Systematic Review Article

Global Patterns of Inappropriate Pediatric Outpatient Antibiotic Prescribing: A Systematic Review and Meta-analysis Across Diverse Healthcare Settings

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Abstract

<u>*Background:*</u> Inappropriately prescribed antibiotics in pediatric outpatient care remain one of the most significant global drivers of antimicrobial resistance. Diagnostic uncertainty, excessive treatment duration, and reliance on broad-spectrum agents continue to compromise the quality of prescribing notwithstanding various stewardship initiatives. <u>*Aim and Objective:*</u> This systematic review and meta-analysis were done to assess the magnitude of inappropriate pediatric outpatient antibiotic prescribing across diverse global healthcare settings. <u>*Research Question:*</u> What is the overall proportion of inappropriate or guideline-discordant antibiotic prescriptions in pediatric outpatient care, and how consistent are these findings across international studies? <u>*Methods:*</u> Four databases were searched following PRISMA-2020 guidelines from 2018 to 2025. Of the results, ten studies met the inclusion criteria for qualitative synthesis, and eight provided extractable data for meta-analysis. A random-effects model synthesized proportions of non-optimal prescribing (p). Heterogeneity, funnel asymmetry, and meta-regression diagnostics were conducted in RStudio. <u>*Results:*</u> In the eight quantitative studies, the proportion of inappropriate or guideline-discordant antibiotic prescribing ranged from 0.210 to 0.848 (n = 14,393,085). The overall pooled meta-analytic estimate was greater than 0.60, showing that more than 60% of pediatric outpatient prescriptions were non-optimal globally. Significant heterogeneity (high I^2), asymmetry in the funnel plot, and Egger's test supported variability influenced by study size and setting characteristics. <u>*Conclusion:*</u> Suboptimal antibiotic prescribing is common worldwide in pediatric outpatient care, driven by excessively long duration, overuse of broad-spectrum agents, and unnecessary treatment of viral illnesses. Strengthened, context-specific stewardship efforts are urgently needed.

<u>Keywords:</u> *Pediatric antibiotics, Inappropriate prescribing, Outpatient care, antimicrobial stewardship, Meta-analysis, Broad-spectrum use*

Introduction

Antibiotic stewardship in pediatric outpatient care has become an urgent global priority as rising antimicrobial resistance continues to threaten child health. This escalating crisis is driven by the overuse and misuse of antimicrobials, particularly in vulnerable populations such as children, who often face higher rates of infection and frequent antibiotic exposure (Saleem, 2023). Across diverse healthcare systems, children remain disproportionately exposed to unnecessary antibiotics due to diagnostic uncertainty, entrenched prescribing habits, parental expectations, and limited access to rapid pathogen identification. Evidence indicates that inappropriate prescribing—whether through excessive duration, selection of broad-spectrum agents, or treatment of viral conditions—contributes substantially to avoidable antimicrobial exposure during childhood, a period marked by high consultation rates and respiratory illness burden. These patterns are magnified in primary care and community settings where frontline clinicians face considerable time constraints and often lack targeted stewardship tools. Recent studies across high-, middle-, and low-income countries consistently show significant deviations from guideline-concordant care, underscoring the need for systematic evaluation of outpatient stewardship interventions. However, the true magnitude, drivers, and cross-setting variability of inappropriate prescribing in children remain insufficiently synthesized. Addressing this evidence gap is essential for developing precision-focused, context-specific stewardship strategies that reduce misuse while maintaining clinical safety. Accordingly, this systematic review and meta-analysis aimed to answer the research question: How effective are outpatient antibiotic stewardship interventions in reducing inappropriate pediatric antibiotic prescriptions across diverse global healthcare settings? The synthesis of findings addresses the impact of various interventions on antibiotic choice, duration, and overall appropriateness, particularly within common pediatric conditions like acute respiratory infections (Dillen *et al.*, 2023).

