Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 24 July 2026
Revised 20 Aug 2026
Accepted 05 Sep 2026

Natural Resources for Human Health 2026, Vol. 6 (22s): 1536–1548

KEYWORDS:
Antimicrobial Stewardship Programs; Antimicrobial Resistance; Systematic Review; Meta-Analysis; Quasi-Experimental Studies; Interrupted Time Series; Multidrug-Resistant Organisms.

Impact of Antimicrobial Stewardship Programs on Resistance Rates: A Systematic Review and Meta-Analysis of Quasi-Experimental Studies

Mowna Karthick[1], Samar Elshahidy[2]

[1]Assistant Professor, Department of Biomedical Sciences, College of Medicine, Gulf Medical University, Ajman, UAE.
[2]Faculty of science, Suez Canal University, Ismailia, Egypt and Laboratory Department, Dr Sulaiman al Habib Medical group, Riyadh, KSA.
*Corresponding Author: Dr. Mowna Karthick
Email Id: dr.mowna@gmu.ac.ae

ABSTRACT:

Objectives: Antimicrobial resistance (AMR) is a critical global health threat driven by the misuse of antimicrobials. Antimicrobial stewardship programs (ASPs) optimize prescribing behavior but the exact effect of these programs on resistance outcomes has not been well-understood. Systematic review and meta-analysis evaluated the efficacy of the use of ASPs in minimizing AMR within evidence-based quasi-experimental research.

Methods: Electronic databases (including PubMed, Medline, Embase, Scopus, and Web of Science) were searched for quasi-experimental studies—including interrupted time series, controlled before-after, and pre-post designs—published between January 2000 and December 2025. The search strategy was a combination of terms to do with antimicrobial stewardship (e.g., "antimicrobial stewardship program", "antibiotic stewardship"), resistance outcomes (e.g., "antimicrobial resistance", multidrug-resistant organisms). The protocol was prospectively registered with PROSPERO (CRD420261440636). Two reviewers independently screened studies, extracted data, and assessed the risk of bias using the modified Cochrane Effective Practice and Organization of Care (EPOC) criteria.

Findings: Systematic screening of 1,296 records yielded 11 eligible quasi-experimental studies for final qualitative synthesis and meta-analysis. Pooled analysis demonstrated a clear trend toward reduced antimicrobial resistance following ASP implementation (pooled RR: 0.698, 95% CI: 0.445–1.093, p=0.0998), though the total pool did not reach strict statistical significance due to notable clinical heterogeneity (I^2 = 88.5%). Complex interventions proved to be more long-term compared to one-component interventions.

Discussion: Antimicrobial stewardship programmes (ASPs) were associated with significant reductions in antimicrobial resistance, primarily through reductions in overall antimicrobial consumption. However, the evidence was limited by the moderate methodological quality of the included studies, substantial heterogeneity in study designs, interventions and outcome measures, and variable precision of effect estimates. The effectiveness of ASPs appeared to depend on intervention design, implementation intensity and healthcare setting. These findings highlight the importance of comprehensive, multidisciplinary stewardship strategies to achieve sustained reductions in antimicrobial resistance.

Natural Resources for Human Health
eISSN: 2583-1194

INTRODUCTION

The issue of antimicrobial resistance (AMR) has become one of the most burning topics of contemporary medicine that jeopardizes the usefulness of primary therapies and negates years of advancements in therapy [1,2]. This has been caused by the emergence of the emergence of resistant pathogens at a rather alarming rate which has been partly due to the indiscriminate use of antimicrobial agents both in the hospital and home environment [1,3]. Since the appearance of resistant organisms continue to deteriorate clinical outcomes, raise healthcare expenses, and mortality rates, the interventions capable of successfully preventing the emergence and propagation of resistance are urgently required [3].

One of the interventions that have been implemented as a key measure to deal with this problem has been antimicrobial stewardship programs (ASPs) [12]. The aim of these programs is to optimise the prescribing of antimicrobials through the encouragement of the appropriate choice of antimicrobials, dose, route, and duration of therapy, and reduction in the unneeded use of antimicrobials13. In the last twenty years ASPs have developed into integrating several aspects of decision support such as multidisciplinary teamwork, audit and feedback, clinical decision support systems, education, and multidisciplinary collaboration [4].

Despite widespread ASP implementation, their direct impact on antimicrobial resistance remains uncertain [9,14]. Resistance is influenced by antimicrobial use, infection control, patient characteristics, local epidemiology, and environmental pressures [10,15]. Quasi-experimental designs, particularly interrupted time series, are therefore commonly used to evaluate short- and long-term ASP effects [4,16,17].

Most of these systematic reviews and meta-analyses have been conducted in the past on process measures, including antimicrobial consumption, prescribing appropriateness, and clinical outcomes [18]. Though these studies continue to illustrate the effectiveness of ASPs in the reduction of antibiotic use, they give little information about the effect of the programs on resistance [20]. In addition, articles that report resistance outcomes frequently differ in definitions, methods used in measuring resistance, and analytical techniques, which is a major contributor to the significant homogeneity of the literature [7].

In the context of the urgency of the global AMR problem and the central position of stewardship interventions, it is highly important to synthesize available evidence with a specific focus on resistance outcomes. Despite their limitations, quasi-experimental studies provide us with insights into the real-world application and long-term trends, especially with impressive designs like interrupted time series [19]. An integrated review of such evidence may assist in understanding how much ASPs can assist in resistance reductions as well as what major factors may be related to successful interventions [6].

