Antibiotic stewardship and point-of-care testing for children in 25 low-income and lower-middle-income countries: a systematic review and meta-analysis

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Summary

Background Inappropriate antibiotic use is a key driver of antimicrobial resistance (AMR), a growing global threat that disproportionately affects children in low and lower-middle-income countries (LLMICs). In response, the WHO Global Research Agenda for Antimicrobial Resistance in Human Health prioritises research on antimicrobial stewardship programs (ASPs, formally introduced in 2007) and feasible point-of-care testing (POCT) in paediatric populations, where evidence on implementation and effectiveness remains limited. We aimed to address this gap and inform the design and scale-up of paediatric-focused strategies via a systematic review and meta-analysis on the impact of ASPs and POCTs in children in LLMICs.

Methods For this systematic review and meta-analysis, we searched MEDLINE, Embase, Cochrane Library, Scopus, Global Health, CINAHL, African Journals Online (AJOL), and Latin American and Caribbean Health Sciences Literature (LILACS) for relevant studies published between January 1, 2007, and December 31, 2024. A search update was conducted on September 1, 2025. The search strategy included a combination of Medical Subject Heading (MeSH) and free text terms for 'children', 'antibiotic', 'stewardship program', and 'point-of-care', without any language restrictions. Eligible studies included children (aged <18 years) and were conducted in healthcare settings (inpatient or outpatient) within LLMICs, as per 2024 World Bank classification. Randomised controlled trials, before-and-after, and cohort studies were eligible for inclusion. Outcomes were antibiotic use, guideline adherence, costs, antimicrobial resistance, and clinical outcomes. When three or more reports assessed the same intervention and outcome, a random-effects meta-analysis was performed, and odds ratios (ORs) with 95% confidence intervals (CIs) were reported. This work is registered with PROSPERO, CRD42024491248.

Findings Of the 11,191 records identified, 78 reports from 13 countries in Africa and 12 countries in Asia were included in the evidence synthesis. These studies evaluated 68 ASPs and 30 POCTs, either alone or in combination. Most reported improvements in antibiotic prescribing (77%) and adherence to guidelines (80%). Success rates were higher when ASPs were combined with POCTs (85%) compared to ASPs (73%) or POCTs alone (80%). Bundled interventions were more effective (81%) than single ones (70%). No increase in adverse clinical outcomes was observed, supporting the safety of ASPs. Meta-analysis showed that clinical decision support systems reduced antibiotic prescribing in primary care (overall OR 0.17, 95% CI 0.07–0.45, I^2 99.7).

Interpretation Evidence shows that ASPs and POCTs are feasible and effective in children in LLMICs, supporting the development of adaptable, paediatric-focused strategies. Future research should focus on large-scale implementation studies and context-specific evaluations to optimise paediatric ASPs and POCTs in LLMICs.

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Keywords: Low and lower-middle-income countries; Antibiotic stewardship programs; Point of care tests; Antimicrobial resistance; Paediatric settings

Research in context

Evidence before this study

Antibiotics are widely used in children, and a substantial proportion are prescribed inappropriately, contributing to the global crisis of antimicrobial resistance (AMR) that is especially pronounced in resource-limited settings. Despite the influence of clinical guidelines, practitioner experience, and drug availability, a gap remains between evidence-based recommendations and actual prescribing practices. To address this, the World Health Organisation (WHO) released the AWaRe Book in 2022, providing standardised treatment guidance for common infections. However, implementation remains challenging in low-income and low-middle-income countries (LLMICs), where stewardship interventions must be feasible, sustainable, and cost-effective. While antimicrobial stewardship programs (ASPs) have proven effective in higher-income settings, their impact in LLMICs is less understood. Point-of-care testing (POCT) holds considerable promise for improving antibiotic use, but its implementation is often constrained in settings where it is most needed. Prior to conducting this study, we performed a literature search in November 2023 on PubMed for systematic reviews using keywords related to 'antimicrobial stewardship programs' and 'diagnostic stewardship programs' in 'paediatric populations' within 'low- and middle-income countries' (LMICs), without language restrictions. This search identified only one relevant systematic review, which included a large proportion of studies from upper-middle-income countries (14 from China), potentially limiting the generalisability of its findings to LMICs with more resource-constrained healthcare systems. We aimed to address this knowledge gap.

Added value of this study

Despite growing awareness of the urgent need for antimicrobial stewardship, the most effective strategies to design and implement ASPs and POCTs in paediatric settings across LMICs are still not well established. By pooling evidence from 25 countries across Asia and Africa, we provide context-specific insights that were previously missing from the global evidence base. Several ASPs and POCTs are associated with meaningful reductions in antibiotic overuse in children across Asia and Africa, without increasing morbidity or mortality. The findings underscore the added value of integrated approaches: interventions combining training programs, clinical pathways, and clinical decision support systems (CDSS) with POCTs were consistently more effective than stand-alone strategies. Notably, CDSS emerged as promising tools to enhance adherence to guidelines and optimise prescribing in both hospital and primary care settings. Our pooled analysis showed that CDSS implementation in primary care for children aged 2–59 months significantly reduced the likelihood of antibiotic prescription compared with usual care.

Implications of all the available evidence

This review offers timely and policy-relevant insights to support the development of large-scale global interventions within LLMICs that are aligned with the WHO Global Research Agenda for Antimicrobial Resistance in Human Health. By systematically evaluating both the characteristics of the interventions and their outcomes, our findings highlight the potential of targeted antimicrobial stewardship strategies to curb antibiotic misuse in paediatric populations, which are often underrepresented in stewardship research, and to inform evidence-based policy and practice in LLMICs. The review also identifies key priorities for future research, including the need for context-specific approaches and the development of standardised, comparable metrics for measuring impact. These findings offer actionable guidance for policymakers and health system stakeholders, underscoring the importance of tailored strategies to advance global health goals and mitigate the burden of antimicrobial resistance in resource-constrained settings. Future research should prioritise large-scale implementation studies and context-specific evaluations to optimise paediatric antimicrobial stewardship and point-of-care testing in LLMICs.

Introduction

Antimicrobial resistance (AMR) represents a major global health threat, with the highest burden observed in low-income and lower-middle-income countries (LLMICs) and among paediatric populations.[1] A global analysis estimated that in 2021, AMR was associated with 840,000 deaths and directly attributable to 193,000 deaths in children under five.[1] Regionally, mortality rates associated with and attributable to AMR were highest in South Asia (68.5 per 100,000 and 18.1 per 100,000, respectively) and Sub-Saharan Africa (81.5 per 100,000 and 18.5 per 100,000, respectively), with regional forecasts predicting differing trends by 2050. In recognition of this growing threat, the 79th United Nations General Assembly (UNGA) in September 2024 set a global target to reduce mortality attributable to AMR by 10% by 2030.[2]

The overuse and misuse of antibiotics are major drivers of AMR, contributing to avoidable healthcare costs for families and health systems, and placing further strain on already overstretched services.[3] To support rational antibiotic use in LLMICs, the World Health Organisation (WHO) published in 2022 the AWaRe Book, providing evidence-based prescribing guidance for more than 30 common infections.[4] Antibiotics recommended are those included in the WHO Essential Medicine Lists, and categorised based on the AWaRe system in Access, Watch and Reserve, according to their spectrum of activities and risk of inducing resistance.[5] Additionally, the Integrated Management of Childhood Illness (IMCI) guidelines, created in collaboration with UNICEF, provide care recommendations for children under five, especially in low-resource settings.[6]