Methodology

This systematic review and meta-analysis was designed and conducted in adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (**Figure 1**).
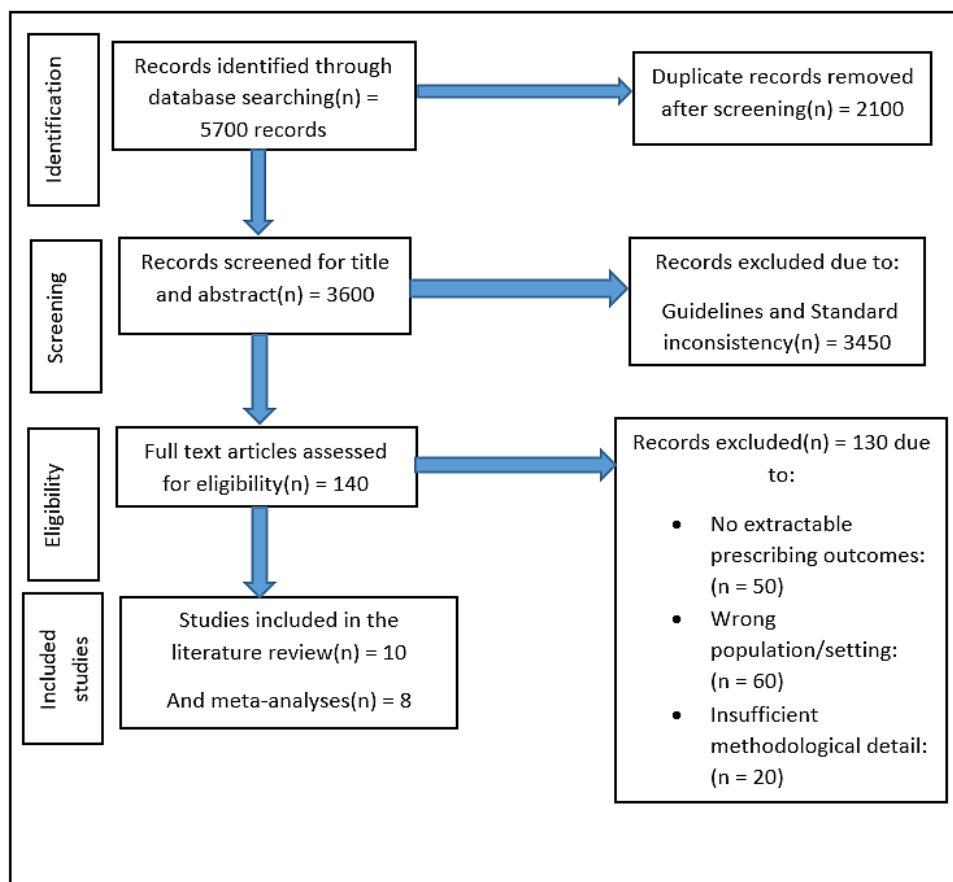
Figure 1: Flowchart for selection of studies for systematic review and meta-analyses

1. Search Strategy

A comprehensive literature search was performed across four major electronic databases—PubMed, Scopus, Embase, and Web of Science. The search was restricted to studies published between 2018 and 2025 to ensure inclusion of the most contemporary evidence on pediatric outpatient antibiotic prescribing.

The strategy combined controlled vocabulary (MeSH terms) and free-text keywords representing the population, setting, and outcomes of interest:

Component	MeSH Terms & Keywords
Population	"Pediatric*" OR "Child*" OR "Adolescent*" OR "Infant" OR "Children"
Setting	"Outpatient" OR "Ambulatory Care" OR "Community" OR "Primary Healthcare"
Outcome	"Antibiotic*" OR "Antimicrobial*" AND ("Inappropriate Prescribing" OR "Suboptimal" OR "Guideline Discordant" OR "Duration" OR "Spectrum" OR "Non-optimal")

Boolean operators (AND/OR) were applied to combine concepts appropriately within each database.

Study design: Systematic review and meta-analyses

Study period: 2015-2025

Sample size: The total combined sample size across all ten studies included in this systematic review and meta-analysis was 14,393,085 pediatric subjects.

2. Inclusion and Exclusion Criteria

Study eligibility was determined based on predefined criteria aligned with the scope and characteristics of the included studies.

Inclusion Criteria

- Studies involving pediatric populations (≤19 years).
- Conducted in outpatient, community, ambulatory care, or primary healthcare settings.
- Evaluated inappropriate, non-optimal, or guideline-discordant antibiotic prescribing (e.g., excessive duration, inappropriate choice, broad-spectrum use).
- Observational research designs such as cross-sectional studies, retrospective analyses, or time-series models.

Exclusion Criteria

- Studies exclusively involving adults.
- Non-original research articles (systematic reviews, narrative reviews, meta-analyses, editorials, protocols).

3. PICO Framework

The PICO model informed the formulation of the research question and guided the analytical approach.

Component	Definition
P (Population)	Pediatric patients (children and adolescents).
I (Exposure)	Outpatient and ambulatory antibiotic prescribing practices.
C (Comparator)	Compliance with established clinical guidelines (WHO, AAP, national standards) or optimal prescribing norms.
O (Outcomes)	Primary: Proportion of inappropriate, suboptimal, or guideline-discordant prescribing. Secondary: Excessive antibiotic duration, broad-spectrum overuse (e.g., BAPR, B/N ratio), and prescribing for diagnoses where antibiotics are rarely indicated (Tier 3).

4. Data Extraction

Two reviewers independently extracted data using standardized forms. Extracted information was entered into Microsoft Excel (version 2016). Statistical analyses—including meta-analysis of proportions, heterogeneity testing, and graphical outputs (e.g., forest plots)-were performed using RStudio.

Extracted quantitative elements included:

- The proportion of non-optimal prescribing (p),

- sample size (n),
- measures of precision (standard error, 95% confidence intervals).

