ecological niche for resistant organisms and resistance genes, even in the absence of clinical infection [33]. Community-level antibiotic exposure—often undocumented—can select for resistant enteric flora, which may later cause invasive disease or be transmitted within households and communities. Thus, AMR in community-acquired diarrhea is not only a therapeutic challenge but also a sentinel indicator of broader antimicrobial misuse and environmental dissemination [34].

Implications for clinical practice and public health

Clinically, these findings reinforce that antibiotics should be reserved for clearly indicated diarrheal syndromes, such as dysentery, suspected cholera with severe dehydration, and severe or high-risk cases, in line with international guidance [26,35]. When antibiotics are indicated, reliance on older oral agents is increasingly untenable. Fluoroquinolones, macrolides, or third-generation cephalosporins may still retain activity in some settings, but their use should ideally be guided by local outpatient antibiograms.

From a public health perspective, strengthening community-based surveillance is critical. Global initiatives such as WHO GLASS have expanded to include enteric pathogens, but outpatient representation remains limited in many regions [36]. Investment in basic microbiological capacity, standardized susceptibility testing, and integration of community data into national AMR strategies is essential. Concurrently, non-pharmacologic interventions—safe water, sanitation, hygiene, and vaccination where available—remain foundational in reducing diarrheal incidence and downstream antibiotic exposure [37].

Strengths and limitations

This study benefits from a large pooled sample size, strict community-acquired inclusion criteria, and pathogen-specific quantitative synthesis. However, several limitations warrant consideration. High heterogeneity limits the precision of pooled estimates, and variability in antibiotic panels and testing standards constrained some analyses. Additionally, limited data from certain regions restrict global generalizability. Finally, resistance proportions could not be consistently linked to clinical outcomes such as treatment failure or mortality.

In summary, this meta-analysis demonstrates that antimicrobial resistance among enteric pathogens causing community-acquired diarrhea is widespread and clinically significant, particularly for traditionally used first-line agents. Emerging resistance to fluoroquinolones and macrolides further threatens effective management of severe bacterial diarrhea. These findings underscore the urgent need for region-specific empiric guidelines, strengthened community surveillance, and robust antimicrobial stewardship to preserve remaining therapeutic options and mitigate the growing burden of enteric AMR.

CONCLUSION

This systematic review and meta-analysis demonstrates widespread antimicrobial resistance among enteric pathogens causing community-acquired diarrhea, with particularly high resistance to traditionally used first-line oral agents such as ampicillin and trimethoprim–sulfamethoxazole. Although resistance to fluoroquinolones and third-generation cephalosporins remains comparatively lower, emerging regional and pathogen-specific resistance signals pose a growing threat to effective empiric therapy. These findings highlight the urgent need for community-based antimicrobial surveillance, region-specific treatment guidelines, and strengthened antimicrobial stewardship to preserve the effectiveness of available therapies and improve diarrheal disease management.

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