Despite global efforts, major gaps remain in the implementation of strategies to curb AMR. The recently published WHO Global Research Agenda for Antimicrobial Resistance in Human Health identifies 40 research priorities with the greatest potential to mitigate AMR, placing strong emphasis on the development of context-specific Antimicrobial Stewardship Programs (ASPs) and Point of Care Tests (POCTs) in paediatric populations, particularly in resource-constrained settings.[7–10] ASPs, formally introduced in 2007 by the Infectious Diseases Society of America, have demonstrated success in high-income countries across both inpatient and outpatient care.[9,11,12] However, their translation to LLMICs is hampered by unique challenges, especially in primary care and rural contexts, where diagnostic capacity is often limited and health systems are under-resourced. Consequently, a large proportion of antibiotic prescriptions remain inappropriate or suboptimal.[7,13] While antibiotic consumption in LLMICs is still lower overall than in high-income settings, since 2018, these countries have reported higher use of Watch group antibiotics, reaching 8.2 defined daily doses per 1000 inhabitants per day in 2023, the highest globally.[14–16] This trend may in part reflect poor adherence to guidelines and widespread access to antibiotics via unregulated channels, such as informal drug vendors, traditional healers, and supermarkets, especially in outpatient contexts where proper clinical evaluation is lacking.[16]

Despite increasing recognition of the urgent need for antimicrobial stewardship, the optimal approach to designing and implementing ASPs and POCTs in paediatric care across LLMICs remains poorly defined. To address this gap, we aimed to conduct a systematic review and meta-analysis on ASPs and POCTs in paediatric settings across LLMICs. Our objective was to assess their impact on antibiotic use, guideline adherence, costs, antimicrobial resistance, and clinical outcomes, thereby providing evidence to inform the development of context-appropriate interventions and global initiatives aimed at reducing AMR in resource-limited settings.

Methods

Study design, ethics, and search strategy

This systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA 2020) guidelines (Supplementary File 1).[17]

Ethics approval and informed consent were not required for this study, owing to the study design. This systematic review and meta-analysis used only previously published data, with no new human participants involved.

A systematic search was conducted in MEDLINE, Embase, Cochrane Library, Scopus, Global Health, CINAHL, African Journals Online, and Latin American and Caribbean Health Sciences Literature. The search strategy included a combination of Medical Subject Heading (MeSH) and free text terms for ‘children’, ‘antibiotic’, ‘stewardship program’, and ‘point-of-care’, with restriction date (1 January 2007–31 December 2024) without language restriction. This search was updated on September 1, 2025. For articles not in English, translations were performed using DeepL (DeepL SE, Germany, version 25.8.2.17787). The complete search strategy is available in Supplementary File 1. The review protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) in February 2024 (CRD42024491248) and updated on September 25, 2025.

Inclusion and exclusion criteria

Reports were eligible for full-text review if they included participants under 18 years of age and were conducted in healthcare settings (inpatient or outpatient) within LLMICs. We used the latest World Bank classification (2024) to select countries for inclusion (as explained in Supplementary Files 1).[18] Randomised controlled trials (RCTs), controlled and uncontrolled before and after studies, controlled and uncontrolled interrupted time series, and cohort studies were included. Review articles, case series, letters, notes, conference abstracts, and opinion articles were excluded. Reports that included adults and children where paediatric data could not be extracted were also excluded. We excluded reports published before 2007, as the concept of ASP was formally introduced that year.[19]

Selection of the reports

In line with the PRISMA guidelines for systematic reviews, the screening for titles, abstracts, and full texts was conducted independently by two investigators (EG and EZ) using Covidence software (Covidence, Australia, 2024).[20] Discussion with a third reviewer (EB or GB) resolved any disagreement regarding the selection of reports. Duplicate reports were excluded after identification by the software and manually.

Data collection and analysis

Data were extracted and recorded using a standardised data collection form, which summarised information about author, publication year, country, study period, study design, sample size, patient age, gender reported, setting, intervention, and outcomes. Outcomes considered were any changes in antibiotic prescribing practices following the intervention, as well as changes in compliance with guidelines, healthcare costs, bacterial resistance, and clinical outcomes. We conducted a synthesis of the evidence stratified by intervention setting—primary care (public health centres and community-based services), hospitals, and private healthcare facilities (pharmacies or private primary care)—to account for variations in available healthcare resources. Successful implementation was defined according to the criteria or judgment provided by the authors of each included report.

Quality assessment (risk of bias)

The risk of bias for randomised controlled trials was evaluated with the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2). Non-randomised studies were assessed using National Institutes of Health tools for Case-Control, Cohort, Cross-Sectional, and Pre-Post studies based on the study design.[21,22] The risk of bias judgments did not affect study inclusion.

Statistical analysis

A meta-analysis was performed when more than three reports on the same intervention assessed the same outcome. Random-effects models were used to pool effect estimates. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for each study. The pooled effect was estimated using a generalised linear mixed model (GLMM) with restricted maximum likelihood (REML) to estimate between-study variance. Statistical heterogeneity was assessed using Cochran's Q test and quantified with the I^2 statistic. Tests for funnel plot asymmetry were planned if at least 10 studies were available. To assess the robustness of the findings, analyses were stratified by study design, and sensitivity analyses restricted to studies evaluating the same specific type of intervention were planned. In addition, a post-hoc analysis was conducted excluding studies deemed to be at high risk of bias. All analyses were conducted in R Studio (version 4.1.3) using the meta package.

Role of the funding resource

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Of the 11,191 records identified, 5383 duplicates were removed, leaving 5808 articles for screening. Among these, 341 (3.0%) articles were assessed in full text, and 78 (22.9%) articles—including five added through the updated search conducted on September 1, 2025—were included in the final evidence synthesis (percentage agreement between reviews: 92% and 81% respectively, Cohen's kappa: 0.44 and 0.56 respectively) (Fig. 1).

Study characteristics

The 78 included reports, encompassing data from 25 countries (13 countries in Africa and 12 countries in Asia), are summarised in Table 1. Most of them (75.6%, 59/78) were conducted in lower middle-income countries (LMICs), while 24.4% (19/78) were conducted in low-income countries (LICs). More than half were conducted in Africa (56.4%, 44/78)[26–28,30,44,46,49–54,56,57,62,65–70,72–77,79,80,85–95,97–100] and 43.6% (34/78) in Asia, mainly in India.[23–25,29,31–43,45,47,48,55,56,58–61,63,64,71,78,81–83,96] The geographical distribution is shown in Fig. 2. Most publications were in English and released after 2020 (59.0%, 46/78). A range of study designs was represented, with before–after studies being the most common (47.4%, 37/78), followed by randomised controlled trials (37.2%, 29/78). 64.1% focused on children under five years of age, and 24.4% specifically targeted neonates. Results stratified by age group are available in Supplementary File 2.

Setting and types of interventions

Studies were more commonly conducted in hospital settings (50.0%, 39/78), with 17 of these conducted in intensive care units, and primary care settings (43.6%, 34/78)–28 in public health centres, six in the community — whereas only five (6.4%) in private care (Table 1). Of the 78 reports, 48 (61.5%) implemented an ASP intervention only, 20 (25.6%) combined ASP with POCTs, while 10 (12.8%) focused solely on diagnostic tests.

Nearly 70% of the included reports documented the implementation of bundled interventions (69.1%, 47/68).