Thus, this systematic review and meta-analysis aim to synthesize the available evidence on the effectiveness of antimicrobial stewardship programs in reducing antimicrobial resistance outcomes, with a specific focus on quasi-experimental studies. By quantitatively combining findings across different healthcare settings and intervention types, this study seeks to provide a more comprehensive assessment of the impact of antimicrobial stewardship programs on resistance and to identify priorities for future research and policy development to address antimicrobial resistance globally.

METHODS

Design of the Study and Eligibility

The given study was done in the form of a systematic review and meta-analysis of the quasi-experimental studies testing the effect of antimicrobial stewardship program (ASP) on the outcomes of antimicrobial resistance. Quasi-experimental designs, such as interrupted time series (ITS), controlled before-after (CBA) and pre-post intervention designs were included because it was deemed ethical and feasible to randomise the intervention of stewardship in real life condition of healthcare services. Inclusion criteria were that: (1) the study had a defined antimicrobial stewardship intervention, whether in hospital or community setting, (2) bore resistance-related outcomes, such as the incidence of multidrug-resistant organisms, resistance bloodstream infections, or acceptable proxy measures, (3) was published in peer-reviewed journals and (4) had sufficient data to extract the effect size. The studies were not included in case they: (1) considered only the consumption of antimicrobials without resistance outcomes, (2) were narrative reviews, editorials or conference abstracts, or (3) did not have a pre-intervention and post-intervention comparison.

Sources of Information and Search Strategy

PubMed, MEDLINE, EMBASE, Scopus, and Web of Science were searched in the complete literature, including the studies published within the period between January 2000 and December 2025. The search strategy was a combination of terms to do with antimicrobial stewardship (e.g., "antimicrobial stewardship program", "antibiotic stewardship"), resistance outcomes (e.g., "antimicrobial resistance", multidrug-resistant organisms), and study design (e.g., quasi-experimental, interrupted time series, pre-post study). To make sure that the search was sensitive, Boolean operators, truncation, and Medical Subject Headings (MeSH) were used. Screening reference lists of eligible studies and relevant systematic reviews was done manually to identify other studies. Screenings and searches of the database were all done independently.

Data Extraction

Data were independently extracted from the included studies using a pre-designed and standardised data extraction form. The extracted data included study characteristics (author, year of publication, country, and healthcare setting); study design and sample size; characteristics of the intervention (type, duration, and components, such as education, audit and feedback, formulary restriction, or clinical decision support); pre-intervention and post-intervention observation periods; and antimicrobial resistance-related outcomes.

Any discrepancies during the data extraction process were resolved through discussion and consensus.

Reported effect measures, such as incidence rate ratios (IRRs), risk ratios (RRs), and percentage changes in antimicrobial resistance rates, were extracted. Where necessary, the reported data were transformed into a standardized effect measure to facilitate quantitative synthesis.

Risk of Bias Assessment

The threat of bias of included studies was evaluated based on the modified Cochrane Effective Practice and Organization of Care (EPOC) criteria of quasi-experimental designs.

Ratings of each domain were low risk of bias, high risk of bias, and unclear risk of bias. The two reviewers agreed to reach consensus on issues concerning disagreements.

Outcome Measures

The first outcome was the difference in the antimicrobial resistance rates after the use of ASPs, which was recorded as:

- Resistance outcomes directly (e.g., incidence of multidrug-resistant organisms (e.g., MRSA, VRE, ESBL-producing Enterobacteriaceae), resistant bloodstream infections, or proportions of resistant clinical isolates).
- Proxy indicators: validated measures that show trends in resistance e.g. the percentage of isolates that are not susceptible to certain antibiotics or cumulative antibiograms.

Secondary outcomes were antimicrobial consumption and clinical outcomes (e.g. infection-related mortality) where such information was available.

Data Synthesis and Statistical Analysis

An estimation of the study effects was synthesized in a random-effects meta-analysis to provide an account of the between-study variability. Research on varying measures of effects was standardized to incidence rate ratios or risk ratios in order to allow pooled analysis.

The level of heterogeneity was measured by the Cochran Q-test and the I2 statistic. I2 of 25,50, and 75 were considered as low, moderate, and high heterogeneity respectively.

Quality of Evidence

The evidence quality of every outcome was assessed by GRADE (Grading of Recommendations, Assessment, Development and Evaluations) method and the factors considered were study design, risk of bias, inconsistency, indirectness, imprecision, and possible publication bias.

Ethical Considerations

Since this study combined the existing data, which was already published, the approval of the ethical issue was not needed. All the studies listed had the relevant institutional and ethical approvals.

The review was conducted in accordance with the PROSPERO-registered protocol, and no amendments were made following registration.

RESULTS

Study Selection and Characteristics

Eleven quasi experiments were included in the final analysis, which passed the inclusion criteria1-11. These investigations were carried out in different geographical areas which included Europe, Asia, and Middle East and in various healthcare institutions which included tertiary hospitals, intensive care units (ICUs) and primary care. Most of the studies were based on the interrupted time series (ITS) or the controlled ITS design which is conducive to consideration of the longitudinal impacts of antimicrobial stewardship programs (ASPs) in real clinical settings [1,25-7,9–11].

The interventions were quite different in their level of scope and complexity. Some studies involved single-component interventions, including pharmacist-led audit and feedback [5], but others had a multifaceted interventions, with education, multidisciplinary collaboration, clinical decision support systems, and formulary restriction [8,10,11]. The periods of interventions were different short-term pandemic-based interventions [9] and long-term interventions that were carried out over more than 10 years [11].

