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REVIEW

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Barriers, facilitators, perceptions and impact of interventions in implementing antimicrobial stewardship programs in hospitals of low-middle and middle countries: a scoping review

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Abstract

Background Antimicrobial stewardship programs (ASPs) are pivotal components of the World Health Organization's Global Action Plan to combat antimicrobial resistance (AMR). ASPs advocate rational antibiotic usage to enhance patient-centered outcomes. However, existing evidence on ASPs and their determinants is largely limited to well-equipped hospitals in high-income nations.

Objective This scoping review aimed to examine the current state of hospital-based ASPs in low- and middle-income countries (LMICs), shedding light on barriers, facilitators, prescribers' perceptions and practices, and the impact of ASP interventions.

Design Scoping review on ASP.

Methods Adhering to PRISMA guidelines, we conducted electronic database searches on PubMed, Scopus, and Google Scholar, covering ASP articles published between January 2015 and October 2023. Our review focused on four key domains: barriers to ASP implementation, facilitators for establishing ASP, ASP perceptions and practices of prescribers, and the impact of ASP interventions. Three reviewers separately retrieved relevant data from the included citations using EndNote 21.0.

Results Among the 7016 articles searched, 84 met the inclusion criteria, representing 34 LMICs. Notably, 58% (49/84) of these studies were published after 2020. Barriers to ASP implementation, including human-resources shortage, lack of microbiology laboratory support, absence of leadership, and limited governmental support, were reported by 26% (22/84) of the studies. Facilitators for hospital ASP implementation identified in five publications included the availability of antibiotic guidelines, ASP protocol, dedicated multidisciplinary ASP committee, and prompt laboratory support. The majority of the research (63%, 53/84) explored the impacts of ASP intervention on clinical, microbiological,

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and economic aspects. Key outcomes included increased antibiotic prescription appropriateness, reduced antimicrobial consumption, shorter hospital stays, decreased mortality rate, and reduced antibiotic therapy cost.

Conclusions The published data underscores the imperative need for widespread antimicrobial stewardship in LMIC hospital settings. Substantial ASP success can be achieved through increasing human resources, context-specific interventions, the development of accessible antibiotic usage guidelines, and heightened awareness via training and education.

Keywords Antimicrobial stewardship program (ASP), Scoping review, Low- and middle-income countries (LMIC)

Background

Antimicrobial resistance (AMR) has emerged as one of the top ten global public health threats of the twenty-first century according to the World Health Organization (WHO) [1, 2]. In 2019, approximately 1.3 million deaths were directly attributable to AMR [3, 4]. If no measures are taken, it is projected that by 2050 AMR could lead to the deaths of 10 million people annually, with up to 90% of these fatalities occurring in low- and middle-income countries (LMICs) [4]. In addition to the health consequences, AMR also carries significant financial implications at both patient and societal levels. According to a World Bank projection, AMR could reduce gross domestic product (GDP) by 1.1–3.8% by 2050, necessitating an annual investment of US$9 billion to counteract AMR effectively [5, 6].

The primary drivers of AMR in LMICs include the absence of antibiotic guidelines to regulate prescribing practices [7], irrational use of antibiotics [8], the financial incentive of prescribers, easy accessibility and 'over the counter access' of antibiotics, self-medication, patient pressure, lack of sanitation, poor infection prevention and control (IPC) practices, and the lack of an antimicrobial stewardship program (ASP) [9]. To address AMR, WHO formulated a global action plan (GAP) in 2015 [10] which identified ASP as a cornerstone to curtail the inappropriate use of antibiotics for therapeutic use [11, 12]. Antibiotic stewardship involves a set of coordinated actions that promote the appropriate use of antimicrobials through evidence-based, multidisciplinary interventions against AMR [12, 13]. In hospital settings, along with infection control measures, ASPs are considered a fundamental strategy to limit the emergence and escalation of AMR [14], improve clinical outcomes, and reduce healthcare costs by promoting the rational use of antibiotics [15, 16].

ASP features may vary [17] but typically include a range of interventions tailored to fit the hospital's infrastructure [18]. Stewardship interventions can be categorized as persuasive (education and feedback), structural (introduction of new diagnostic tests to guide antibiotic treatment), enabling (guidelines on antibiotic use), or restrictive (expert approval for the use of certain antibiotics) [2, 16, 19]. The key components identified in successful ASPs include leadership commitment, drug expertise, prescribers' accountability, and orientation training for prescribers [13]. Most of the recent evidence on ASP comes from resource-intensive hospitals in high-income countries [20, 21], making it uncertain whether these findings apply to resource-constrained hospitals [22, 23].

This scoping review aimed to map and summarize published data on ASPs deployed in hospital settings in LMICs. It focuses on sequentially integrating four key domains: barriers to implementing ASP, facilitators to establishing ASP, ASP perceptions and practices of prescribers, and the impact of ASP interventions in LMICs. Prior reviews on LMICs mostly focused on the impact of ASP interventions or the ASP methods most widely employed in hospital settings [10, 15, 24]. The findings from this review would be valuable for key stakeholders and policymakers to get an insight into the common obstacles encountered in hospital settings across LMICs, and the key areas on which they need to focus prior to ASP implementation. The review will also help the stakeholders get an idea of where we stand in terms of prescribers' knowledge and perception of ASP across LMIC.

Methods

Search strategy

This scoping review adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for scoping reviews (PRISMA-ScR) guidelines [25]. We developed a systematic search strategy using keywords and medical subject headings (MeSH) terms to identify relevant articles published between January 2015 and December 2023 in MEDLINE, Scopus, and Google Scholar databases. Our search focused on articles related to ASP published after the WHO GAP Plan on AMR in 2015 [13], as this led to increased hospital-based ASP publications in LMICs [10, 24]. We only included articles published in the English language. The review encompassed countries classified as low, and lower-middle income, according to the World Bank classification system [26].

Study inclusion criteria

Based on our research questions, we established the following inclusion and exclusion criteria to select relevant articles.

Inclusion criteria

- ASP interventions for adult patients conducted in hospital settings in LMICs
- Articles, abstracts, poster presentations, preprints, and grey literature
- Antimicrobial or antibiotic stewardship in the human population
- Published articles limited to the English language

Exclusion criteria

- Case studies, narrative reviews, editorials, discussion articles, conference papers, invited articles, special reports on ASP
- Reviews, commentaries, or expert opinions on ASP
- ASP in animal, agriculture, or community settings
- Articles focusing solely on the use of antifungal or antiviral stewardships

Our search strategy employed a combination of first, second, and third-string terms. The first string included keywords such as 'antimicrobial' 'antibiotic' 'antimicrobial resistance' and 'antibiotic resistance.' The second string is composed of keywords related to antimicrobial stewardship, such as 'stewardship' 'formulary restriction' and 'prospective audit.' The third string included the terms 'low-middle income countries' 'less developed countries' 'underdeveloped' and 'developing nation.' These search terms were combined using Boolean operators "OR" or "AND" to refine search results. Detailed search strategies can be found in the supplementary file (Additional file 1: Appendix 1. Search strategy).