The various interventions and their combinations, stratified by setting (hospital, primary care, and private), are shown in Fig. 3. The main interventions implemented at the hospital level were audit and feedback (58.3, 21/36) and guidelines and protocols (58.3, 21/36).

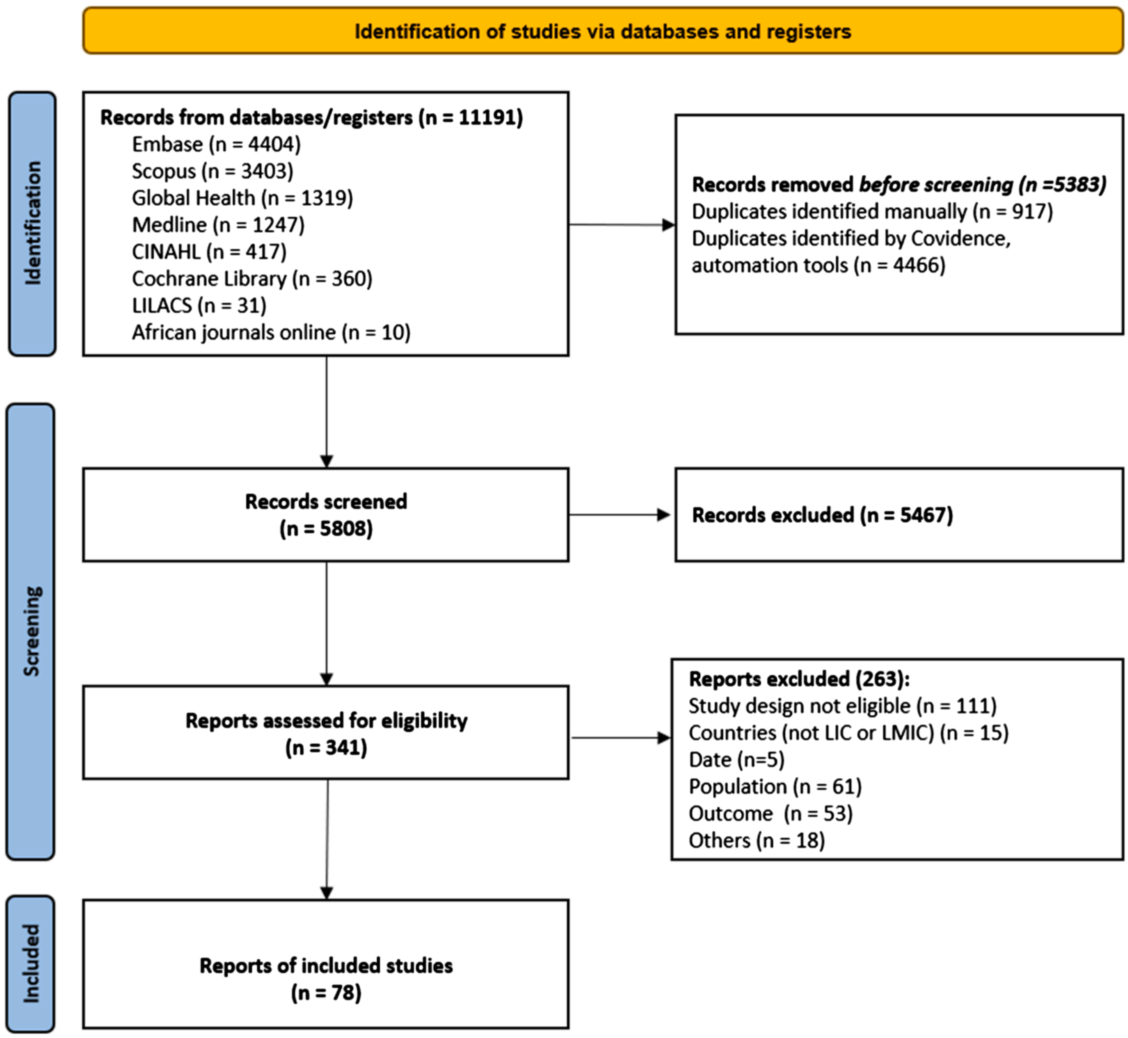

Fig. 1: PRISMA flowchart of the report's selection process.

In primary care, healthcare workers' education was reported in 24 out of 27 reports (88.9%). In most cases, it was implemented in association with clinical decision support systems (CDSS) (36.0%, 10/26) and clinical pathways (38.4%, 9/25). CDSS were mainly ePOCT (electronic Point-Of-Care Tool) and ALMANACH (Algorithm for the Management of Childhood Illnesses). Regarding the implementation of POCTs, 30 reports were identified. The most frequently reported were malaria rapid diagnostic tests (50.0%, 15/30) and C-reactive protein tests (46.7%, 14/30). In 13 studies, these were used alongside additional tests, including urine dipsticks, diagnostics for typhoid fever, influenza A and B, group A Streptococcus, *Streptococcus pneumoniae*, and haematological counts. Of the 78 reports, 47 implemented disease-specific interventions: 15 focused on febrile illnesses, 11 on respiratory diseases, five on diarrhoea management (mainly in hospitals), and seven on sepsis management in neonates (<28 days, hospital level). In over 85% of these interventions, stewardship targeted overall antibiotic prescribing for the treatment of infectious diseases rather than specific antibiotics. No reports regarding the use of antibiotics for prophylaxis were included.

Outcomes

78.2% reports (61/78) analysed the impact of interventions on antibiotic prescribing, 35 (44.9%) the compliance of antibiotic prescribing with current guidelines, three (3.8%) the changes in healthcare costs and three (3.8%) the bacterial resistance to antibiotics. Overall, 60 of the 78 studies (76.9%) reported successful implementation of an ASP or POCT, seven (9.0%) yielded inconclusive results, while 11 (14.1%) reported unfavourable results (Fig. 4). The success rate was notably higher in studies where an ASP was combined