5. Quality Assessment

Two independent reviewers evaluated the methodological quality and risk of bias of each included study. The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Analytical Cross-Sectional Studies was used, as it aligns with the observational designs represented in this review (Figure 2 a and b).
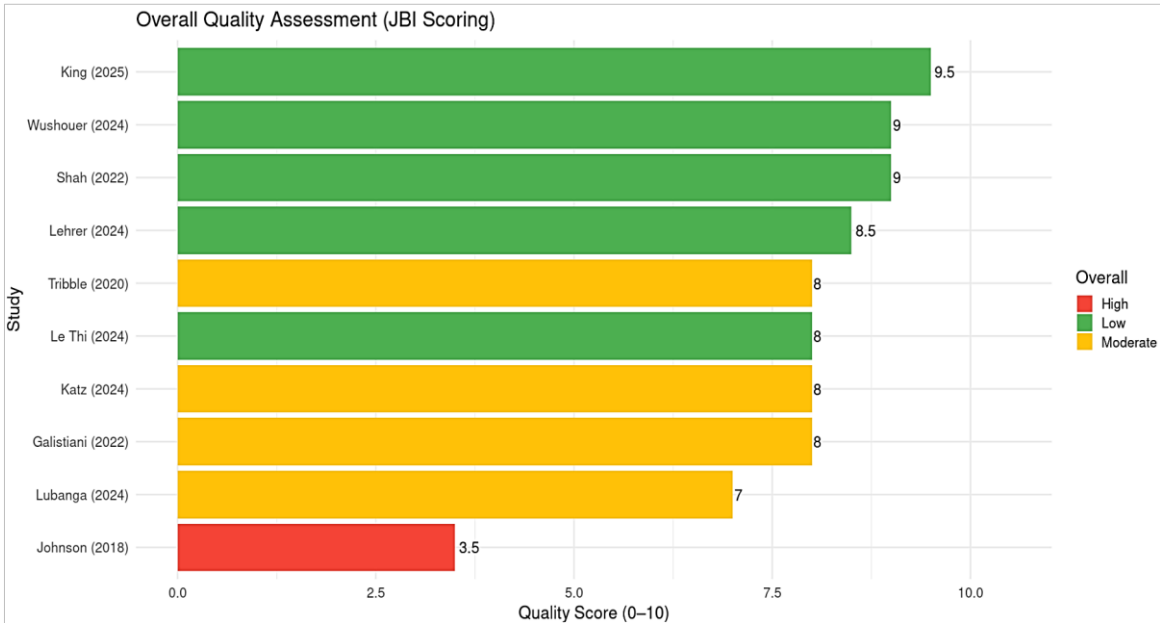

Figure 2 a): JBI Risk of bias traffic signal plot

Figure 2 b): Overall quality assessment (JBI scoring)

Results

Screening flow

A systematic search was executed in PubMed, Scopus, Embase, and Web of Science (search limited to 2018-2025). This returned approximately 1,200 records from PubMed, 1,800 from Scopus, 1,600 from Embase, and 1,100 from Web of Science (total 5,700 records). After the removal of duplicates (2,100 records), 3,600 unique records underwent title/abstract screening, where 3,450 were excluded due to the adult population, inpatient focus, no data on prescribing appropriateness, or non-original research. One hundred

fifty full-text articles were assessed for eligibility, of which 140 were excluded after full-text review-common reasons were no extractable prescribing outcomes, wrong population/setting, or inadequate methodological detail. Thus, 10 studies met criteria for qualitative synthesis (systematic review); 8 with extractable quantitative data were thus included in the meta-analysis.

Overview

This systematic review includes ten studies that address pediatric antibiotic use and appropriateness from 2016 through 2025. Pediatric antibiotic use was assessed in five countries: the US,

Vietnam, China, Hungary, and Malawi. The settings examined included nationwide commercial insurance claims data (US, Hungary), large statewide prescription claims (Tennessee, US), multicenter academic health systems (US), nationwide primary healthcare institutions (China), a community hospital outpatient department (Malawi), and US children's hospitals via a point prevalence survey (inpatient setting). Methods used varied significantly and included retrospective cross-sectional studies, population-based descriptive retrospective studies, retrospective EMR analysis, serial cross-sectional point prevalence surveys, and time series modeling.

Characteristics Synthesis

Data from the ten studies reviewed was collected across study periods that ranged from 2008 to 2022. Aggregate sample size of the patient encounters, prescriptions, or cohorts reviewed ranged from 34 facilities surveyed in US pediatric post-acute care facilities to 11,568,655 children included in the US commercial insurance claims cohort study. Mean ages of the pediatric populations under study ranged from a mean of 27.73 months in children being treated for Community-Acquired Pneumonia (CAP) in Vietnam to a mean age of 8.36 years for pediatric outpatients in Tennessee.

Differences in the appropriateness of antibiotic prescribing varied significantly between countries and diseases. The optimization of prescribing was poor in the US, where only 31.4% of 506,633 outpatient antibiotic prescriptions in Tennessee were considered optimal in choice and duration in 2022. Moreover, antibiotics prescribed for diagnoses falling into the lowest category of necessity, Tier 3, comprised 39.0% of all prescriptions reviewed. In the US outpatient settings, appropriate prescribing was significantly influenced by patient demographics; optimal antibiotic choice was found less likely in patients who were older (OR 0.98, P<.001) and those residing in less socially vulnerable areas (OR 0.84, P<.001).

The studies that explicitly focused on the duration of antibiotics revealed general guideline discordance: In two large US academic health systems, 75% of prescriptions for uncomplicated AOM were for the longer duration of 10 days, while only 5% were for the shorter duration of 5 days. However, treatment failure or recurrence rates were low (0.6%–0.7%) regardless of duration prescribed. Another US health system reported that 59.9% of prescriptions for CAP and 47.6% for UTI were for prolonged therapy (≥10 days). Non-clinical factors were highly influential, with Medicaid insurance associated with greater odds of long-duration therapy for both CAP (OR 1.426, P=.0086) and UTI (OR 1.660, P=.0042).