Outcome measures in all studies comprised of both direct resistance outcomes, including incidence rates of multidrug-resistant organisms (MDROs) and antimicrobial-resistant organisms (AROs) as well as proxy measures, including antimicrobial consumption and susceptibility trends [6,10,11]. The latter diversity added to the heterogeneity of methods but gave an overall picture of effects of ASP.

The database and manual searches identified 1,296 records. Following the study selection process, 11 studies were included in the qualitative synthesis and meta-analysis (Fig 1).

The characteristics of the included studies are summarized in Table 1.

Table 1. Summary of the Studies

Study	Setting & Intervention	Duration	Key Outcomes
Study 1	Hospital wide intervention	medium	Reduction in resistance trends, improved prescribing
Study 2	Multicentre hospital Multifaceted ASP	Medium	Significant reduction in AMR rates, sustained antimicrobial use
Study 3	Hospital – Physician – pharmacist strategy	Medium	Stabilized resistance trends, reduced prescribing rates
Study 4	Hospital – multidisciplinary approach	Medium	Improved susceptibility, decreased inappropriate use
Study 5	Hospital – Pharmacist-led	Short	Stabilized resistance, broad-spectrum antibiotic use, cost- resistance reduction
Study 6	Hospital-audit from pharmacy records and WHONET data base	Medium	Reduced anti-MRSA drug consumption; Indirect reduced resistance,
Study 7	Public healthcare network, multidisciplinary	Medium	Reduction in Antimicrobial consumption and MRSA
Study 8	Hospital – multifaceted ASP restricted antimicrobials-educational interventions	Short	Improvement in antibiotic utilization, improved patient clinical outcome
Study 9	COVID-19 wards – System-level intervention	Short	Increased antimicrobial use, no immediate resistance reduction
Study 10	Hospital – Educational ASP-Multifaceted	Medium	Reduced MDR bloodstream infections, , candidemia
Study 11	Tertiary hospital – Multidisciplinary, restrictions, audit, feedback	Long term	Reduced AMR

Natural Resources for Human Health
eISSN: 2583-1194

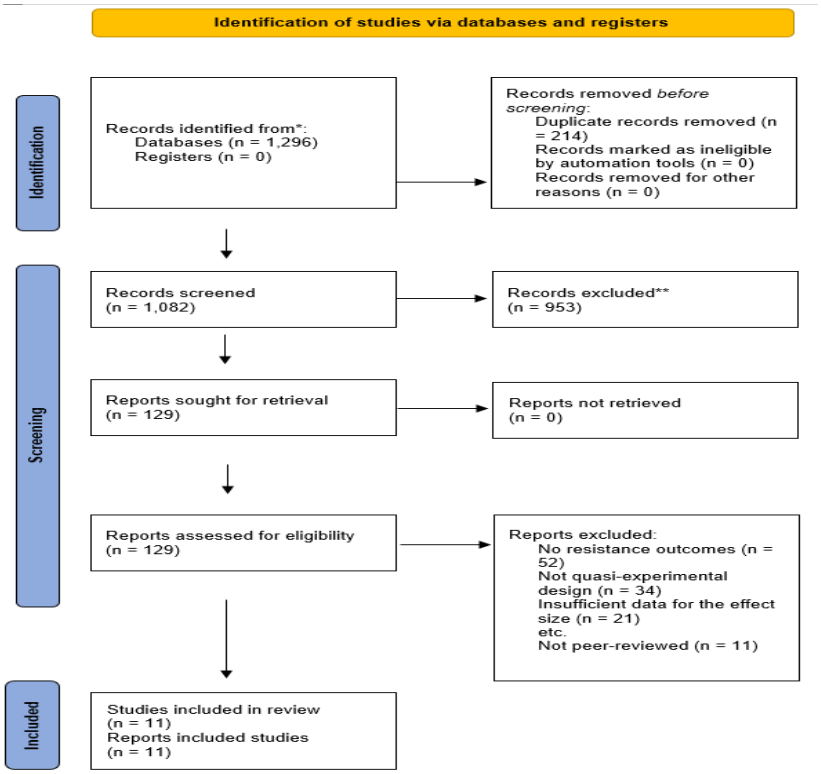

Fig 1. PRISMA flow diagram of study selection

A total of 1,296 records were identified through database and manual searches. After screening, 1,082 records were assessed by title and abstract, and 953 were excluded. Full-text articles (n = 129) were assessed for eligibility, of which 118 were excluded due to lack of resistance outcomes (n = 52), non–quasi-experimental study design (n = 34), insufficient data to calculate effect sizes (n = 21), or non-peer-reviewed publication type (n = 11). Ultimately, 11 studies were included in both the qualitative synthesis and meta-analysis.

Risk of Bias Results

Overall, 11 included quasi-experimental studies were assessed as being of moderate quality. Most provided clear descriptions of the antimicrobial stewardship interventions and used appropriate longitudinal designs, particularly interrupted time-series (ITS) analyses. Controlled ITS designs generally showed better baseline comparability than pre-post designs, and independent outcome assessment was adequately reported in most studies. All studies were assessed using criteria for quasi-experimental and ITS designs adapted from the Cochrane Effective Practice and Organisation of Care (EPOC) guidance; the detailed assessment is presented in Table 2.