Study selection

Three reviewers (MGDH, SAS, IH) conducted a systematic title screening of the databases using the specified keywords. Duplicate records were removed and then imported into a citation management program (EndNote 21.0). IH and SAS independently assessed titles and abstracts, while MGDH reviewed the final list. Subsequently, full texts of potentially relevant articles were obtained and evaluated for eligibility.

Data extraction

We extracted and organized data into four domains listed below:

- Domain 1: Barriers to ASP implementation
- Domain 2: Facilitators for establishing ASP
- Domain 3: ASP perceptions and practices of prescribers (physicians or pharmacists)
- Domain 4: Impact of ASP interventions

The retrieved data included the name of the first author, year of publication, place of study, study design, setting, type of hospital (public, private, or university), study population, and measured outcomes (Table 1). Barriers to ASP implementation (Domain 1, Table 2) and facilitators for establishing ASP (Domain 2, Table 3) were categorized based on constraints and contributing factors described in the articles. The identified impediments or lack of facilities or resources for ASP implementation from the mentioned studies were assembled in Domain 1 as barriers, whereas the availability of facilities or resources to execute ASP was considered in Domain 2 as facilitators. Physicians' perception and practices related to ASP were categorized into knowledge, attitude, and practices (KAP) (Domain 3, Table 4). The impact of ASP interventions was described into five subcategories (Domain 4, Table 5): (1) antibiotic prescription by prescribers (physicians or pharmacists), (2) antibiotic consumption (defined daily doses or days on therapy), (3) clinical outcomes (e.g., length of hospital stay, in-hospital mortality), (4) microbiological outcomes (multi-drug resistance, bacterial resistance patterns), and (5) economic outcomes (hospital antibiotic procurement cost, cost of antibiotic therapy). Antibiotic prescription refers to the quality of antibiotic use (proportion of prescriptions with inappropriate antibiotic use, inappropriate use without clinical indications, unnecessary double coverage, incorrect frequency, dosage, timing, broad-spectrum and expensive antibiotics when inexpensive and narrow-spectrum alternatives were available), which was prescribed by hospital physicians or pharmacists.

Results

Characteristics of included studies

We initially retrieved 7016 relevant articles through comprehensive and systematic database searches in Pubmed, Google Scholar, and Scopus. After removing duplicates, 6497 records remained for screening. Title and abstract screening resulted in the identification of 182 relevant articles, of which 84 met the inclusion criteria (References 27–110). Ninety-eight articles were excluded based on the exclusion criteria (Fig. 1). The majority of studies (63%, 53/84) reported the impact of ASP interventions, followed by barriers to ASP implementation (26%, 22/84), ASP perceptions and practices of prescribers (25%, 21/84), and facilitators for ASP establishment (6%,

Table 1 Summary of characteristics of included studies in the scoping review of antimicrobial stewardship programs in low and middle-income countries, 2015–2023

Sl	Year	Country	Author	Ref	Design	Setting, Population	Measured metrics	Barrier	Facilitator	KAP	Intervention
1	2023	China	Yuan et al.	103	Randomized controlled trial	Tertiary Public hospital, Hospital inpatients	Antibiotic consumption, clinical, economic outcomes				■
2	2023	China	Zheng et al.	110	Intervention	Tertiary hospital, Physicians, Nurses	Antibiotic use, microbiological and economic outcome				■
3	2023	Egypt	Salem et al.	48	Cross-sectional	University hospitals, Physicians, and Clinical Pharmacists	Barriers to ASP	■			
4	2023	Ghana	Sefah et al.	52	Cross-sectional	Public hospitals, Physicians, Nurses	Perception and practice toward ASP			■	
5	2023	India	Zacchaeus et al.	101	Intervention	Secondary-care hospitals, Hospital inpatients	Antibiotic consumption, clinical and microbiological outcome				■
6	2023	India	Zirpe et al.	102	Quasi-experimental	Tertiary Private hospital, Hospital inpatients	Antibiotic consumption, clinical outcomes				■
7	2023	Jordan	Hassan et al.	57	Cross-sectional	Public hospitals, Physicians, Nurses	Practice towards ASP			■	
8	2023	Palestine	Aiesh et al.	100	Quasi-experimental	University Hospital, Hospital inpatients	Antibiotic consumption, clinical, microbiological economic outcomes.				■
9	2023	Panama	Fabre et al.	36	Mixed-method	Public and Private hospitals, Physicians, pharmacists, microbiologists	Barriers and facilitators to ASP implementation	■	■		
10	2023	South Africa	Scheepers et al.	35	Qualitative	Public hospitals, Physicians, pharmacists, nurses	Barriers and facilitators to ASP implementation	■			
11	2022	Banglade sh	Sumon et al.	45	Mixed-method	Tertiary care public hospital; Physicians	Perceptions about ASP, antibiotic prescribing patterns	■		■	
12	2022	China	Chang et al et al.	37	Cross-sectional	Secondary and tertiary acute-care hospitals	The barrier to ASP implementation, practice levels of ASP	■			
13	2022	Columbia	Pallares et al.	82	Retrospective observational	Public and private tertiary hospitals; Hospital inpatients	Antibiotic consumption				■
14	2022	India	Borde et al.	80	Quasi-experimental	Private hospitals; Hospital inpatients	Antibiotic consumption, antibiotic prescription				■
15	2022	India	Kaur et al.	50	Cross-sectional	Tertiary care referral hospital; Physicians	Perception and practice of ASP			■	
16	2022	Indonesia	Limato et al.	49	Cross-sectional	Public and private hospitals; Physicians	Perception and practice toward ASP			■	

Table 1 (continued)