Author	Countries[b]	Setting	F (%)	Age	Study period	Study design	ASP	POCT	ASP intervention implemented (bundled intervention in case of multiple dots)							Outcomes					Quality assessment
									EP	CG	EPa	AF	CP	CDSS	Others	AP	C	Co	Cl	R	
Hospital settings (N = 39)																					
Agarwal et al. (2021)[23]	India	Hospital	26.9	<28 d	January–March 2019, April 2019–November 2020	BAF	Yes	No	•	•		•	•		•	+	+				Fair
Awad et al. (2020)[24]	Jordan	Hospital	33.7	<24 m	January–March 2016, January–March 2017	BAF	Yes	No		•						+	+		+		Poor
Azeez et al. (2020)[25]	India	Hospital	40.0	<14 y	September 2016–August 2017	BAF	Yes	No	•	•		•					a				Poor
Bassiouny et al. (2020)[26]	Egypt	Hospital	36.2	<28 d	July–September 2016, October 2016–March 2017	BAF	Yes	No	•	•		•				+	+	+	+	+	Fair
Bastiaens et al. (2011)[27]	Tanzania[b]	Hospital	NR	<10 y	September 2009–January 2010, January–February 2010	BAF	Yes	Yes	•							–					Fair
Chimhini et al. (2020)[28]	Zimbabwe	Hospital	46.9	NA	May–June 2018, October–November 2018	BAF	Yes	No	•			•				+	+		+		Fair
Deorari et al. (2022)[29]	India[b]	Hospital	44.2	<28 d	February–August 2017, August 2017–February 2019	BAF	Yes	No	•			•				+			+		Fair
El Baky et al. (2020)[30]	Egypt	Hospital	41.8	<28 d	August 2016–April 2017, June 2017–February 2018	BAF	Yes	No		•						+	+	+	+	a	Poor
Hembade et al. (2024)[31]	India	Hospital	NR	1 m–18 y	December 2019–August 2021	BAF	Yes	No	•			•				+	+				Fair
Jain et al. (2021)[32]	India	Hospital	NR	<28 d	March 2018–August 2018	BAF	Yes	No	•	•		•			•	+			+		Poor
Jinka et al. (2017)[33]	India	Hospital	40.0	<28 d	January 2013–December 2013, January 2014–December 2014	BAF	Yes	No		•						a			+		Fair
Joshi et al. (2020)[34]	India	Hospital	36.7	<18 y	January–December 2012, January–December 2014	BAF	Yes	No		•		•			•	a	a		+		Fair
Khorshidi-Malahmadi et al. (2021)[35]	Iran	Hospital	NR	NA	February 2017–January 2018, February 2019–January 2020	BAF	Yes	No	•			•			•	+		–		+	Poor
Kommalur et al. (2021)[36]	India	Hospital	NR	<28 d	April 2019, May–September 2019	BAF	Yes	No	•	•		•			•	+	+		+		Good
Konda et al. (2021)[37]	India	Hospital	NR	<28 d	November 2019, November 2019–January 2020	BAF	Yes	No	•	•		•			•		+				Fair
Kushala et al. (2023)[38]	India	Hospital	41.3	<18 y	November–December 2017, January–June 2018	BAF	Yes	No	•	•		•	•		•		+				Good
Lapitan et al. (2021)[39]	Philippine	Hospital	53.5	<18 y	January–February 2019, February–March 2019	BAF	Yes	No		•							a		+		Fair
Maalouf et al. (2023)[40]	Lebanon	Hospital	42.8	<28 d	January–December 2015, April 2017–March 2022	BAF	Yes	No	•	•		•	•	•	•	+			+		Fair
Mishra et al. (2022)[41]	India	Hospital	NR	NA	July 2019, October 2019–March 2020	BAF	Yes	No	•	•	•	•				+					Poor
Mohammadi et al. (2015)[42]	Pakistan	Hospital	NR	NR	April 2011–November 2013	BAF	Yes	No				•				+			+		Poor
Nguyen et al. (2022)[43]	Vietnam	Hospital	41.1	<17 y	April 2016–March 2018	BAF	Yes	No		•		•				–	+		+		Good
Ola-Bello et al. (2023)[44]	Nigeria	Hospital	42.0	<16 y	April 2019–September 2019	BAF	Yes	No				•			•		+				Fair
Rahbarimanesh et al. (2019)[45]	Iran	Hospital	45.2	NA	September 2014–September 2015, October 2015–October 2016	BAF	Yes	No				•				+	+		+		Fair

(Table 1 continues on next page)

Author	Countries[b]	Setting	F (%)	Age	Study period	Study design	ASP	POCT	ASP intervention implemented (bundled intervention in case of multiple dots)							Outcomes					Quality assessment
									EP	CG	EPa	AF	CP	CDSS	Others	AP	C	Co	Cl	R	
(Continued from previous page)																					
Senbanjo et al. (2017)[46]	Nigeria	Hospital	43.5	<5 y	March 2011–April 2012, October–December 2013	BAF	Yes	No	•			•					+				Fair
Venugopal et al. (2023)[47]	India	Hospital	45.5	<28 d	April 2019, May 2019–June 2020	BAF	Yes	No	•								+		+		Good
Ahmed et al. (2017)[48]	Pakistan	Hospital	42.9	<28 d	September 2016–May 2017	Others	No	Yes								+					Fair
Fileccia et al. (2022)[49]	Kenya	Hospital	48.0	<5 d	2018–2020	Others	Yes	No		•			•			+			+		Fair
Khan et al. (2025)[50]	Zimbabwe, Malawi[b]	Hospital	44.6	<28 d	January 2021–June 2022	Others	Yes	No		•						–					Fair
Rasti et al. (2025)[51]	Uganda[b]	Hospital	37.0	0–12 y	March 2019–July 2020	Others	No	Yes											+		Fair
Salama et al. (2020)[52]	Egypt	Hospital	NR	<28 d	Not specified	Others	Yes	No		•						+			+		Fair
Ameyaw et al. (2014)[53]	Ghana	Hospital	43.3	6 m–12 y	August–October 2009	RCT	No	Yes								+			+		Low risk
Ayieko et al. (2019)[54]	Kenya[b]	Hospital	44.7	2 m–59 m	March 2016–December 2016	RCT	Yes	No			•						–		+		Low risk
Khan et al. (2020)[55]	Bangladesh[b]	Hospital	50.6	<18 y	March–September 2018	RCT	Yes	No	•				•	•			+		+		High risk
Nelson et al. (2022)[56]	Bangladesh, Mali[b]	Hospital	42.9	2 m–59 m	November 2020–March 2021	RCT	Yes	No	•					•		–			+		Low risk
Opondo et al. (2011)[57]	Kenya[b]	Hospital	38.0	2 m–59 m	2006–2009	RCT	Yes	No	•	•		•					+				Some concerns
Saini et al. (2011)[58]	India	Hospital	NR	<28 d	September 2006–November 2007	RCT	Yes	No		•					•	–			+		Some concerns
Sathyan et al. (2023)[59]	India	Hospital	37.3	<28 d	January 2019–August 2021	RCT	Yes	No							•	+			+		Fair
Rohatgi et al. (2017)[60]	India	Hospital	31.1	<28 d	November 2012–April 2014	RCT	Yes	No		•					•	+					Low risk
Unni et al. (2023)[61]	India	Hospital	54.0	<18 y	November 2021–January 2022	RCT	Yes	No				•					+		+		Some concerns
Primary care setting (N = 34)																					
Berhanu et al. (2021)[62]	Ethiopia[b]	Primary care	NR	3 m–15 m	October–December 2013, November–December 2017	BAF	Yes	No	•	•						+			+		Fair
Bernasconi et al. (2018)[63]	Afghanistan[b]	Primary care	45.7	2 m–59 m	January–February 2016, May–December 2017	BAF	Yes	No						•		+	+				Poor
Bernasconi et al. (2018)[64]	Afghanistan[b]	Primary care	46.3	2 m–59 m	January–February 2016 and July 2016, May–September 2017	BAF	Yes	Yes	•					•		+					Poor
Daka et al. (2023)[65]	Ethiopia[b]	Primary care	45.6	2 m–59 m	December 2016–February 2017, December 2018–February 2019	BAF	Yes	No	•	•	•						–				Good
Nanyonjo et al. (2015)[66]	Uganda[b]	Primary care	NR	2 m–59 m	January–December 2009, January–December 2012	BAF	Yes	No	•	•						+					Fair
Nyamu et al. (2021)[67]	Kenya[b]	Primary care	NR	<5 y	Not specified	BAF	Yes	No	•							+					Poor
Bonko et al. (2022)[68]	Burkina Faso[b]	Primary care	43.7	<5 y	April 2016–December 2016	Others	No	Yes								+					Fair
El Mahalli et al. (2011)[69]	Egypt[b]	Primary care	NR	<5 y	January 2010–June 2010	Others	Yes	No		•						+	a				Fair
Langet et al. (2025)[70]	Kenya, Senegal[b]	Primary care	47.5	<5 y	August 2021–March 2023	BAF	Yes	Yes	•					•		+					Fair