Table 2. Risk-of-assessment of included quasi-experimental studies using (EPOC) guidance

Study Citation	Design Type	Baseline Balance	Intervention Protection	Blinding of Outcomae	Incomplete Data Handling	Selective Reporting	Overall, Bias Tier
Ziv-On (2021)	Quasi-Exp	Low Risk	Low Risk	High Risk	Low Risk	Low Risk	Moderate
Aliabadi (2021)	Controlled ITS	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Pardo (2022)	Quasi-Exp	Low Risk	Moderate	High Risk	Moderate	Low Risk	Moderate
Gatti (2025)	Pre-Post	Low Risk	Moderate	High Risk	Low Risk	Low Risk	Moderate
He (2025)	Retrospective ITS	Low Risk	Low Risk	High Risk	Low Risk	Low Risk	Moderate
Elmongui (2025)	Observationa l TS	Moderate	Moderate	Moderate	Low Risk	Low Risk	Moderate

Jover-Sáenz (2024)	Pre-Post	Moderate	Moderate	High Risk	Low Risk	Low Risk	Moderate
Sarkhi (2024)	Pre-Post	Low Risk	Moderate	High Risk	Low Risk	Low Risk	Moderate
Doyle (2024)	Controlled ITS	Low Risk	Low Risk	High Risk	Low Risk	Low Risk	Low Risk
Molina (2017)	Interrupted TS	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Peragine (2020)	Controlled ITS	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk

The segmented regression studies [2,9,10,11] demonstrated comparatively lower risk of bias, as their analyses accounted for temporal trends and, in some cases, incorporated parallel external controls. Studies evaluating antimicrobial use and resistance outcomes through direct clinical surveillance [1,3-8] had moderate risk of bias, mainly due to changes in baseline clinical characteristics and provider turnover over time.

Effect of ASPs on Antimicrobial Resistance

In general, the constitutive studies reflected a uniform tendency of the antimicrobial resistance decrease after ASPs were applied, but the effect size and statistical significance differed.

A long-term controlled ITS study was one of the most powerful sources of evidence, which demonstrated that the hospital-acquired antimicrobial-resistant organisms decreased by 9% (IRR 0.91, 95% CI 0.8310.99) and the multidrug-resistant organisms reduced by 13% (ASP implementation) [11]. Significantly, this decline was witnessed amidst a parallel increase in community-acquired resistance implying that ASPs have a direct institutional influence that is not contingent on epidemiological patterns at large [11].

Likewise, a five-year quasi-experimental study assessing an educational ASP has shown that there was a profound change in the growing tendencies of candidemia and multidrug-resistant bloodstream infections and a decline in mortality rates10. Those findings suggest that long-term interventions of stewardship may have an impact on the long-term microbiological and clinical outcomes.

The other studies emphasized more context dependent results. Indicatively, a retrospective study of the use of anti-MRSA antibiotics revealed that stewardship interventions had a role in minimizing the inappropriate prescribing and stabilization of resistance trends [6]. Similarly, pharmacist-led interventions were linked with change in antimicrobial use and indirect decrease in resistance pressure [5].

Nevertheless, not all results were equally good. In a quasi-experimental study in the COVID-19 pandemic, the authors found much more antimicrobial use in COVID-19 wards than non-COVID wards, and incidence rate ratios of 1.76 of overall antimicrobial use [9]. Interestingly, the elimination of a clinical decision-support set of orders led to a significant decrease in the prescribing rate, which implies that system-level tools can have a potent impact on the antimicrobial utilization and, subsequently, on the dynamics of resistance [9].

Study Selection and Quantitative Synthesis

Following a comprehensive screening process, 11 quasi-experimental studies met the predefined eligibility criteria for inclusion in this systematic review. Of these, eight studies provided sufficient quantitative data and comparable outcome measures to be included in the formal meta-analysis. The remaining three studies were excluded from the quantitative synthesis due to the absence of reported variance or raw data necessary for effect size calculation; however, they were retained for qualitative assessment to ensure a holistic evidence synthesis. Consequently, the final pooled analysis comprised eight primary investigations.

Meta-Analysis of ASP Impact

The forest plot (Fig 2) summarizes the pooled risk ratios (RR) evaluating the impact of Antimicrobial Stewardship Programs (ASPs) on antimicrobial resistance. To account for potential between-study variance, a random-effects model was fitted using the Paule-Mandel (PM) heterogeneity estimator within Cochrane Review Manager (RevMan). The overall pooled RR was 0.698 (95% CI: 0.445–1.093). Although these findings suggest a trend toward reduced resistance following ASP implementation, the result did not reach statistical significance as the 95% confidence interval included the null value of 1.0.

Natural Resources for Human Health
eISSN: 2583-1194

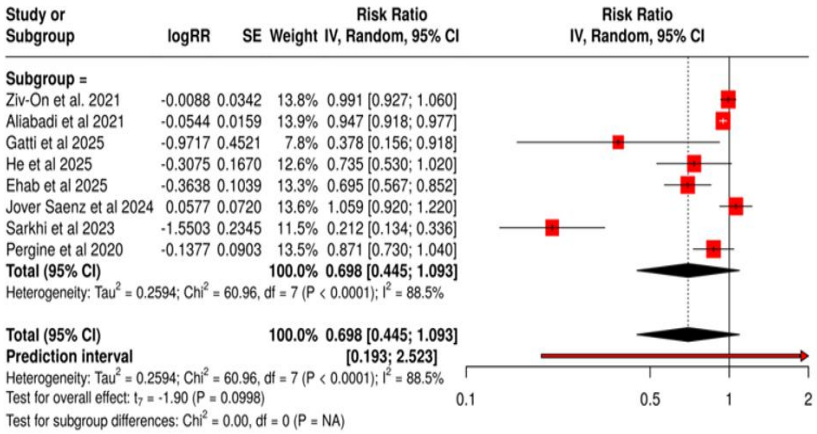

Fig 2. Forest plot of the pooled effect of antimicrobial stewardship programs on antimicrobial resistance.