17	2022	Indonesia	Limito et al.	40	Qualitative	Public and Private hospitals; Physicians, Microbiologists, Pharmacists	Barriers to ASP implementation				
18	2022	Indonesia	Setiawan et al.	47	Cross-sectional	Tertiary teaching hospital; Physicians, Pharmacists	Perceptions and barriers to ASP				
19	2022	Jordan	Darwish et al.	79	Retrospective observational	Private hospitals; Hospital inpatients	Antibiotic consumption, microbiological outcomes				
20	2022	Jordan	Nassar et al.	32	Cross-sectional	Public and private hospitals; Physicians, Pharmacists, Nurses	Barriers to ASP implementation, practice levels of ASP				
21	2022	Pakistan	Ashraf et al.	59	Cross-sectional	Public hospital; Physicians	Perception and practice of ASP				
22	2022	Uganda	Kimbowa et al.	41	Cross-sectional	Public and private hospitals; Physicians, Pharmacists	The barrier to ASP implementation, practice levels of ASP				
23	2022	Uganda	Kimbowa et al.	60	Cross-sectional	Public hospitals; Physicians, Pharmacists, Technicians	Perception and practice of ASP				
24	2021	India	Garg et al.	87	Cross-sectional	Public and private hospitals; Hospital inpatients	Antibiotic use, microbiological outcomes				
25	2021	India	Nampoot hiri et al.	34	Pre-post intervention*	Private hospital; Physician, Microbiologist, Pharmacist	Barriers to ASP, antibiotic consumption				
26	2021	India	Panditrao et al.	64	Cross-sectional	Public hospital; Hospital inpatients	Antimicrobial usage				
27	2021	India	Thakkar et al.	105	Prospective observation	Private hospital; Hospital inpatients	The practice of ASP, antibiotic use				
28	2021	Jordan	Yusef et al.	83	Retrospective	Public hospital; Hospital inpatients	Antibiotic usage				
29	2021	Lagos	Oshun et al.	33	Cross-sectional	University teaching hospital; Hospital inpatients	Barriers to ASP, antimicrobial prescription pattern				
30	2021	Lebanon	Sayegh et al.	27	Cross-sectional	Public hospital; Physicians	Antimicrobial prescription pattern				
31	2021	Nigeria	Chukwu et al.	56	Cross-sectional	Public and private hospitals; Physicians	Practice of ASP				
32	2021	Pakistan	Atif et al.	44	Qualitative	Public hospital; Physicians	Knowledge, perception, and practices of ASP				
33	2021	Pakistan	Mubarak et al.	53	Cross-sectional	Public and private hospitals; Physicians, Pharmacists, Nurses	ASP Practice				
34	2021	SouthAfri ca	Bashar et al.	84	Cross-sectional	Public hospital; Hospital inpatients	Antibiotic consumption, economic outcomes				
35	2021	SriLanka	Rolfe Jr et al.	38	Qualitative	Public hospital; Physicians	Barriers to ASPs				

Table 1 (continued)

36	2020	China	Du et al.	73	Quasi-experimental	Public hospital; Hospital inpatients	Antibiotic use				
37	2020	China	Xiao et al.	89	Observational	Public hospitals; Hospital outpatients	Antibiotic consumption, economic outcomes				
38	2020	CostaRica	Madriz et al.	85	Retrospective observational	Private hospital; Hospital inpatients	Antibiotic consumption				
39	2020	Egypt	Sokkary et al.	65	Cross-sectional	University Hospital; Hospital inpatients	Antibiotics use, microbiological, economic outcome				
40	2020	India	Banerjee et al.	66	Pre-post intervention*	Public hospital; Hospital inpatients	Clinical, microbiological outcomes				
41	2020	India	Mathew et al.	28	Qualitative	Public hospitals; Physicians, Pharmacologist, pharmacists	Barriers to implementing ASP				
42	2020	India	Patel et al.	74	Observational	Tertiary teaching hospital; Hospital inpatients	Antibiotic prescribing pattern, clinical outcomes				
43	2020	Iran	Mahmoud i et al.	88	Cross-sectional	University hospital; Hospital inpatients	Antibiotic consumption, economic outcome				
44	2020	Iran	Mardani et al.	75	Quasi-experimental	University hospital; Hospital inpatients	Antibiotic prescription, clinical, microbiological outcomes				
45	2020	Lebanon	Moghnieh et al.	81	Retrospective	Public hospital; Hospital inpatients	Antibiotic consumption, clinical, economic outcomes				
46	2020	Malawi	Lester et al.	39	Cross-sectional	Public hospital; Hospital inpatients	Barriers and facilitators of ASP				
47	2020	Nepal	Nauriyal et al.	62	Pre-post intervention*	Community referral hospital: Hospital inpatients	Antibiotic usage				
48	2020	Pakistan	Hussain et al.	86	Quasi-experimental	University hospital; Hospital inpatients from SICU	Clinical and economic outcomes				
49	2020	Pakistan	Raheem et al.	55	Cross-sectional	Public and private hospitals; Physicians, pharmacists	ASP practice				
50	2020	SouthAfrica	Bergh et al.	108	Prospective cohort	Public and private hospitals; Hospital inpatients	Clinical outcomes				
51	2019	Brazil	Dos Santos et al.	71	Quasi-experimental	Tertiary care public hospital; Physicians	Antibiotic prescription, clinical, economic outcome				
52	2019	China	Wang et al.	76	Retrospective observational	Tertiary care public hospital; Hospital inpatients and outpatients	Antibiotic prescription, microbiological outcome				

Table 1 (continued)

53	2019	China	Zhang et al.	99	Retrospective	Public hospital; Hospital inpatients	Antimicrobial use				
54	2019	India	Baubie et al.	30	Qualitative	Private hospital; Physicians, Pharmacists, Microbiologists.	Barriers and facilitators to ASP implementation				
55	2019	India	Charani et al.	43	Qualitative	University Hospital; Healthcare worker	Barriers and facilitators to ASP implementation				
56	2019	India	Joshi et al.	68	Quasi-experimental	Community referral hospital; Hospital inpatients	Antibiotic prescription pattern, antibiotic consumption				
57	2019	India	Sarang et al.	107	Prospective observation	Public and private hospitals; Hospital inpatients	Clinical and economic outcomes				
58	2019	India	Singh et al.	42	Mixed-method	Public and private hospitals; Physicians, Microbiologists	Barriers				
59	2019	India	Swamy et al.	63	Quasi-experimental	Public hospital; Hospital inpatients	Antibiotic prescription, consumption, clinical outcome				
60	2019	India	Verma et al.	46	Pre-Post intervention	Public hospital; Hospital inpatients	Antibiotic prescription, barriers to ASP				
61	2019	Nigeria	Abubakar et al.	67	Pre-post intervention	Public hospitals; Hospital inpatients	Antibiotic usage, economic outcomes				
62	2019	Pakistan	Hayat et al.	31	Qualitative	Tertiary care public hospitals; Physicians	Barriers and perception towards ASP				
63	2019	Pakistan	Hayat et al.	61	Cross-sectional	Tertiary care public hospitals; Physicians	Perception towards ASP				
64	2019	Pakistan	Saleem et al.	54	Cross-sectional	Public hospitals; Physicians	Knowledge and perception towards ASP				
65	2019	Turkey	Karaali et al.	70	Intervention	Tertiary training and research hospital; Hospital inpatients	Antibiotic prescription pattern				
66	2019	Turkey	Şengel et al.	96	Quasi-experimental	University hospital; Hospital inpatient	Antibiotic consumption, clinical outcomes				
67	2019	Zambia	Kalungia et al.	58	Cross-sectional	Public hospitals; Physicians, Pharmacists	Knowledge and perceptions of ASP				
68	2018	Chile	Fica et al.	90	Observational	Tertiary care public hospital; Hospital inpatients	Antimicrobial consumption, economic outcomes				
69	2018	Ethiopia	Gebretekle et al.	29	Mixed-method	Tertiary care public hospital; Physicians	Barriers, facilitators, perception and practice to ASP				