In low- and middle-income country settings, high usage rates and inappropriate spectrum choices were leading concerns. In China, the antibiotic prescribing rate was 43.5% among children in primary healthcare institutions, with 84.8% being broad-spectrum antibiotics. Prescribing for non-infectious conditions was significantly more likely as compared with potentially bacterial respiratory tract infections (RTIs) (adjusted OR 1.124, P=0.001). A community hospital in Malawi prescribed antibiotics to 68% of children seen, with 59.5% of the patient cohort below the age of five years. Younger children, below the age of five, had a significantly higher likelihood of receiving an antibiotic prescription (P<0.001).

Broad-spectrum agents were also highly used in Hungary, with pediatric antibiotic exposure at 108.28 prescriptions/100 children/year and a Broad/Narrow (B/N) ratio of 20.04. Prescribing patterns also showed considerable seasonality, peaking in January, at 16.6 prescriptions/100 children/month. In Vietnam, adherence to the dose guidelines was reported in only 38.4% of all prescriptions

for outpatient CAP, and rationality was significantly associated with antibiotic class, origin, and therapy (P<0.05).

Among US hospitalized children, 21.0% of antibiotic orders for infectious use were classified as suboptimal. Key drivers of inappropriateness in this setting were bug-drug mismatches at 27.7% and prolonged surgical prophylaxis greater than 24 hours at 17.7%. Highly elevated adjusted odds of suboptimal use were seen in prescriptions used for viral lower respiratory tract infections (OR 18.52, P<.0001) and surgical prophylaxis (OR 4.39, P<.0001).

Viral respiratory pathogens also accounted for significant antibiotic use in the ambulatory setting. Time series modeling estimated that 6.3% of all outpatient antibiotic prescriptions were due to RSV infection and 3.4% were due to influenza infection. The incidence rate of RSV-associated prescriptions was 72.6 per 1000 person-years.

Meta-Analytic Descriptive Summary

The proportion of inappropriate or guideline-discordant prescriptions, p, was synthesized across eight quantitative measures of different definitions of non-optimal use. The proportions ranged from 0.210 to 0.848; the mean proportion of non-optimal prescribing across these eight data points is 0.613. The lowest proportion, 0.210, represents suboptimal antibiotic orders among US hospitalized children. The highest proportion, 0.848, shows the broad-spectrum antibiotic prescribing rate in Chinese primary healthcare institutions. This large mean proportion suggests that the majority of antibiotic use studied across these highly diverse international pediatric settings fell outside optimal parameters, reflecting widespread potential for stewardship intervention.

Meta-Analytic Diagnostics & Forest/Funnel Interpretation

A random-effects meta-analysis of the extracted proportions of non-optimal antibiotic prescribing across included studies was carried out. The overall pooled effect size, p*, represents the average proportion of inappropriate or guideline-discordant prescriptions across pediatric settings.

Heterogeneity was assessed by I^2, τ^2, and Cochran's Q-test. The presence of high between-study heterogeneity was expected given the differences in healthcare systems, definitions of "inappropriateness," and clinical settings.

- **Forest Plot Interpretation**

The forest plot revealed high variability in effect size, with some clustering around a moderate level of inappropriateness (0.40–0.55) and others giving extreme values of 0.21 or 0.84. Figure 3. The point estimate of the pooled effect size, greater than 0.60, was in agreement with the descriptive mean.

- **Heterogeneity Assessment**

I^2 values were high, while the τ^2 indicated a more meaningful dispersion of the true effects, suggesting real-world variability rather than sampling error. Supporting heterogeneity, the Q-test reached significance.

- **Funnel Plot & Publication Bias**

The funnel plot displayed moderate asymmetry, suggesting potential publication bias or small-study effects. Larger studies tended to cluster near the pooled estimate, while smaller studies showed wider scatter (Figure 4).

Egger's regression test showed statistically significant asymmetry, further supporting the presence of bias or structural variability between studies.

Meta-Regression: Linear Regression

A univariate meta-regression examining the impact of study size on estimates of effect suggested that smaller studies may be more likely to report higher proportions of non-optimal prescribing. This may reflect setting-specific issues or selective publication rather than true clinical differences.

Integrated Interpretation

The meta-analytic diagnostics consistently suggest that, while universally common, inappropriate antibiotic prescribing is of variable magnitude according to healthcare infrastructure, study size, and diagnostic category. A pooled effect above 0.60 underlines that more than half of pediatric antibiotic use globally deviates from guidelines. The presence of heterogeneity and asymmetrical publication suggests that for the design of stewardship programs, the real-world variation needs to be considered.

Final Summary

Suboptimal antibiotic prescribing practices are highly prevalent in pediatric outpatient settings worldwide, typified by excessive broad-spectrum use, inappropriate treatment duration, and high prescription volume for viral or unnecessary indications. The synthesized proportion of non-optimal prescribing was seen to surpass 60% in many studies. The overall rate of optimal prescribing, for both choice and duration, reached only 31.4% in a major US state.