(Table 1 continues on next page)

Author	Countries[b]	Setting	F (%)	Age	Study period	Study design	ASP	POCT	ASP intervention implemented (bundled intervention in case of multiple dots)							Outcomes					Quality assessment
									EP	CG	EPa	AF	CP	CDSS	Others	AP	C	Co	Cl	R	
(Continued from previous page)																					
Mansoor et al. (2017)[71]	Afghanistan[b]	Primary care	45.0	2 m–59 m	December 2014–February 2015	Others	Yes	No	•	•							+				Fair
Msellem et al. (2009)[72]	Tanzania[b]	Primary care	NR	<15 y	February–August 2005	Others	No	Yes								+			+		Fair
Schmitz et al. (2022)[73]	Nigeria[b]	Primary care	48.7	2 m–59 m	3 March–28 March, 17 July–30 September 2020	Others	Yes	No	•					•		a			+		Fair
Shao et al. (2015)[74]	Tanzania[b]	Primary care	48.2	2 m–59 m	December 2010–June 2011	Others	Yes	Yes	•					•		+			+		Good
Tarimo et al. (2015)[75]	Tanzania[b]	Primary care	47.2	<5 y	April–May 2012	Others	No	Yes								–					Fair
Adjei et al. (2023)[76]	Ghana[b]	Primary care	46.5	6 m–18 y	September 2020–September 2021	RCT	Yes	Yes	•		•		•			+					Low risk
Beynon et al. (2025)[77]	India, Tanzania[b]	Primary care	47.0	<5 y	March 2022–April 2023	RCT	Yes	Yes	•					•		a					Low risk
Rambaud Althaus et al. (2018)[78]	Myanmar Thailand[b]	Primary care	54.1	1 y–12 y	June 2016–August 2017	RCT	No	Yes								+			+		Some concerns
Ansah et al. (2010)[79]	Ghana[b]	Primary care	59.7	<18 y	August 2007–December 2008	RCT	No	Yes								a			+		Some concerns
Ciccone et al. (2024)[80]	Uganda[b]	Primary care	52.4	2 m–59 m	November 2021–May 2022	RCT	Yes	Yes	•				•			+			+		Low risk
Do et al. (2016)[81]	Vietnam[b]	Primary care	60.1	1 y–15 y	March 2014–July 2015	RCT	No	Yes								+			+		Low risk
Do et al. (2023)[82]	Vietnam[b]	Primary care	54.1	1 y–15 y	June 2020–May 2021	RCT	Yes	Yes	•		•					+			+		Low risk
Isaeva et al. (2024)[83]	Kyrgyzstan[b]	Primary care	53.1	6 m–12 y	November–December 2021	RCT	Yes	Yes	•				•			+			+		Low risk
Isaeva et al. (2025)[84]	Kyrgyzstan[b]	Primary care	48.1	6 m–12 y	November 2022–April 2023	RCT	No	Yes								+					Low risk
Kapisi et al. (2023)[66]	Uganda[b]	Primary care	60.8	1 y–15 y	July 2020–September 2021	RCT	Yes	Yes	•				•			–			+		Some concerns
Keitel et al. (2017)[85]	Tanzania[b]	Primary care	45.8	2 m–59 m	December 2014–February 2016	RCT	Yes	Yes	•					•		+			+		Low risk
Keitel et al. (2019)[86]	Tanzania[b]	Primary care	44.9	2 m–59 m	December 2014–February 2016	RCT	Yes	Yes	•					•		+			+		Low risk
Kiemde et al. (2023)[87]	Burkina Faso[b]	Primary care	51.1	6 m–18 y	September 2020–September 2021	RCT	Yes	Yes	•		•		•			+	+		+		Some concerns
Kiemde et al. (2024)[88]	Burkina Faso[b]	Primary care	50.5	6 m–18 y	February–September 2022	RCT	Yes	Yes	•				•			+					Some concerns
Mukanga et al. (2012)[89]	Burkina Faso, Ghana, Uganda[b]	Primary care	49.3	6 m–59 m	April 2009–October 2010	RCT	Yes	Yes	•				•				+		+		Some concerns
Rambaud Althaus et al. (2017)[90]	Tanzania[b]	Primary care	48.0	2 m–59 m	April–September 2011, September–October 2011	RCT	Yes	Yes	•				•	•		+	+				Low risk
Steinhardt et al. (2019)[91]	Malawi[b]	Primary care	NR	<5 y	January–February 2015, April–September 2015, November–December 2015	RCT	Yes	No							•	–					Some concerns
Tan et al. (2023)[92]	Tanzania[b]	Primary care	51.3	<15 y	December 2021–October 2022	RCT	Yes	Yes	•					•		+			+		Low risk
Tan el al (2024)[93]	Tanzania[b]	Primary care	50.0	2 m–59 m	March–June 2022	RCT	Yes	No	•					•		+	+				Low risk
Yeboah-Antwi et al. (2010)[94]	Zambia[b]	Primary care	48.4	6 m–5 y	December 2007–November 2008	RCT	Yes	Yes	•			•	•				+		+		Some concerns
Private facilities setting (N = 5)																					
Awor et al. (2014)[95]	Uganda[b]	Private facilities	51.4	<5 y	May 2011–June 2012, September 2011–August 2012	BAF	Yes	Yes	•		•		•			+	+				Fair
Chowdhury et al. (2018)[96]	Bangladesh[b]	Private facilities	NR	<5 y	June 2012–December 2013, June 2014	BAF	Yes	No	•	•			•			+					Fair

(Table 1 continues on next page)

Author	Countries[b]	Setting	F (%)	Age	Study period	Study design	ASP	POCT	ASP intervention implemented (bundled intervention in case of multiple dots)							Outcomes					Quality assessment
									EP	CG	EPa	AF	CP	CDSS	Others	AP	C	Co	Cl	R	
(Continued from previous page)																					
El-Khoury et al. (2016)[97]	Ghana[b]	Private facilities	NR	6 m–59 m	May–June 2012, August–September 2014	BAF	Yes	No	•	•	•					+					Good
Kitutu et al. (2017)[98]	Uganda[b]	Private facilities	51.3	<5 y	June–August 2013, February 2014–September 2015, May–June 2015	BAF	Yes	Yes	•				•			+	+				Fair
Mbonye et al. (2020)[99]	Uganda[b]	Private facilities	50.4	<5 y	June 2015–July 2017	RCT	Yes	No	•		•						+				Low risk

ASP, Antimicrobial stewardship program; POCT, Point of care test. Intervention: EP, Physician education; GP, Guidelines and protocol; EPa, Parent education; AF, Audit and feedback; CP, Clinical pathways; CDSS, clinical decision support systems; Oth, Other (restriction, pre-authorisation, reminder messages ...). Result on outcomes: AP, antibiotic prescription; C, compliance; Co, cost; Cl, clinical outcome; R, resistance; +: Success, Significant improvement after the implementation of the intervention; –, Unfavourable results, opposite of what was expected. [a]Inconclusive results: results are not significant. [b]Multicentric, F, Females (%), Age: d, days; m, months; y, years; BAF, before-after study; RCT, Randomised Clinical trial.