Table 1 (continued)

70	2018	India	Rupali et al.	77	Prospective cohort	Tertiary care public hospital; Hospital inpatients	Antibiotic prescription pattern, consumption, clinical outcome				
71	2018	Malaysia	Sze et al.	69	Cross-sectional	Tertiary care public hospital; Hospital inpatients	Antibiotic prescription pattern, clinical, economic outcome				
72	2017	Bangladesh	Sultana et al.	91	Pre-Post intervention	Tertiary care public hospital; Hospital inpatients	Antibiotic prescribing, consumption				
73	2017	China	Li et al.	109	Prospective Cohort	University hospitals; Hospital inpatients	Antibiotic consumption, clinical, microbiological outcome				
74	2017	Ethiopia	Tegagn et al.	51	Cross-sectional	Public Hospital; Physicians, Nurses	Knowledge, perception and practice toward ASP				
75	2017	India	Shah et al.	78	Cross-sectional	Tertiary care public hospital; Hospital inpatients	Antimicrobial use				
76	2017	India	Wattal et al.	98	Qualitative	Public hospital; Physicians	Antibiotic prescribing, antibiotic consumption				
77	2017	SouthAfrica	Boyles et al.	104	Observational	Tertiary care public hospital; Hospital inpatients	Antibiotic consumption, clinical and economic outcome				
78	2016	China	Ma et al.	97	Pre-post intervention	Tertiary care public hospital; Hospital inpatients	Antibiotic consumption, clinical, microbiological outcomes				
79	2016	India	Shafiq et al.	95	Pre-post intervention	Tertiary care public hospital; Hospital inpatients	Antibiotic consumption				
80	2016	Jordan	Bhalla et al.	93	Pre-Post intervention*	Public hospital; Hospital inpatients	Antibiotic consumption, economic outcomes				
81	2016	SouthAfrica	Brink et al.	92	Pre-Post intervention	Private hospitals; Hospital inpatients	Antibiotic consumption				
82	2015	China	Zhou et al.	94	Pre-Post intervention*	Public hospital; Hospital inpatients	Antibiotic consumption, economic outcomes				
83	2015	Egypt	Saied et al.	72	Pre-post intervention	Public hospital; Hospital inpatients	Prescription pattern, antibiotic use				
84	2015	SouthAfrica	Messina et al.	106	Pre-Post intervention*	Private hospital; Hospital inpatients	Clinical outcome				

*Assessment by the authors as the study design was not specified in the reference

5/84). The studies included in the review were conducted in 34 countries, with India (26%, 22/84), China (12%, 10/84), and Pakistan (10%, 8/84) being the most represented. South Asia had the highest number of articles (40%, 34/84) followed by the Middle East (15%, 13/84) and East Asia (12%, 10/84). The Caribbean region has no representation in our review. In terms of study design, most of the studies were cross-sectional (33%, 28/84),

Table 2 Barriers to implementing ASP of included studies in the scoping review of antimicrobial stewardship programs in low and middle-income countries, 2015–2023

Barriers	Atif et al.	Baubie et al.	Chang et al.	Charani et al.	Fabre et al.	Gebretekle et al.	Hayat et al.	Kimbowa et al.	Lester et al.	Limato et al.	Mathew et al.	Nampoothiri et al.	Nassar et al.	Oshun et al.	Rolfe Jr et al.	Salem et al.	Sayegh et al.	Scheepers et al.	Setiawan et al.	Singh et al.	Sumon et al.	Verma et al.
Lack of human resource		■	■		■	■	■				■	■	■	■			■	■				
Lack of laboratory support, uncertainty	■			■	■	■	■			■	■				■			■		■	■	
Lack of leadership, Interdepartmental coordination			■		■			■	■	■	■				■		■	■				
Inadequate orientation training on rational antibiotic use	■	■			■			■									■			■		■
Physician negative attitude to ASP		■	■	■										■			■	■	■			
Lack of fund			■		■			■			■		■	■						■		
Lack of guidelines/ educational program				■	■											■	■				■	
Time-constraint		■			■			■			■					■						
Conflict between prescribers						■					■								■			
Physician lack of knowledge			■												■						■	
Unrestricted access to antimicrobial		■													■							
Physician workload/ patient load		■					■															
Aggressive Pharmaceutical Marketing Campaign				■							■											
Rigid Hierarchy					■	■			■													
Other (Lengthy test, overcrowding, incomplete record, high staff turnover, shortage of antimicrobials)		■			■								■					■				■

followed by pre-post (14%, 12/84) and quasi-experimental (12%, 10/84). More than half of the studies were single-centered (52%, 44/84) and, 58% (49/84) of the studies were conducted between 2020 and 2023 (Table 1).