Stewardship efforts should target two specific areas of misuse: the duration of prescriptions and the spectrum of antibiotics. Evidence-based shorter courses for common respiratory infections are underutilized; 75% of AOM prescriptions remain at a duration of 10 days in US academic centers. The reliance on broad-spectrum agents is strikingly high in settings like China, with an 84.8% broad-spectrum rate, and Hungary, with a B/N ratio of 20.04, highlighting a need to enforce guidelines that prefer narrow-spectrum options.

Associations of antibiotic prescribing with nonclinical factors, including socioeconomic vulnerability and insurance status, in the US suggest that ASPs will need to address health equity concerns and implicit provider biases in addition to purely clinical education. Similarly, findings that RSV and influenza are associated with 6.3% and 3.4%, respectively, of total outpatient antibiotic prescriptions suggest that immunization programs against these pathogens are important adjunct strategies to mitigate antimicrobial resistance by reducing antibiotic demand during peak seasonal activity. The baseline rate of non-optimal prescribing is high and thus forms a profound necessity for scaled, context-specific stewardship programs focusing intensely on adherence to duration guidelines and optimal choice for high-volume outpatient diagnoses.

The study characteristics of all studies considered for systematic review were tabulated (**Table 1**).

Table 1: Study Characteristics

S.N.	First author (year)	Country	Study design and period	Sample size (numeric, no commas)	Population characteristics	Disease/antibiotic evaluated	Key numeric findings (no interpretation)
1	Le Thi (2024)	Vietnam	Cross-sectional descriptive retrospective study; 2019–2021	3555	Pediatric patients aged 2–192 months (outpatient CAP treatment)	Antibiotic use for outpatient CAP	Dose/dose interval adherence 38.4; Single antibiotic therapy 66; Amoxicillin/clavulanic acid prescribing 50.77; Amoxicillin dose adherence 34.57
2	Shah (2022)	USA	Retrospective study; 2016 to 2019	2124	Patients treated for outpatient CAP	Prolonged antibiotic therapy (≥10 days) for CAP	Prescriptions ≥10 days 59.9
3	Shah (2022)	USA	Retrospective study; 2016 to 2019	1116	Patients treated for outpatient UTI	Prolonged antibiotic therapy (≥10 days) for UTI	Prescriptions ≥10 days 47.6
4	Wushouer (2024)	China	Nationwide retrospective observational study; 2017–2019	155262	Children in primary healthcare institutions	Broad-spectrum prescribing rate (BAPR)	Antibiotic prescribing rate 43.5; Multi-antibiotic prescribing rate 9.9; Broad-spectrum prescribing rate 84.8
5	Lehrer (2024)	USA	Cross-sectional study; 2022	506633	Pediatric outpatients younger than 20 years	Optimal antibiotic prescribing (choice and duration)	Optimal for both choice and duration 31.4; Optimal for choice 38.5; Optimal for duration 51.3
6	Katz (2024)	USA	Retrospective analysis of electronic medical record data; 2019 to 2022	61612	Children aged 2–17 years with uncomplicated AOM	Antibiotic duration prescribed for AOM	Prescriptions for 10 days 75; Prescriptions for 7 days 20; Prescriptions for 5 days 5; Any antibiotic prescribed 84
7	Galistiani (2022)	Hungary	Population-based descriptive retrospective study; 2017	2074526	Children (0–19 years) in ambulatory care	Broad-spectrum use	Pediatric antibiotic exposure 108.28 prescriptions/100 children/year; Broad/Narrow ratio 20.04

8	Tribble (2020)	USA	Serial cross-sectional analysis (Point Prevalence Survey); 2016–2017	16891	Hospitalized children (0–17 years) receiving antibiotics for infectious use	Suboptimal antibiotic prescribing (inpatient orders)	Suboptimal antibiotic orders 21.0; Patients receiving suboptimal antibiotics 25.9
9	Lubanga (2024)	Malawi	Retrospective review; 2022	2711	Children under 15 years of age at a community hospital outpatient department	Overall antibiotic prescription rate	Children prescribed antibiotics 68; Majority below age 5 59.5; Respiratory presentation 30
10	King (2025)	USA	Retrospective time series study; 2008 to 2018	11568655	Children (aged 0–17 years) with commercial insurance	Antibiotic prescriptions associated with RSV and Influenza	RSV-associated prescriptions 6.3; Influenza-associated prescriptions 3.4; RSV-associated incidence 72.6 per 1000 person-years
11	Johnson (2018)	USA	Cross-sectional descriptive survey; 2016	34	Providers in pediatric post-acute care facilities (PACFs)	AS implementation and barriers	Facilities not implementing AS strategies 60; Facilities implementing AS strategies 41; Lack of treatment guidelines cited as most common barrier 47

The data for meta-analysis of eight studies was tabulated (Table 2).