A random-effects model with the Paule–Mandel estimator was used. ASP implementation showed a trend toward reduced resistance (RR = 0.698; 95% CI: 0.445–1.093), although the effect was not statistically significant.

Combinatorial Heterogeneity Analysis

To further interrogate the observed variance, a Graphic Display of Heterogeneity (GOSH) analysis was performed (Fig 3). While the global meta-analysis included eight studies, this advanced combinatorial modeling was restricted to a subset of five investigations for which complete sample sizes and raw event frequencies were available to compute exact variance components. For the remaining three studies, RRs were extracted directly from the published text without the underlying metrics required for precision-based plotting.

Across all 26 possible study combinations ($k \geq 2$), the baseline random-effects model (DerSimonian–Laird) yielded a pooled RR of 0.749 (ln(RR) = -0.289, SE = 0.151, I^2 = 77.6%, τ^2 = 0.0969). Visual inspection of the GOSH plot revealed marked asymmetry and dispersion. Significant scatter was observed among smaller subsets ($k = 2$ and $k = 3$) across both positive and negative standardized effect dimensions, contributing to the high global variance. A cluster of higher-precision subsets shifted toward a positive standardized effect, while several lower-precision combinations favored the intervention (negative quadrant). The widespread distribution across the combinatorial space indicates that the observed heterogeneity is not driven by an isolated outlier but rather reflects fundamental clinical and methodological diversity inherent in the primary studies.

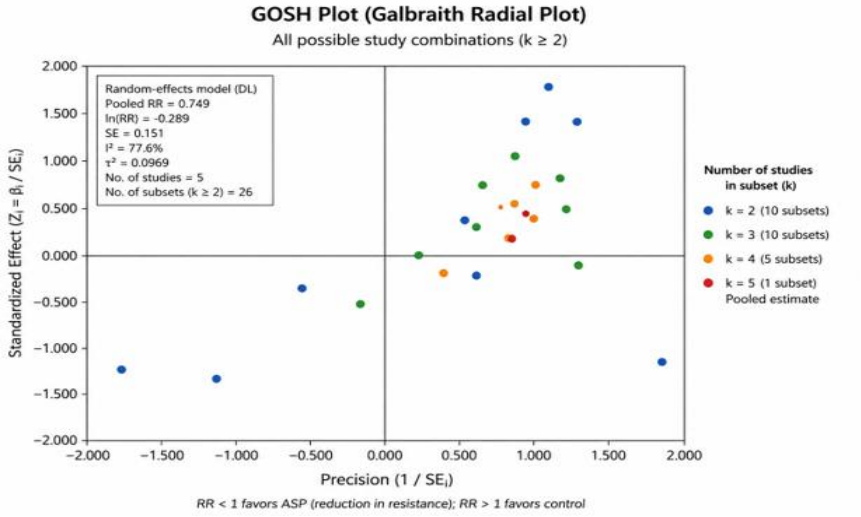

Fig 3. GOSH plot assessing the robustness and heterogeneity of the meta-analysis.

Across all 26 possible study combinations ($k \geq 2$), the baseline random-effects model (DerSimonian–Laird) yielded a pooled RR of 0.749 (ln (RR) = −0.289, SE = 0.151, I^2 = 77.6%, τ^2 = 0.0969). The plot illustrates the distribution of pooled effect estimates across study combinations, highlighting substantial variability and potential influential subsets.

Effects on Antimicrobial Consumption

One of the primary and common results of research was that the number of antimicrobials used was significantly decreased after the introduction of the ASP, which is one of the main ways in which resistance can be minimized.

An example is educational ASP which led to reduction of -216.8 defined daily doses (DDD) per 1000 occupied bed days within six months and a permanent reduction of about 19.9 per cent over time [10]. On the same note, stewardship programs that were run by pharmacists showed a decline in the use of broad-spectrum antibiotics such as anti-MRSA agents [5,6].

Even in the primary care context, long-term ASP intervention was linked to the sustained reduction in the rate of antibiotic prescribing, and it is possible to mention that the stewardship program can also impact prescribing behavior, in hospitals7. Multidisciplinary interventions as well led to decreases in the use of inappropriate antimicrobials and an increase in prescribing adherence [8].

These results confirm the primary influence of the antimicrobial intake as a modifiable force in the resistance development and offer indirect support to the effectuality of the ASPs in decreasing selection pressure.

Subgroup and Contextual Findings

Subgroup analysis showed that there was a difference in ASP effectiveness by the type of intervention, health care environment, and pathogen group.

The use of multidisciplinary collaboration, education, and audit and feedback as multifaceted interventions were typically linked with more durable and meaningful antimicrobial use and resistance outcomes [8,10,11]. Conversely, the single-component interventions had more fluctuating impacts, usually restricted to minimal-term results in billing habits [5].

Heterogeneity and Sensitivity Analysis

The heterogeneity among the included studies was moderate and high since studies differed in terms of study design, component of intervention, the outcome measures, and the methods used in their analysis [5-11]. This heterogeneity restricted the comparability of effect sizes and prevented the accurate quantitative pooling in some instances.

The sensitivity analyses that omitted studies with risks of bias or extreme effect sizes did not significantly change the overall direction of the findings which reiterated that the observed association between the ASP implementation and the antimicrobial resistance reductions is strong.