Table 1: **Characteristics of studies included in the review (N = 78), 2009–2025.**

with POCT (17/20 studies, 85.0%) compared to ASP alone (35/48 studies, 72.9%) or POCT alone (8/10 studies, 80.0%) (Supplementary File 3). Moreover, studies with the implementation of bundled interventions showed a higher success rate (39/48 studies, 81.3%) compared to studies with single interventions. Stratifying results by outcomes, over 75% of papers showed significant improvements in antibiotic prescribing, including reduced prescriptions (77%) and better guideline compliance (80%) (Fig. 4). Instead, stratifying by disease-specific interventions, 12 out of 15 interventions were successfully implemented for the management of febrile illnesses, nine out of 11 for respiratory diseases, 4 out of 5 for diarrheal diseases, and 4 out of 7 in sepsis. Among the 78 reports, 50 reported results regarding clinical outcomes: 23 reports specifically assessed the impact on mortality and found no increase in mortality rates in the intervention groups. Other studies evaluated clinical indicators, such as length of hospital stay, time to symptom resolution (15/50), treatment failure (23/50), and adverse events (10/50), with none reporting an increase in these outcomes.

Meta-analysis

Since more than three reports with the same outcome were found for the implementation of CDSS, a meta-analysis was performed. Overall, the implementation of a CDSS in primary care for children aged 2–59 months was associated with a significant reduction in antibiotic prescribing (OR 0.17, 95% CI 0.07–0.45, I^2 99.7%) (Fig. 5). The reduction in antibiotic prescribing was most pronounced in RCTs (OR 0.14, 95% CI 0.03–0.62, I^2 99.5%), followed by observational studies (OR 0.37, 95% CI 0.16–0.85, I^2 98.9%), and non-randomised controlled trials (OR 0.03, 95% CI 0.03–0.05). Only one sensitivity analysis, restricted to studies using the ALMANACH tool, was performed and showed results consistent with the primary analysis. A post hoc analysis excluding studies of poor quality yielded similar findings (Supplementary File 4).

Risk of bias assessment

We identified 24 studies with an overall risk of bias rated as low/good, while 11 studies were considered to have a high/poor risk of bias (Table 1 and Supplementary File 5). In studies with a before-and-after design, almost all reports were judged to have a moderate risk of bias in outcome measurement, as in all these reports, the outcome assessors were aware of the intervention received by participants.

Discussion

Infections remain the leading cause of death among children under five in LLMICs, a burden compounded by overcrowding, inadequate sanitation, and limited access to clean water.[101] In these settings,

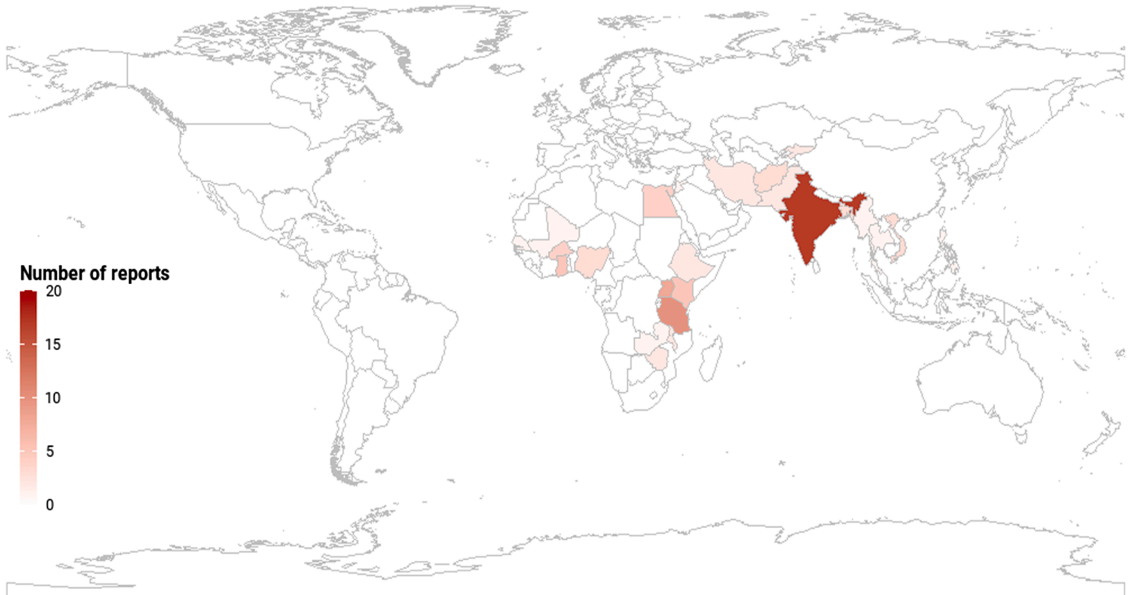

Fig. 2: Geographical distribution of the 78 reports included in this review (2007–2025).

antimicrobial therapy is often indispensable and life-saving. However, the complexity of care environments frequently undermines appropriate prescribing practices.

Although overall antibiotic consumption in LLMICs remains lower than in high-income nations, the use of WHO Watch group antibiotics has risen steadily in these settings.[15,102,103] Recognising the urgent need to shift prescribing patterns, the 79th UNGA (2024) set a global target: by 2030, 70% of human antibiotic use should belong to the Access group—a benchmark for responsible antimicrobial stewardship.[2,104] Translating policy into practice requires effective mechanisms to disseminate AWaRe-aligned guidance and ensure adherence across healthcare levels. Antimicrobial stewardship programmes, particularly when integrated with context-appropriate strategies and rapid diagnostics, represent a key tool to enhance uptake and promote rational antibiotic use.

Previous studies have identified numerous barriers to ASP implementation, including health system limitations, supply chain and regulatory challenges, restricted access to quality antimicrobials, workforce shortages, inadequate infrastructure, and weak intersectoral collaboration.[105] A more recent review highlighted further obstacles such as staffing shortages, lack of governmental support, limited laboratory capacity, inadequate training, prescriber resistance to change, funding deficiencies, absence of national guidelines or programs, and time constraints.[106]

Previous research from LMICs has demonstrated the potential of ASPs in paediatric populations. Our review strengthens and expands this evidence by focusing specifically on LLMICs and incorporating studies evaluating POCT's use, an area not previously assessed systematically.[107] Furthermore, earlier analyses included studies conducted in several upper-middle-income countries, such as China, which limits their applicability to more resource-constrained and operationally challenging settings.

Our systematic review demonstrates that several ASPs and POCTs can be successfully implemented in LLMICs, as has been previously shown in HICs.[12,108] Since January 2020, there has been growing interest in strategies to optimise antibiotic use. Several context-adapted interventions have been implemented effectively, resulting in significant reductions in antibiotic prescriptions and improved adherence to clinical guidelines, without adverse effects on child health.