Barriers to implementing ASP

Table 2 summarizes the reported barriers to ASP implementation. Of the 22 studies that documented barriers to ASP adoption, 50% (11/22) reported a

Table 3 Facilitators for implementing ASP of included studies in the scoping review of antimicrobial stewardship programs in low and middle-income countries, 2015–2023

Facilitators	Authors				
	Baubie et al.	Charani et al.	Fabre et al.	Gebretekle et al.	Lester et al.
Availability of antibiotics guidelines, ASP implementation protocol	■	■		■	■
Dedicated multidisciplinary ASP committee/ organizational leadership	■	■	■		
Prompt Microbiology laboratory	■		■		
Presence of electronic health record		■	■		
Reserved Antimicrobial List		■			
Easily accessible Antibiogram	■				
High level of ASP understanding among staff	■				
Prescribing Hierarchy (interns-residents-senior consultants)				■	
Others (IPC guidelines/External audits/Empowering pharmacists)		■	■		■

Table 4 Physicians' perception and practices on ASP of included studies in the scoping review of antimicrobial stewardship programs in low and middle-income countries, 2015–2023

Variables	Ashraf et al.	Atif et al.	Chukwu et al.	Gebretekle et al.	Hassan et al.	Hayat et al.	Hayat et al.	Kalungia et al.	Kaur et al.	Kimbowa et al.	Limato et al.	Mubarak et al.	Nassar et al.	Raheem et al.	Saleem et al.	Sayegh et al.	Sefah et al.	Setiawan et al.	Sumon et al.	Tegagn et al.
Knowledge																				
Familiarity with ASP		■				■		■								■	■		■	■
Knowledge about the Indication of antibiotics (antibiotic spectrum, indication, dosage, route)	■								■								■			■
Know about the AMR mechanism									■											■
Familiarity with ASP intervention types									■		■						■			
Attitude																				
Positive attitude toward ASP		■		■		■	■	■	■	■	■					■	■	■		■
Prefer feedback						■										■	■		■	
Fear of loss of physician autonomy									■								■	■		
Implementation of ASP									■											
Practice																				
Involvement with ASP			■		■					■		■	■	■	■	■	■	■	■	
Prescribing pattern				■					■							■	■			■
Tracking and reporting antibiotic use		■	■		■							■		■						
Providing education and expertise					■							■	■	■						

Table 5 Impact of ASP intervention of included studies in the scoping review of antimicrobial stewardship programs in low and middle-income countries, 2015–2023

Year	Author, Country	Antibiotic Prescription Pattern	Antibiotic Consumption	Clinical Outcomes	Microbiological Outcomes	Economic Outcomes
2023	Aiesh et al. Palestine		■			
2023	Yuan et al. China		■	■		■
2023	Zacchaeus et al. India		■	■	■	
2023	Zheng et al. China				■	■
2023	Zirpe et al. India		■	■		
2022	Borde et al. India	■	■	■		
2022	Darwish et al. Jordan	■	■	■	■	
2022	Pallares et al. Columbia		■		■	
2021	Bashar et al. South Africa		■		■	
2021	Garg et al. India		■	■	■	
2021	Nampoothiri et al. India	■				
2021	Oshun et al. Lagos	■				
2021	Panditrao et al. India	■	■			
2021	Thakkar et al. India		■			
2021	Yusef et al. Jordan		■		■	
2020	Banerjee et al. India	■	■	■		
2020	Bergh et al. South Africa			■		
2020	Du et al. China		■	■		
2020	Hussain et al. Pakistan		■	■		■
2020	Lester et al. Malawi	■				■
2020	Madriz et al. Costa Rica		■		■	
2020	Mahmoudi et al. Iran		■	■	■	■
2020	Mardani et al. Iran	■		■	■	
2020	Moghnieh et al. Lebanon		■	■	■	■
2020	Nauriyal et al. Nepal	■	■	■		
2020	Patel et al. India	■	■			
2020	Sokkary et al. Egypt	■			■	■
2020	Xiao et al. China		■		■	■
2019	Abubakar et al. Nigeria	■	■	■	■	■
2019	Dos Santos et al. Brazil	■	■		■	
2019	Joshi et al. India	■	■			
2019	Karaali et al. Turkey	■				
2019	Sarang et al. India			■		■
2019	Şengel et al. Turkey		■			
2019	Swamy et al. India	■	■	■	■	
2019	Verma et al. India	■	■			
2019	Wang et al. China	■	■		■	
2019	Zhang et al. China		■		■	
2018	Fica et al. Chile		■			■
2018	Rupali et al. India	■	■	■		
2018	Sze et al. Malaysia	■	■	■		■
2017	Boyles et al. South Africa		■	■		■
2017	Li et al. China		■	■	■	
2017	Shah et al. India	■				
2017	Sultana et al. Bangladesh	■	■			
2017	Wattal et al. India		■			
2016	Bhalla et al. Jordan		■			■
2016	Brink et al. South Africa		■			
2016	Ma et al. China		■	■	■	
2016	Shafiq et al. India		■			
2015	Messina et al. South Africa			■		
2015	Saied et al. Egypt	■	■			
2015	Zhou et al. China		■			■