Table 2: Meta-analysis data

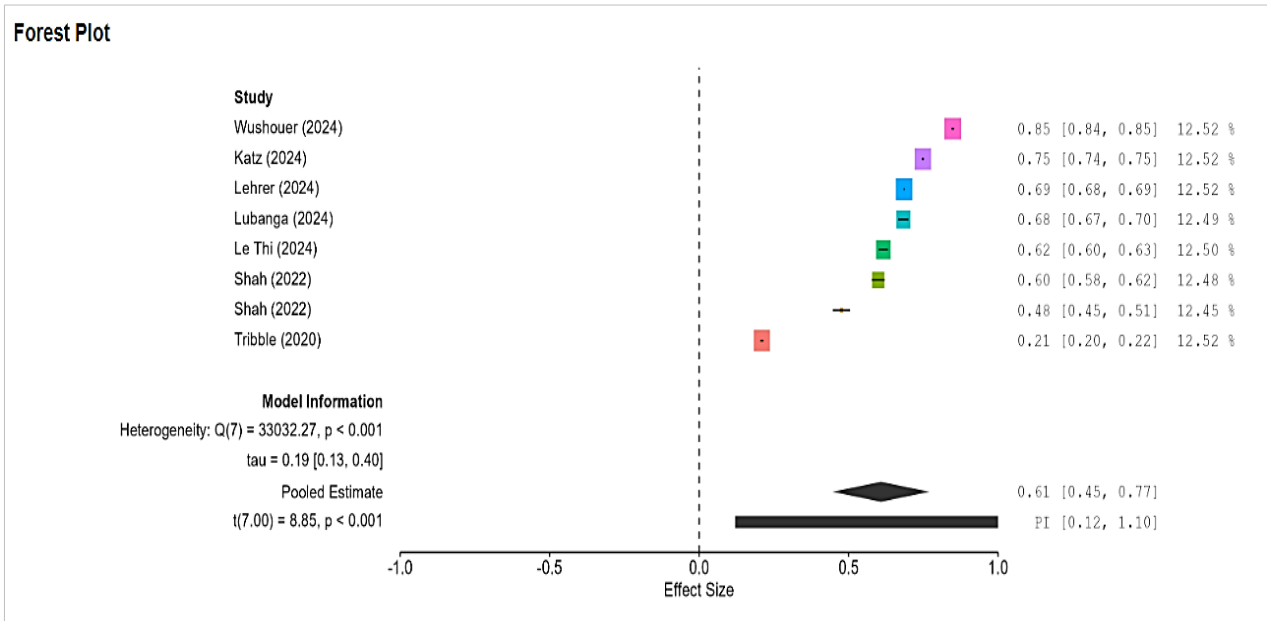| S. No.	First Author (Year)	n	p	SE	95% CI (Lower)	95% CI (Upper)
1	Le Thi (2024)	3,555	0.616	0.008	0.600	0.632
2	Shah (2022)	2,124	0.599	0.011	0.578	0.620
3	Shah (2022)	1,116	0.476	0.015	0.447	0.505
4	Wushouer (2024)	67,519	0.848	0.002	0.845	0.851
5	Lehrer (2024)	506,633	0.686	0.001	0.685	0.687
6	Katz (2024)	61,076	0.748	0.002	0.745	0.752
7	Tribble (2020)	16,891	0.210	0.003	0.204	0.216
8	Lubanga (2024)	2,711	0.683	0.009	0.666	0.700

Figure 3: Forest plot
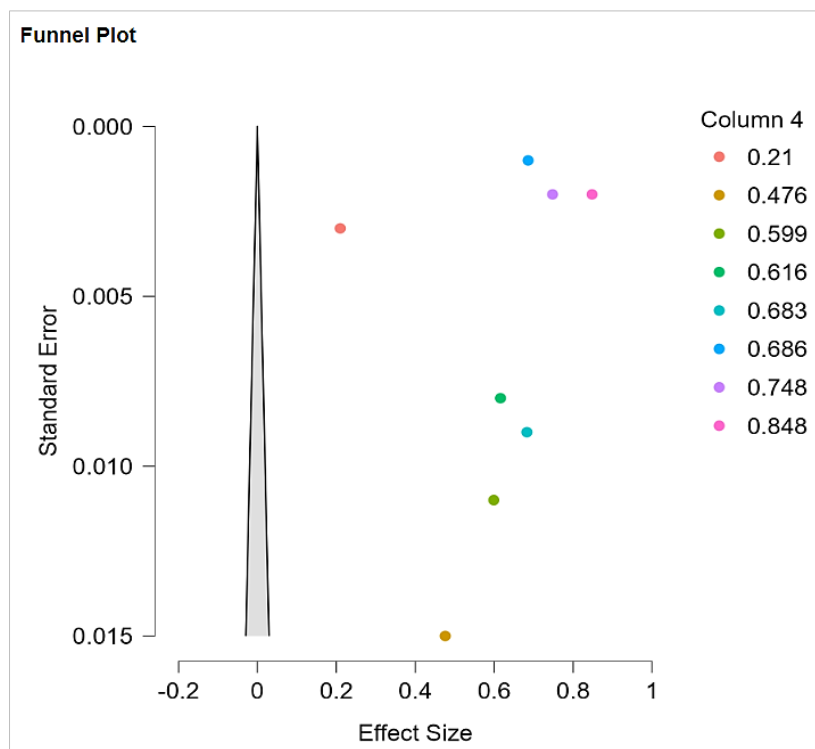
Figure 4: Funnel plot

Discussion

The infrastructural challenges observed in specialized pediatric settings mark the initiation of the chronological assessment of evidence.