Furthermore, within LLMICs, it is essential to consider the specific challenges at each level of care. In urban hospital settings, the presence of trained healthcare professionals—including physicians, pharmacists, and microbiologists—together with advanced diagnostic tools, and stronger financial infrastructure enables the implementation of more complex ASPs.[109] Hospital-based healthcare professionals typically have better training and access to up-to-date evidence, facilitating the establishment of multidisciplinary antimicrobial stewardship teams[43,47] and the development of evidence-based protocols.[24,39,43] Audit and feedback interventions are more commonly implemented in hospitals, supported by the expertise required to evaluate prescribing practices against clinical standards.[44,54]

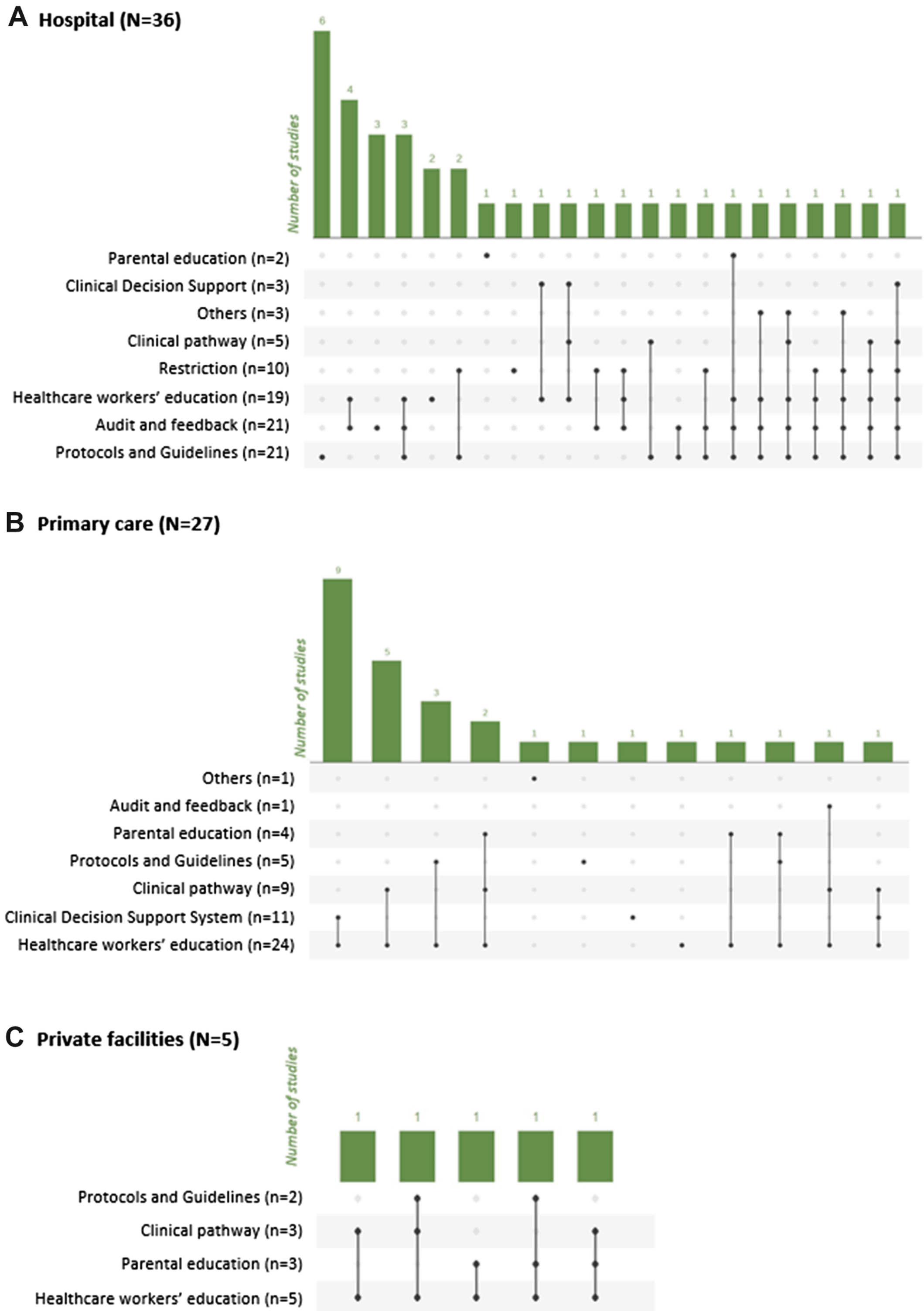

Fig. 3: Types of interventions (single or bundled) of antimicrobial stewardship programs (ASP) included in this systematic review and implemented in hospitals (A), primary care (PHC and community) (B) and private facilities (C) (N = 68 interventions presented/78 reports).

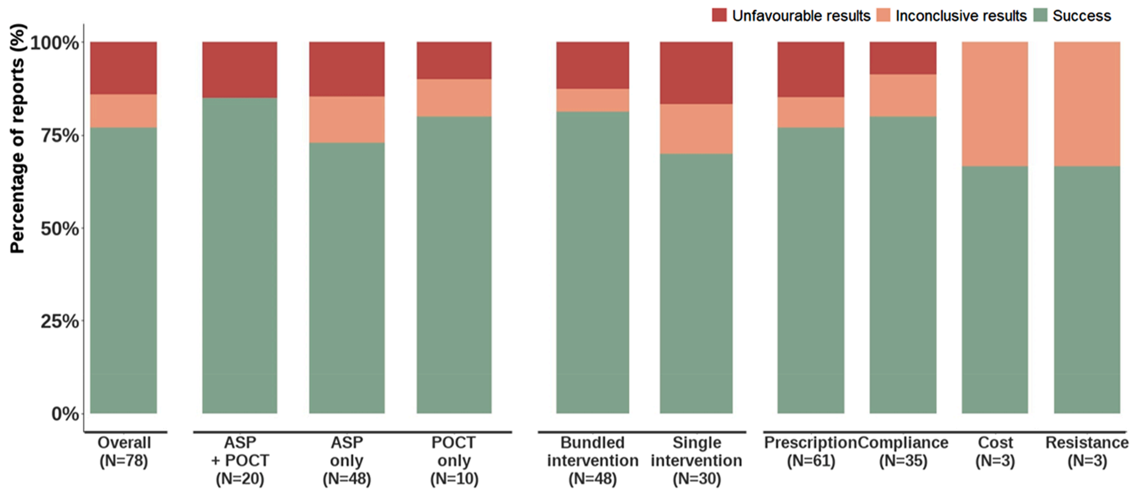

Fig. 4: Bar chart illustrating the percentage of studies reporting success, inconclusive results and unfavourable results, by type of intervention and reported outcomes (N = 78). Unfavourable results = a statistically significant effect in the opposite direction to that expected, Inconclusive results: results that were not statistically significant, Success = a statistically significant improvement following the implementation of the intervention. ASP, Antimicrobial Stewardship Program; POCT, Point of Care Test.