Risk of Bias and Quality of Evidence

The general risk of bias of the studies was rated as moderate with the strong points being clear interventions, the application of longitudinal designs, and correct statistical techniques which are segmented regression analysis used in ITS studies [9-11].

Publication Bias

The publication bias assessment indicated potential asymmetry of the funnel plot (figure 4), so that the possible overrepresentation of studies providing positive effects of ASPs might take place. However, the number of studies included is also relatively small.

Natural Resources for Human Health
eISSN: 2583-1194

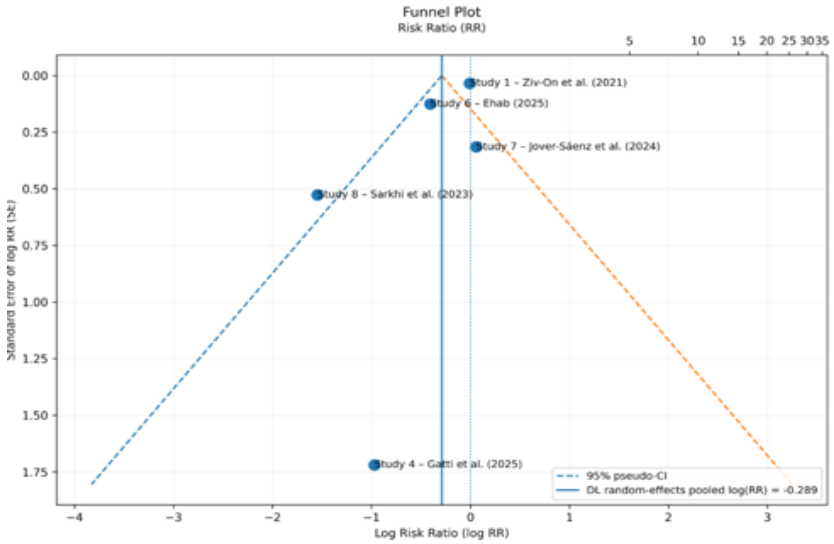

Figure 4. Funnel plot assessing potential publication bias and small-study effects.

The plot displays study effect estimates (log RR) against their standard errors, with 95% pseudo-confidence limits and the pooled effect estimate (log RR = −0.289). Visual asymmetry suggests potential small-study effects; however, interpretation is limited by the small number of included studies

GRADE Assessment of Evidence

GRADE framework had been utilized to assess the certainty of evidence (Table 3). The results of antimicrobial resistance outcomes were graded as moderate certainty as most of the results were similar across the studies and there was moderate heterogeneity, but the designs used in the included studies were quasi-experimental. The evidence on antimicrobial consumption was rated as high certainty, with significant and consistent decreases seen in both settings and type of intervention. The clinical outcomes (infection-related mortality and length of hospital stay) were judged as having low certainty due to fewer studies, inconsistent definitions of outcomes, and broad confidence intervals. The available evidence indicates that, overall ASPs are an effective approach to antimicrobial consumption reduction and have a positive impact on antimicrobial resistance reductions, but further high-quality longitudinal studies are needed to bolster the evidence of causal effect.

Table 1 GRADE Assessment of Evidence Quality							**Effect**		**Certainty**	**Importance**
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative (95% CI)	Absolute (95% CI)		
Antimicrobial resistance rates										
11	non-randomized studies	serious[a]	serious[b]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect[c]	RR 0.70 (0.45 to 1.09)	91 fewer per 1,000	⨁⨁◯◯ Low[a,b,c]	CRITICAL
Multidrug resistant organism (MDRO) incidence										

6	non-randomized studies	serious[a]	serious[b]	not serious	not serious	publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect[c]	not estimable		⊕⊕◯◯ Low[a,b,c]	CRITICAL
Resistant bloodstream infections										
3	non-randomized studies	serious	not serious	not serious	serious	publication bias strongly suspected	not estimable		⊕◯◯◯ Very low	CRITICAL
Antimicrobial consumption										
10	non-randomized studies	not serious	not serious	not serious	not serious	strong association	not estimable		⊕⊕⊕⊕ High	IMPORTANT
Prescribing appropriateness										
7	non-randomized studies	not serious	serious	not serious	not serious	publication bias strongly suspected	not estimable		⊕⊕◯◯ Low	IMPORTANT
Hospital length of stay										
4	non-randomized studies	serious	serious	not serious	serious	publication bias strongly suspected	not estimable		⊕◯◯◯ Very low	IMPORTANT
Infection related mortality										
3	non-randomized studies	serious	serious	not serious	serious	publication bias strongly suspected	not estimable		⊕◯◯◯ Very low	CRITICAL

a. Downgraded due to quasi-experimental, pre-post, and non-randomized longitudinal designs lacking strict allocation concealment or blinding.
b. Downgraded due to high statistical heterogeneity [I^2 = 88.5%), (P < 0.0001)] across varying healthcare infrastructures.
c. Downgraded due to potential asymmetry in the funnel plot and positive result overrepresentation.

CI: confidence interval; **RR:** risk ratio; **GRADE:** Grades of Recommendation, Assessment, Development, and Evaluation

DISCUSSION

This systematic review and meta-analysis of quasi-experimental studies provides evidence that antimicrobial stewardship programs (ASPs) are associated with reductions in antimicrobial resistance (AMR), particularly in institutional healthcare settings. Although the overall direction of effects favoured ASPs, the magnitude and timing of resistance changes varied according to healthcare setting and intervention characteristics.