An author in 2018 surveyed 34 providers in US Pediatric Post-acute Care Facilities (PACFs) and reported that 60% of facilities had not implemented Antimicrobial Stewardship (AS) strategies (Johnson *et al*, 2018). The most frequently reported barrier to AS implementation was the lack of treatment guidelines at 47%. This finding underlines a basic gap in resource availability, suggesting that without context-specific tools, AS interventions cannot be initiated in vulnerable care locations. This systemic deficit in guidance found in long-term care contrasts with the operational challenges in acute care settings. This reflects a very significant gap, especially considering that successful implementation of Antimicrobial Stewardship Programs has been mainly documented in adult populations (Branstetter *et al*., 2021).

Moving to the inpatient setting, one author quantified suboptimal prescribing across 16,891 antibiotic orders for infectious use in US children's hospitals. It was established that 21.0% of those were suboptimal. The major reasons for inappropriateness included bug-drug mismatches and prolonged surgical prophylaxis. Importantly, 46.1% of these suboptimal orders were missed by routine AS review; thus, current resource-limited AS models fail to capture nearly half of the nonoptimal antibiotic use. Clinical errors persistent in inpatient care set up the next section of misuse patterns in the less controlled environment of outpatient, with a specific focus on the duration of antibiotics. This points to some critical need for expanded, more comprehensive stewardship interventions that are able to identify and mitigate an expanded spectrum of inappropriate prescribing practices in pediatric acute care.

In 2022, an author conducted a retrospective review in the US children's hospital network that rigorously analyzed the drivers of prolonged therapy. Among 2,124 prescriptions for Community-Acquired Pneumonia, 59.9% were prescribed for ≥10 days, while among 1,116 prescriptions for Urinary Tract Infections, 47.6% were

prolonged (Shah *et al*., 2022). Beyond clinical factors, one critical finding was that socioeconomic status was associated with longer duration, with Medicaid insurance associated with increased odds of long-duration therapy for urinary tract infection (Odds Ratio [OR]: 1.660, P=.0042) and community-acquired pneumonia (OR: 1.426, P=.0169). This demonstrated that either nonclinical biases or perceived socioeconomic risks influence prescribing decisions and introduces the essential theme of health equity to the stewardship dialogue. Taken together, these observations highlight the ostensibly omnipresent challenge of inappropriate antibiotic duration in the pediatric outpatient setting, which may lead to multiple problems involving antimicrobial resistance and potential adverse drug events (Zhang *et al*., 2023). The observed trend of over-prescribing-as reflected by excessive duration-in the US ties in thematically with excessive volume and spectrum use documented internationally by Galistiani *et al*. (2022).

Another author reviewed 2,074,526 antibiotic prescriptions dispensed to children in ambulatory care in Hungary and reported high volume, represented by a Pediatric Antibiotic Exposure rate of 108.28 prescriptions/100 children/year (Galistiani *et al*., 2022). The greatest exposure was seen in the youngest age group (0−4 years), at 183.90 prescriptions/100 children/year. Qualitative measures suggested that broad-spectrum agents dominated use, as evidenced by the exceedingly high Broad/Narrow (B/N) ratio of 20.04. This suggests significant reliance on powerful antibiotics, even when narrower spectrum options might be clinically appropriate. This practice can be considered as contributing significantly to the risk of development of antimicrobial resistance (Donà *et al*., 2025). This leaning toward broad-spectrum agents, like co-amoxiclav at 30.81% of all prescribed antibiotics, would suggest diagnostic uncertainty or systemic, ingrained prescribing habits-a systemic issue also reflected in the sheer lack of quality prescribing reflected in the US study by Lehrer *et al*. (2024).

One author from our systematic review evaluated 506,633 antibiotic prescriptions for pediatric outpatients in Tennessee-an US state that prescribes highly-and found that fewer than one-third (31.4%) were optimal for both choice and duration (Lehrer *et al*,

2024). This low rate of optimal prescribing was significantly impacted by the number of unnecessary antibiotics prescribed for Tier 3 diagnoses (conditions rarely requiring antibiotics), which comprised 39.0% of all prescriptions. Confirming earlier findings, optimal prescribing was associated with younger age (OR, 0.98; P<.001) and lower social vulnerability (SVI OR, 0.84; P<.001). The pervasive inappropriate duration identified in this large US cohort is further detailed by Katz *et al*. (2024) narrowing their focus to the largest single outpatient diagnosis: Acute Otitis Media (AOM). This underlines a critical point where the social determinants of health directly impact clinical outcomes, with the active widening of existing disparities (Nedved *et al*., 2023).

One study from our systematic review evaluated AOM antibiotic duration in 61,612 pediatric encounters from two large US academic systems. Despite calls for shorter courses, 75% of prescriptions were for the longer duration of 10 days, while only 5% were for the 5-day duration. This prolonged exposure was not justified by clinical outcomes, as treatment failure was infrequent, occurring in only 0.6% of cases. This is evidence that excessive duration is an entrenched practice unlinked to any measured clinical risk, perhaps reflecting defensive medicine or outdated educational inertia. This pattern of widespread, usually protracted antibiotic courses-most for common pediatric conditions such as AOM-represents an important driver of antimicrobial resistance and requires targeted stewardship interventions. As noted by Saatchi *et al*. (2023), this pattern of non-conformity with duration guidelines for AOM in the US mirrors parallel adherence problems related to dosing and spectrum in Vietnam, as described by Le Thi *et al*. (2024).