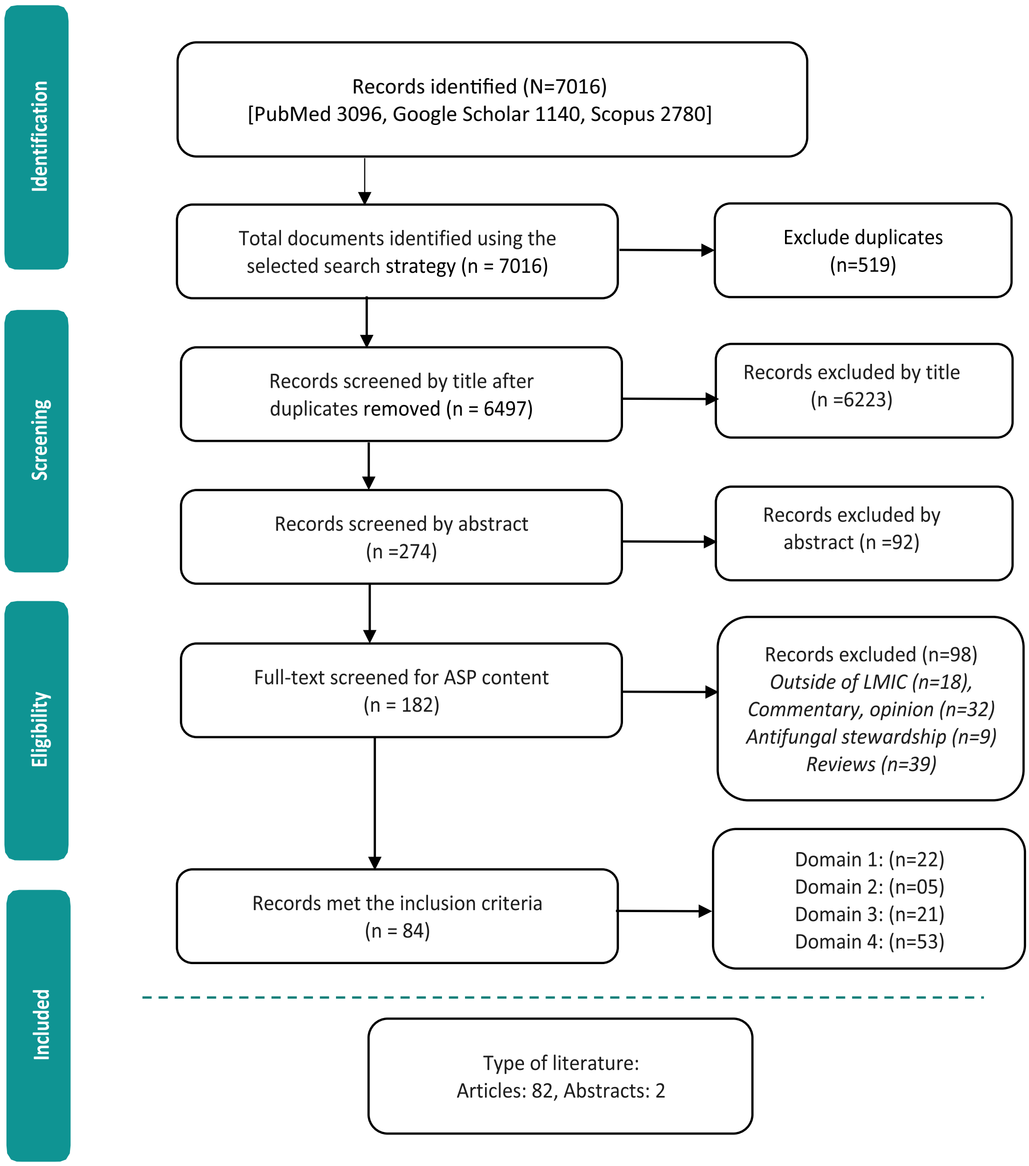

Fig. 1 PRISMA flowchart of the selection of studies in the scoping review of antimicrobial stewardship programs in low and middle-income countries, 2015–2023

shortage of human resources [27–37]. Eleven studies each identified the absence of leadership and minimal governmental support [27, 28, 35–42], and a lack of reliable laboratory infrastructure and microbiology laboratory support as challenges to effective ASP implementation [28, 29, 31, 35, 36, 38, 40, 42–45]. Other identified barriers included inadequate orientation and training on ASP including rational antimicrobial use [27, 30, 36, 41, 44, 46], prescribers' negative attitudes to changes in antibiotic practices [27, 30, 33, 35, 37, 43, 47], and a lack of dedicated ASP funds [28, 32, 33, 36, 37, 41]. Five studies each cited the absence of approved national guidelines or educational programs [27, 36, 43, 45, 48], and time constraints for prescribers [28, 30, 36, 41, 48] as barriers. The 'Others' category included challenges like incomplete electronic medical records (EMR), long waiting times for tests, overcrowding in wards [30, 46], the perception of AMR as an 'external problem' [49], frequent staff turnover, lack of specific ASP goals [36], stock shortage of antimicrobials [35], and suboptimal salary [36].

Facilitators to establishing ASP

The facilitators of hospital ASP implementation are shown in Table 3. Of the five studies documenting ASP enablers, the availability of antibiotic guidelines based on WHO AWaRe classification and ASP protocols was cited as a facilitator for the hospital's ASP implementation in four studies [29, 30, 39, 43]. The establishment of a dedicated multidisciplinary ASP committee [30, 36, 43] was mentioned as an enabling factor for ASP implementation in three studies. Prompt access to microbiology laboratory facilities with institutional antibiograms [30, 36], the presence of electronic health records [36, 43], and a restricted antimicrobial list in hospitals [43] were also noted as enablers for stewardship implementation. The hospital antibiogram is a periodic summary of antimicrobial susceptibilities of local bacterial isolates which are used by prescribers to determine local susceptibility rates, monitor antibiotic resistance trends over time within the institution, and compare antibiotic resistance trends between hospitals [36]. 'Others' facilitating factors included the presence of a guideline for infection prevention and control [39, 43], external audits with feedback, and empowerment of pharmacists [36].

ASP perception and practices of physicians

Table 4 presents the 21 publications related to physicians' perceptions and practices (i.e. KAP) regarding ASP. Six of these studies (29%, 6/21) reported on all three elements: knowledge, attitude, and practice [27, 45, 47, 50–52], and six others exclusively assessed ASP practice compliance [32, 53–57]. The majority of the studies revealed that prescribers (physicians or pharmacists) had a sub-optimal knowledge of ASP and its basic principles [31, 45, 47, 51, 52, 58]. However, four studies stated that prescribers had sufficient knowledge of the correct antibiotic indication (i.e. correct dose, diagnosis, and duration of antibiotic) [50–52, 59]. In terms of attitude towards ASP implementation, the majority of prescribers showed positive attitudes, as they felt ASP is beneficial for both prescribers and patients [27, 29, 31, 45, 49, 51, 52, 60, 61], and were interested receive feedback on their antibiotic prescriptions [27, 31, 45, 52]. However, some studies also revealed the physicians' concern that implementation of ASP would limit their prescribing autonomy [47, 50, 52]. Regarding ASP practice, studies reported that prescribers mostly had a substandard level of involvement in ASP activities or previously worked in ASP facilities [44, 45, 51, 52, 56]. Prescribers also had a low level of compliancein sending specimens for culture and susceptibility tests [44, 45, 52, 60]. However, tracking, reporting, and documenting antibacterial use in patient care had a better level of implementation among prescribers [29, 32, 52, 53, 60].

Impact of ASP intervention

The majority of studies (63%, 53/84) measured the impact of ASP interventions, which is displayed in five categories in Table 5. The impact of ASP interventions on the appropriateness of antibiotic prescriptions administered was reported in (43%, 23/53) of studies [33, 34, 39, 46, 62–80]. Metrics used to measure appropriate prescriptions included dose adjustment or dose optimization [46, 63, 64], antibiotic de-escalation [62, 63, 68, 74, 80, 81], and timing and duration of antibiotic prophylaxis [67, 70, 76]. Most studies (79%, 42/53) primarily documented a decrease in antibiotic consumption and an improvement in rational antibiotic use after ASP implementation in hospitals [39, 46, 62, 64, 66–69, 71, 73, 76–104]. Metrics for evaluating antibiotic consumption included defined daily doses (DDDs) or days of therapy (DOT) per 1,000 patient-days [62–64, 68, 72, 77, 79–81, 84–86, 88, 100, 104, 105] while some studies used defined daily doses (DDDs) per 100 patient-days or Days of therapy/DOT per 100 patient-days [66, 67, 76, 90, 97, 102].