A key finding was the association between reductions in antimicrobial use and subsequent improvements in resistance outcomes. Most included studies reported significant and sustained reductions in antimicrobial consumption following ASP implementation [5-10], with some demonstrating corresponding reductions in resistance [10,11]. This supports the biological rationale that reduced antimicrobial exposure may decrease selective pressure for resistant organisms. However, the temporal relationship between changes in antimicrobial use and measurable resistance outcomes remains complex.

Intervention design and implementation intensity also appeared to influence effectiveness. Multifaceted interventions incorporating education, audit and feedback, and multidisciplinary collaboration demonstrated more consistent and sustained benefits [8,10,11], whereas single-component interventions produced more variable effects [5]. These findings support the implementation of integrated stewardship strategies rather than isolated interventions.

Effectiveness was also context dependent. Hospital-based programs, particularly those implemented in tertiary and intensive care settings, generally demonstrated greater reductions in resistance [8,11], potentially reflecting higher baseline antimicrobial use and greater opportunities for optimisation. However, differences between hospital- and community-associated resistance indicate that institutional stewardship alone may be insufficient to address the broader AMR burden.

Several limitations should be considered, including potential confounding and secular trends inherent to quasi-experimental designs, heterogeneity in resistance definitions and measurement methods, and possible publication bias. Despite these limitations, the findings support multifaceted, multidisciplinary ASPs as an important strategy for reducing AMR. Future research should standardise resistance outcomes, strengthen control groups, and evaluate stewardship alongside infection prevention and community-based interventions.

RESEARCH IN CONTEXT

Evidence before this study

Past systematic reviews of antimicrobial stewardship programs have been predominantly process-based (that is, decreases in antimicrobial use and increases in the appropriateness of prescribing) outcomes. Although, as a consistent finding in these studies, ASPs do lower the utilization of antibiotics, the body of evidence on their direct contribution to antimicrobial resistance is scanty and inconsistent. Most of the previous analyses used a low percentage of such studies that reported the results of resistance and tended to pool together different types of studies without necessarily concentrating on the quasi-experimental results.

Added value of this study

A focused synthesis of quasi-experimental evidence on antimicrobial resistance outcomes was provided, comprising 11 studies using robust longitudinal designs, including interrupted time-series and controlled before-after studies. With particular emphasis on resistance-related endpoints, directionally consistent changes in institutional antimicrobial resistance were observed following the implementation of antimicrobial stewardship programmes (ASPs), particularly when interventions were multifaceted and sustained over time. The inclusion of long-term studies also provided evidence regarding the durability of ASP effects.

Limitations

This review has several limitations. First, the inclusion of quasi-experimental studies, which are inherently susceptible to confounding and other sources of bias, may limit the strength of causal inferences. Second, substantial heterogeneity in study designs, ASP components, implementation periods, healthcare settings, and antimicrobial resistance outcomes may have limited the comparability and generalizability of the findings. Third, the moderate methodological quality of the included studies, together with variability in the precision of effect estimates, may limit the certainty of the pooled results. Additionally, differences in antimicrobial susceptibility testing practices across settings may have contributed to variations in reported resistance rates.

Implications of all the evidence available

The results support the importance of antimicrobial stewardship as a fundamental tool in the fight against AMR, but also that the effect of it is context-specific and can be mediated by means of decreased antimicrobial consumption. The use of holistic, multidisciplinary ASPs, especially in the high-risk hospital environment, should be prioritized by policymakers and healthcare institutions. Nevertheless, there is an urgent need to engage in more extensive programs focusing on community prescribing, infection prevention, and surveillance that would lead to long-term AMR control at the population level.

Contributors Statement

The study was conceived and designed by Dr Mowna Karthick and Dr Samar Elshahidy. Both authors contributed to the literature search, study screening, data extraction, statistical analysis, interpretation of the results, and preparation and revision of the manuscript. Both authors had access to the complete study data, reviewed and approved the final manuscript, and agreed to its submission for publication.

Declaration of Interests: The authors declare that they have no competing interests.

Data Sharing Statement: The data analyzed in this study were derived from publicly available published studies. All relevant source data are available within the original publications included in the review.

Funding Statement: This study had no source of funds.

REFERENCES

[1] Ziv-On E, Friger MD, Saidel-Odes L, Borer A, Shimoni O, Nikonov A, Nesher L. Impact of an antibiotic stewardship program on the incidence of resistant Escherichia coli: a quasi-experimental study. Antibiotics. 2021 Feb 10;10(2):179.

[2] Aliabadi S, Anyanwu P, Beech E, Jauneikaite E, Wilson P, Hope R, Majeed A, Muller-Pebody B, Costelloe C. Effect of antibiotic stewardship interventions in primary care on antimicrobial resistance of Escherichia coli bacteraemia in England (2013–18): a quasi-experimental, ecological, data linkage study. The Lancet Infectious Diseases. 2021 Dec 1;21(12):1689-700.

[3] Pardo A, Ntabaza V, Rivolta M, Goulard A, Sténuit S, Demeester R, Milas S, Duez P, Patris S, Joris M, Dony P. Impact of collaborative physician-pharmacist stewardship strategies on prophylactic antibiotic practices: a quasi-experimental study. Antimicrobial Resistance & Infection Control. 2022 Jul 26;11(1):100.