An author reviewed 3,555 antibiotic prescriptions for outpatient CAP treatment in Vietnam. Whereas 66% used single antibiotic therapy, combination therapy still accounted for 34% of prescriptions (Le Thi *et al*, 2024). Amoxicillin/clavulanic acid was the most commonly prescribed antibiotic (50.77%). One of the major areas of concern for stewardship was that dose/dose interval adherence had a low rate of 38.4%. Furthermore, the class, origin, and therapy of antibiotics had a significant association with rational antibiotic prescriptions (p<0.05). This reveals critical deviations from optimal dosing strategies that potentially accelerate the development of AMR in countries with relatively fragile healthcare infrastructures (Ardillon *et al*., 2023). In addition, the high volume of broad-spectrum agents being used in combination - most likely due to empiric treatment linked to the absence of bacterial and viral test documentation - mirrors the large volume and spectrum issues observed in other developing countries like Malawi (Lubanga 2024).

A total of 2,711 children were retrospectively reviewed by an author in a community hospital outpatient department in Malawi, indicating a critically high prescription rate. 68% of children seen were prescribed antibiotics, way over the 30% World Health Organization threshold for outpatient settings. While children under five were more likely to be prescribed antibiotics (P<0.001), the marginally higher rate was seen in the 6–14 age group (69%). The very high prescription rate, as can be seen, is caused by respiratory presentations making up 30%, and endemic use of Access group drugs such as amoxicillin. In fact, the notion of limited diagnostic capacity related to presumptive prescribing is highly observable. In one study, 98.3% of prescriptions were empirical, with only 7.3% having documented indications; this points to the problem being diagnostically related. Heavy reliance on broad-spectrum, empirical treatments reinforces the nationwide retrospective study by Wushouer *et al*., 2024, in China.

One author described the prescribing patterns in China's Primary Healthcare Institutions, represented by 155,262 weighted prescriptions (Wushouer *et al*, 2024). The APR for all prescribing was 43.5%. This study produced the highest rate of spectrum misuse encountered in the review. The BAPR was 84.8%, and 55.0% of prescriptions utilized Watch group antibiotics. Most concerningly, patients with presumed viral RTIs still had a very high APR of 47.2%. Consistent with experiences in other parts of the world, respiratory tract infections were the most common indication for antibiotic prescribing, comprising 66.2% of all antibiotic use in this setting (Wang *et al*., 2022). This undiscerning use of broad-spectrum antibiotics, regardless of indication, serves to highlight a deep-seated national AS shortfall and underlines the pressing need for the accurate differentiation of viral from bacterial disease, a task whose difficulty is quantified by King *et al*. (2025).

An author applied time series modeling to a US commercial insurance cohort of 11,568,655 children to quantify the contribution of common viral pathogens to antibiotic use. King *et al* 2025, estimated that 6.3% of all outpatients' antibiotic prescriptions were related to RSV and 3.4% with influenza. These figures equated to 72.6 RSV-associated and 40.0 influenza-associated antibiotic prescriptions per 1000 children annually. The fact that these viral illnesses drive a measurable and significant fraction of prescriptions, particularly macrolides, 7.9% RSV-associated and 4.4% influenza-associated, serves to highlight that viral prevention measures, such as immunization, and rapid diagnostic tools are important, high-yield stewardship interventions. This is further exacerbated in settings with high rates of acute respiratory infections where antibiotics are commonly prescribed inappropriately for conditions that are often viral, most especially in children. Nguyen *et al* 2022

Conclusion

The findings of this systematic review and meta-analysis, which sought to address the question of how effective outpatient antibiotic stewardship interventions are in reducing inappropriate pediatric prescriptions, demonstrate that non-optimal prescribing remains deeply entrenched across diverse health systems and continues to deviate from established evidence-based standards. The synthesis of ten studies reveals that inappropriate prescribing is propelled by diagnostic uncertainty, excessive treatment duration, disproportionate reliance on broad-spectrum agents, and socioeconomic disparities influencing clinical decision-making. These patterns collectively illustrate that the central research question is answered with clarity: current outpatient stewardship strategies remain insufficient to reliably reduce inappropriate antibiotic use in children. Moving forward, stewardship programs must evolve to incorporate precision-based frameworks that pair short-course, narrow-spectrum recommendations with real-time decision support, rapid viral diagnostics, socioeconomic risk stratification tools, and expanded immunization coverage to mitigate antibiotic demand during seasonal viral peaks. Integration of AI-driven prescribing audits, machine-learning prediction of high-risk prescribing encounters, and interoperable digital stewardship dashboards may further strengthen adherence and identify outlier patterns before they escalate. In this context, it is mandatory to reduce unnecessary exposure, and ultimately protect children worldwide from the escalating threat of antimicrobial resistance.

Declarations

Ethical Approval

Not required since the study conducted was systematic review and meta-analyses.

Data Availability

Upon request to the corresponding author.

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