To assess the impact of ASP interventions, 24 studies (45%, 24/53) assessed clinical or patient-centered outcomes [62–64, 66, 67, 69, 73–75, 77, 79–81, 86–88, 97, 100–104, 106–108]. Metrics used to evaluate the intervention included length of stay in hospital (LOS) in specific units (e.g., ICU) [46, 62, 68, 69, 73, 74, 76, 77, 81, 86, 88, 96, 101–103], hospital mortality [62, 76, 77, 80, 86, 100–102, 106], rehospitalization [77, 81, 83, 86, 104], hospital-acquired infections [63, 64, 67, 81, 97, 107, 109], and device-associated infections [64]. ASPs brought about positive clinical outcomes in hospital inpatients in most cases. Microbiological outcomes to assess the impact of ASP were reported in 42% (22/53) of studies [63, 65, 66, 71, 76, 79, 81–85, 87–89, 100, 101, 109, 110], including a decrease in the prevalence of multi-drug resistance bacterial strains like *Acinetobacter spp*, *Methicillin-Resistant Staphylococcus aureus* (MRSA), *Vancomycin-Resistant Enterococcus* [VRE], increase in the antibiotic susceptibility of bacterial strains such as *Pseudomonas aeruginosa, E. coli* [71, 81, 82, 85]. Studies also documented a reduction in the incidence of bacterial infections such as Clostridioides difficile infections and Candidemia [75, 77], and a decrease in pan-drug resistant isolates [65, 71, 77, 85]. Economic outcomes were assessed in 17 studies [39, 65, 69, 71, 81, 86, 88–90, 93, 94, 96, 100, 103, 104, 107, 110], and reported a decrease in hospital antibiotic procurement cost [65, 71, 81, 90, 93, 94], savings in antibiotic costs [39, 69, 86, 88, 104, 110], decrease in antibiotic therapy and antibiotic prophylaxis cost [67, 107], and hospitalization costs [110].

Discussion

The purpose of this scoping review was to look into the present state of hospital-based ASPs in low-and middle-income countries (LMICs), providing insight into four major domains in a stepwise manner: the obstacles, enablers, attitudes, and behaviors of prescribers, and the outcomes of ASP interventions. Our review identified a shortage of human resources, and a lack of diagnostic facilities as the most commonly encountered barriers to ASP implementation, while the availability of hospital ASP guidelines and dedicated multidisciplinary teams were found to be facilitators. Additionally, the review revealed a substandard baseline about ASP perception among physicians and found that ASP interventions were successful in improving the rational use of antibiotics, reducing antibiotic consumption, and decreasing hospital antibiotic procurement costs.

Our review identified several challenges to implementing ASP in resource-compromised settings, including inadequate human resources, a lack of laboratory infrastructure, unreliable institutional antibiogram, the absence of national guidelines, minimal funding, and a lack of ASP orientation and training [27–30, 35–37, 43, 44]. These findings are in line with a previous review, which documented the presence of substandard microbiology laboratory facilities and unreliable antibiograms [1]. Physicians' lack of trust in microbiology findings poses a serious threat, as prescribers may lean toward broad-spectrum empiric therapy based on anecdotal evidence. Regarding the absence of context-based antibiotic guidelines and lack of ASP training, our findings are reinforced by prior reviews which also documented these factors as impediments [1, 12, 23, 111]. The absence of guidelines implies that prescribers would be unaware of local AMR patterns, leading to the prescription of broad-spectrum antibiotics and the promotion of AMR. Physicians who lack ASP training may administer antibiotics empirically out of habit, and this insufficient training may result in suboptimal ASP understanding among prescribers.

In terms of facilitators toward ASP implementation, existing hospital ASP protocols or guidelines, including their easy access were cited as facilitating factors [29, 30, 39, 43]. The presence of guidelines implies that prescribers have a tool that directs them toward prescribing narrow-spectrum antibiotics. Readily available antibiograms suggest that physicians have a trustworthy source of local, relevant antibiotic patterns, which helps them prescribe antibiotics rationally, instead of resorting to a range of resources.

Studies in our review documented a substandard level of knowledge and familiarity among prescribers with the basic principles of ASP. An inadequate fundamental understanding of ASP and AMR would lead to irrational and improper antimicrobial prescriptions [44]. Regarding perceptions toward ASP, studies reported positive perceptions toward ASP, as physicians felt that ASP made them think more carefully about their antibiotic choices, beneficial in terms of reducing AMR, decreasing patient length of stay, and reducing healthcare costs [27, 31, 49–52, 58]. Our review revealed that prescribers were on board to receive regular monitoring and feedback on rational antibiotic use and recommended tailored ASP training [27, 45, 52, 61]. However, a few studies also revealed that physicians were concerned that ASP implementation might lead to a loss in their prescribing autonomy [27, 47, 52]. Despite the overall favorable perceptions, most countries have yet to align with global efforts to combat increasing AMR through stewardship activities. Studies in this review documented that hospitals either did not have any ASP initiatives in place [24, 45, 50] or had few ASP activities with low compliance levels [44, 53–55]. This low level of ASP compliance might stem from perceiving AMR as an 'external problem', with some prescribers having a notion that AMR is developed by inappropriate antibiotic use elsewhere instead of on their premises.