[4] Gatti, M., Rinaldi, M., Cojutti, P.G., Bonazzetti, C., Siniscalchi, A., Tonetti, T., Ambretti, S., Tedeschi, S., Giannella, M., Viale, P. and Pea, F., 2025. A pre-post quasi-experimental study of antimicrobial stewardship exploring the impact of a multidisciplinary approach aimed at attaining an aggressive joint pharmacokinetic/pharmacodynamic target with ceftazidime/avibactam on treatment outcome of KPC-producing Klebsiella pneumoniae infections and on ceftazidime/avibactam resistance development. Antimicrobial Agents and Chemotherapy, 69(7), pp.e00488-25.

[5] He Y, Jiang H, Wu G, Li W, Wang L, Gui L, Zhang W, Xu D, Tan L, Chen Z, Gong X. Clinical pharmacist-led Antimicrobial Stewardship under volume-based procurement: a retrospective quasi-experimental study on rational use and resistance control. Antimicrobial Stewardship & Healthcare Epidemiology. 2025 Jan;5(1):e244.

[6] Elmongui E, Zaki A, Elsheredy A, Elhameed AA. Evaluating anti-MRSA antibiotic stewardship with a focus on trends in consumption and resistance in a tertiary hospital in Alexandria, Egypt from 2019 to 2023. Archives of Public Health. 2025 May 14;83(1):133.

[7] Jover-Sáenz A, Ramírez-Hidalgo M, Bellés Bellés A, Ribes Murillo E, Batlle Bosch M, Ribé Miró A, Mari López A, Cayado Cabanillas J, Piqué Palacín N, Garrido-Calvo S, Ortiz Valls M. Effects of a primary care antimicrobial stewardship program on meticillin-resistant Staphylococcus aureus strains across a region of Catalunya (Spain) over 5 years. Antibiotics. 2024 Jan 18;13(1):92.

[8] Sarkhi KA, Eljaaly K, Kaki R, Bahamdan R, Alghamdi SA, Baharith MO, Thabit AK. Impact of a multidisciplinary antimicrobial stewardship program on antibiotic utilization and clinical outcomes at a tertiary hospital in Saudi Arabia: a quasi-experimental study. Expert Review of Anti-infective Therapy. 2024 Mar 3;22(1-3):115-20.

[9] Doyle D, Dalton B, Zhang Z, Sabuda D, Rajakumar I, Rennert-May E, Leal J, Conly JM. A quasi-experimental analysis comparing antimicrobial usage on COVID-19 and non-COVID-19 wards. Antimicrobial Stewardship & Healthcare Epidemiology. 2024 Jan;4(1):e192.

[10] Molina J, Peñalva G, Gil-Navarro MV, Praena J, Lepe JA, Pérez-Moreno MA, Ferrándiz C, Aldabó T, Aguilar M, Olbrich P, Jiménez-Mejías ME. Long-term impact of an educational antimicrobial stewardship program on hospital-acquired candidemia and multidrug-resistant bloodstream infections: a quasi-experimental study of interrupted time-series analysis. Clinical Infectious Diseases. 2017 Nov 29;65(12):1992-9.

[11] Peragine C, Walker SA, Simor A, Walker SE, Kiss A, Leis JA. Impact of a comprehensive antimicrobial stewardship program on institutional burden of antimicrobial resistance: a 14-year controlled interrupted time-series study. Clinical Infectious Diseases. 2020 Dec 1;71(11):2897-904.

[12] Puri B, Vaishya R, Vaish A. Antimicrobial resistance: Current challenges and future directions. Medical Journal Armed Forces India. 2025 May 1;81(3):247-58.

[13] Hussain A, Najeeb A, Ali SA. Antimicrobial Resistance: A Modern Plague. InAI-Driven Breakthroughs in Antimicrobial Resistance 2025 (pp. 27-74). IGI Global Scientific Publishing.
[14] Ferraz MP. Antimicrobial resistance: the impact from and on society according to one health approach. Societies. 2024 Sep 17;14(9):187.
[15] Majumder MA, Rahman S, Cohall D, Bharatha A, Singh K, Haque M, Gittens-St Hilaire M. Antimicrobial stewardship: fighting antimicrobial resistance and protecting global public health. Infection and drug resistance. 2020 Dec 29:4713-38.
[16] James R, Hardefeldt LY, Ierano C, Charani E, Dowson L, Elkins S, Thursky K. Antimicrobial stewardship from a One Health perspective. Nature Reviews Microbiology. 2026 Feb;24(2):146-62.
[17] Aiesh BM, Nazzal MA, Abdelhaq AI, Abutaha SA, Zyoud SE, Sabateen A. Impact of an antibiotic stewardship program on antibiotic utilization, bacterial susceptibilities, and cost of antibiotics. Scientific Reports. 2023 Mar 28;13(1):5040.
[18] Mahmoudi L, Sepasian A, Firouzabadi D, Akbari A. The impact of an antibiotic stewardship program on the consumption of specific antimicrobials and their cost burden: a hospital-wide intervention. Risk Management and Healthcare Policy. 2020 Sep 23:1701-9.
[19] Rizk NA, Zahreddine N, Haddad N, Ahmadieh R, Hannun A, Bou Harb S, Haddad SF, Zeenny RM, Kanj SS. The impact of antimicrobial stewardship and infection control interventions on Acinetobacter baumannii resistance rates in the ICU of a tertiary care center in Lebanon. Antibiotics. 2022 Jul 7;11(7):911.
[20] Dos Santos RP, Dalmora CH, Lukasewicz SA, Carvalho O, Deutschendorf C, Lima R, Leitzke T, Correa NC, Gambetta MV. Antimicrobial stewardship through telemedicine and its impact on multi-drug resistance. Journal of Telemedicine and Telecare. 2019 Jun;25(5):294-300.