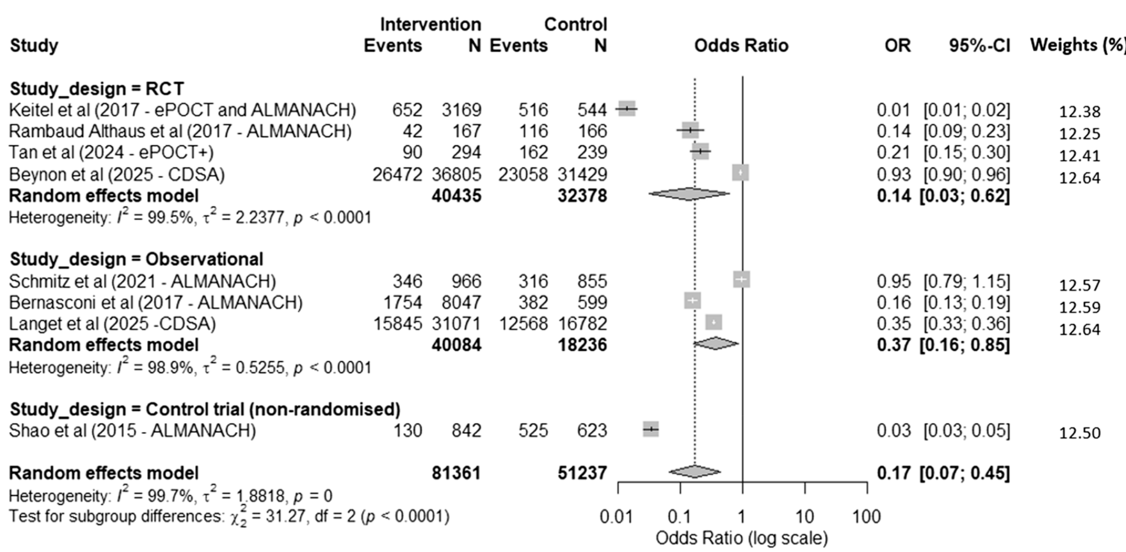

Fig. 5: Forest plot displaying the effect of introducing clinical decision support systems (CDSS) in primary care on antibiotic prescribing in children aged between 2 and 59 months across 8 reports, stratified by study design (i.e., randomized controlled trials, RCT; observational studies, OBS; and non-randomized controlled trials, CT). Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using a random-effects multivariate meta-analysis model (REML). CI, confidence interval; OR, odds ratio.

Hospitals further benefit from stronger surveillance systems compared to primary care, facilitating continuous updates of treatment guidelines aligned with local and national epidemiological trends.[79]

Rural hospitals and primary care facilities, often constrained by limited budgets, lack of POCTs, and personnel trained in microbiology, must prioritise interventions that are both cost-effective and widely applicable. Educational programmes for healthcare providers are among the most economical and impactful strategies.[67,89,100] For instance, a 2021 study in rural Kenya demonstrated that interactive training significantly improved staff awareness of AMR and reduced antibiotic prescriptions for children by 44%.[67]

Given the lower clinical specialisation among primary care staff, training initiatives should be highly practical and adapted to local realities. Integration of clinical pathways and CDSSs can further enhance these programmes by guiding prescribing decisions.[64,74,85,92] Our meta-analysis confirmed that CDSSs in primary care significantly reduce antibiotic prescriptions. ALMANACH and ePOCT are feasible and suitable for LLMICs due to their simplicity and use of affordable POCTs, unlike the more complex, costly tools typical in HICs.[110]

These tools empower non-physician prescribers to better adhere to clinical guidelines, reducing unnecessary antibiotic use. However, reduced prescribing does not automatically improve patient outcomes. In resource-limited settings with restricted follow-up, lower antibiotic use may risk patient safety if timely reassessment is unavailable. Robust safeguarding and follow-up mechanisms are therefore essential to ensure ASPs do not inadvertently compromise care. As primary care is often the first contact for families, community engagement is essential. Educational materials such as leaflets and posters raise parental awareness about proper antibiotic use and discourage self-medication.[41,111] Strengthening routine immunisation and ensuring equitable vaccine access in LLMICs can also significantly reduce antibiotic use, especially for vaccine-preventable diseases.

However, the impact of these interventions remains difficult to assess. First, routine monitoring of antibiotic prescribing is hindered by the lack of electronic data systems outside research settings, complicating the evaluation of intervention. Point prevalence surveys could streamline data collection and support assessments of sustainability and long-term effectiveness of interventions.[112] Second, metrics used to measure antibiotic consumption vary widely across studies, including days of therapy,[56,57,91] defined daily doses,[54,79] and the proportion of children receiving antibiotics.[25,43,75] This variability underscores the urgent need for harmonised metrics to ensure reproducibility and comparability of ASPs. In 2019, WHO released a practical toolkit to support ASP implementation in LMICs,[113] followed in 2020 by a consensus statement on optimal study designs for assessing ASP impact.[114] However, a paediatric-specific version of the toolkit is still lacking. Adult ASPs may not be generalisable to paediatrics due to distinct clinical and pharmacological characteristics, including immune response, diagnostic challenges, and age-specific infection patterns,[9,115] underscoring the need for tailored paediatric stewardship approaches. Third, evaluations of AMR and cost-effectiveness were often lacking, reflecting the challenges of measuring savings and drug-resistant infections in resource-limited settings.

This review has several notable strengths. First, we conducted an extensive and inclusive literature search across major bibliographic databases, including those specifically targeting LLMICs—such as African Journals Online and LILACS—ensuring broad geographic and contextual representation. No language restrictions were applied, minimising selection bias and enhancing global relevance. Second, a pre-specified, standardised protocol guided the review process, applying rigorous eligibility criteria and quality assessment tools. This approach ensured methodological consistency and helped reduce the influence of systematic biases and data heterogeneity.

Finally, sensitivity analyses focusing on studies of CDSS implementation confirmed the robustness of the observed effects of ASP, supporting the generalisability of our findings across diverse healthcare settings. Together, these methodological strengths enhance the reliability and applicability of the evidence, providing a solid foundation for policy development and program design in paediatric antibiotic stewardship across LLMICs.

Several limitations should be noted. First, estimates of ASP effects were limited by data availability, quality, and representativeness. The absence of studies from South America and the Caribbean restricts the global applicability of findings. Second, higher-level healthcare facilities were likely overrepresented due to their greater diagnostic capacity, higher likelihood of publication, and more complex patient populations with higher AMR risks. Third, most interventions were assessed only in the short term, reflecting the limited availability of tools and difficulties in sustaining long-term programs. Fourth, despite rigorous inclusion criteria, heterogeneity in study design, populations, and outcomes limited comparability and constrained broader analyses.

The meta-analysis included only eight reports with comparable interventions, settings, and outcomes, leading to unstable pooled estimates. Despite similarities in settings (primary care), age group (2–59 months), and outcomes (antibiotic prescription), substantial heterogeneity was observed across studies ($I^2 > 75\%$). Several factors likely contributed to this variability. First, effect estimates varied widely, with minimal overlap in confidence intervals and some extreme values, increasing overall variance. Second, study designs varied, and stratification by design did not reduce heterogeneity. Third, the CDSS interventions and their implementation varied, including differences in tool functionalities, integrated POCTs, and user training. Fourth, sample sizes were heterogeneous, and finally, differences in disease prevalence further contributed to variability. These findings highlight that, while the overall direction of effects is consistent, caution is warranted when interpreting pooled results and generalising across different settings. In conclusion, our findings support the use of integrated strategies that combine ASPs with diagnostic tools, demonstrating consistent reductions in inappropriate antibiotic prescribing and improved adherence to treatment guidelines across diverse healthcare settings. Despite these encouraging results, evidence on cost-effectiveness and the long-term impact on AMR remains limited. To translate this evidence into progress toward global targets, coordinated action is urgently needed to develop, adapt, and scale sustainable, context-specific strategies built on ASPs and POCT, ultimately contributing to improved child health outcomes in resource-limited settings.

Contributors

Conceptualisation: GE, BG, BA, DD. Data curation: GE, ZE. Methodology: GE, BG, BE, DD. Formal analysis: GE. Supervision: EB, DD. Writing—original draft: GE, BG. Writing—review & editing: BG, DA, DD, MMH, ZM, HR, LV, BE, DD. EG, EB, and GB accessed and verified the data. All authors had final responsibility for the decision to submit for publication.

Data sharing statement

The data included in this meta-analysis consist of previously published data from other authors and do not represent new data.

Editor note

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Declaration of interests

All authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2025.103667.

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