Our review found that ASP interventions achieved improvement in rational antibiotic prescription through dose optimization, antibiotic de-escalation, and a reduction in antibiotic prescriptions. ASP implementation documented a reduction in the consumption of WATCH category antibiotics such as vancomycin, meropenem, aztreonam, ceftriaxone, and RESERVE category antimicrobials like colistin, carbapenems, teicoplanin, in hospital wards and ICUs [46, 63, 71, 77, 82, 83, 100–102]. Prior systematic reviews demonstrated a decrease in antibiotic consumption after ASP implementation in the ICUs of hospitals [2, 24]. This decline in consumption might have been achieved by a combination of factors like revising existing hospital antibiotic policies, compliance with antimicrobial policies, stopping orders at 48 h, de-escalation of empirical antimicrobial therapy, and a curb-on combination therapy [46, 63]. As observed in the review, there was substantial heterogeneity between studies concerning metrics to quantify antibiotic use and consumption. The consumption metrics used were DDD with different denominators (100 or 1000 patient-days) or Days of therapy/DOT per 100 patient-days or 1000 patient-days. This lack of uniformity makes it difficult to compare, aggregate, and interpret data. While the use of different metrics makes it difficult for an accurate and meaningful comparison, an International multidisciplinary panel recommended the simultaneous use of at least two metrics to quantify antibiotic use in hospital settings. DDDs per 100(0) patient-days and days of therapy per patient-days were identified as the most common metric used in the hospital setting [112]. Clinical outcomes such as a decrease in the length of hospital stay (LOS), in-hospital mortality, and a reduction in Clostridioides difficile infections were observed after ASP implementation [46, 62, 63, 69, 81, 86, 102]. Prior systematic reviews also confirmed that stewardship activities resulted in positive clinical outcomes [19, 113]. These findings imply that ASPs curb needless antibiotic consumption among hospital inpatients, and show a positive impact on microbiological outcomes, such as a reduction in the prevalence of multi-drug resistance [82, 83, 88] and bacterial resistance [82, 83]. Though fewer studies reported ASPs' impact on economic outcomes, the studies in this review showed a positive effect on ASP implementation which was reiterated by prior reviews that revealed the beneficial effects of ASPs in terms of cost reduction in clinical settings [15, 114]. ASPs were able to reduce the needless use of expensive parenteral antibiotics and demonstrated a decrease in the use of high-cost broad-spectrum antibiotics [69, 88]. These pieces of evidence show that ASPs were successful in accomplishing the core objective of reducing inappropriate antibiotic use and antibiotic costs without compromising clinical outcomes.

Clinical outcomes are essential objectives of ASPs that justify the long-term sustainability of any ASP program. Most of the studies included in our review were unable to meet this expectation. Future ASP initiatives should attempt to include and report microbiological, clinical, and cost-effectiveness outcomes. In this review, barring only four studies [77, 103, 108, 109], none of the other citations had a control group. Owing to the lack of a control group and the non-randomized design of most of the studies, confounding effects would be difficult to control. Since hospital settings can also differ across LMICs, this might also result in confounders affecting the prescribing pattern and patient-centered outcomes. If randomization is difficult to conduct, future ASP attempts should at least try to include a control group to minimize confounding and make the results more definitive. The majority of the studies in this scoping review were single-centered, with almost all of them being conducted in tertiary care centers of urban settings. This limits the generalizability of the review since our findings are in line with a recent review that also found that the majority of ASP studies were conducted in urban areas. [24]. Implementation of hospital ASP in rural settings of LMICs might also be more challenging owing to financial and resource constraints. Future efforts should emphasize conducting multi-center trials and if possible in rural settings. Studies in this review had a short follow-up period ranging from 2 to 6 months [46, 65, 67, 69, 72, 77, 86, 102], with some studies having no defined follow-up period [64, 91]. Shortage of the follow-up period would make it difficult to accurately assess microbiological outcomes such as changes in AMR pattern, hospital re-admission, mortality, and determination of the long-term impact of ASP on antimicrobial cost reductions. Long-term evidence of positive economic outcomes would also help to convince stakeholders and policymakers to invest in the ASP program. Furthermore, the implementation of infection prevention and control (IPC) programs to prevent bacterial infections and infections will be necessary to improve patient safety and healthcare quality [14]. This approach is strongly linked to ASP, as co-implemented with IPC measures were successful in curbing AMR [115], and future ASP interventions can integrate basic IPC measures into ASP programs. To implement ASP in a resource-compromised hospital setting, WHO recommends the establishment of a multidisciplinary ASP team, comprising infectious diseases specialists, microbiologists, nurses with IPC expertise, and clinical pharmacists as core members [116]. Of the 53 studies reporting stewardship interventions, only five studies documented the involvement of multidisciplinary teams with such composition [39, 82, 86, 92, 105]. Future ASP efforts should concentrate on forming a more inclusive multidisciplinary team to ensure the long-term sustainability of stewardship activities.

Our scoping review sequentially integrates the four ASP domains of barriers, facilitators, prescriber perceptions and practices, and intervention impact to provide a comprehensive overview of the current state of ASP in LMICs, representing cumulative evidence from almost all LMIC regions except the Caribbean. However, this review has a few limitations. We only included articles published in English due to linguistic constraints, which may have resulted in the exclusion of relevant studies in other languages. Albeit the aforementioned limitation, Indian and Pakistani citations are mostly published in English. In addition, our review included global representation except the Carribean. Additionally, the scope of our review was limited to studies published between 2015 and 2023 and there may be earlier studies that could have provided significant insights. However, since hospital-based ASP articles in LMICs increased following the WHO GAP Plan on AMR in 2015, and we included publication from 2015 onwards, along with the most recent citations, this drawback is negated to a substantial extent. Finally, we did not analyze the possibility of bias for the selected research. We excluded documents such as case studies, commentaries, and expert opinions which have a high potential for bias with weak evidence.

Conclusions

Antimicrobial stewardship programs in LMICs face a range of challenges, including a shortage of human resources, inadequate laboratory infrastructure, limited governmental support, and a lack of national guidelines. However, the availability of hospital ASP guidelines and protocols is a significant facilitator for ASP implementation. Physicians in LMICs generally have a suboptimal level of knowledge and familiarity with antimicrobial stewardship programs, but they hold positive attitudes toward ASP and are willing to receive training and educational sessions. ASP interventions in LMICs have been effective in improving the rational use of antibiotics, leading to reduced antibiotic consumption, improved clinical outcomes, positive microbiological outcomes, and economic benefits. Future efforts should focus on addressing the identified barriers to ASP implementation, involving multidisciplinary teams in stewardship initiatives, and integrating infection prevention and control measures into ASP programs to combat antimicrobial resistance effectively in LMICs.

Abbreviations

ASP	Antimicrobial stewardship program
AMR	Antimicrobial resistance
GAP	Global Action Plan
DOT	Days of therapy
DDDs	Defined daily doses
GDP	Gross Domestic Product
IPC	Infection prevention and control
ICU	Intensive Care Unit
KAP	Knowledge, attitude, and practices
LOS	Length of stay in hospital
LMICs	Low-and-middle-income countries
MeSH	Medical subject headings
PRISMA-ScR	Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for scoping reviews
WHO	World Health Organization

Supplementary Information

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Additional file 1: Appendix 1. Search strategy.

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Author contributions

The initial research questions were developed by MGDH with SAS and IH. SAS and IH conducted the literature search for the inclusion and exclusion of identified articles, and MGDH reviewed the final list. Analysis and overall synthesis of findings for the review, and the initial drafting of the manuscript were conducted by MGDH, SAS, MSI, FMA, MMUA. All authors contributed to revisions of the manuscript and have approved the final version before submission and take responsibility for its content.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare no competing interests.

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