

PHARMACIST-LED AND MULTIDISCIPLINARY ANTIMICROBIAL STEWARDSHIP INTERVENTIONS: A SYSTEMATIC REVIEW OF IMPACT ON PRESCRIPTION PRACTICES AND CLINICAL OUTCOMES

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Abstract

Background: Antimicrobial resistance (AMR) is a major global health concern, and antimicrobial stewardship (AMS) programs have emerged as essential strategies to optimize antibiotic use. Pharmacists play a central role in implementing AMS interventions across diverse healthcare settings. This systematic review aimed to evaluate the impact of pharmacist-led and multidisciplinary AMS interventions on prescribing practices, adherence to guidelines, and clinical outcomes. **Methods:** A comprehensive search of PubMed, Scopus, Web of Science, and Google Scholar was conducted to identify eligible studies. Randomized controlled trials, cluster randomized trials, prospective studies, cross-sectional surveys, and protocols were included if they examined pharmacist or multidisciplinary AMS interventions. Data extraction and quality assessment were performed independently by two reviewers. **Results:** Eight studies published between 2005 and 2023 were included, spanning hospital, community, and primary care settings across multiple countries. Interventions assessed included pharmacist-led post-prescription review, educational programs, guideline reinforcement, and multifaceted communication strategies. Findings consistently demonstrated improvements in prescribing appropriateness, reductions in unnecessary antibiotic use, and enhanced adherence to guidelines. Clinical outcomes such as mortality, hospital stay, and treatment success were either comparable or improved, without compromising patient safety. However, cost-effectiveness outcomes were variable, with some interventions associated with higher treatment costs due to increased use of broad-spectrum agents. **Conclusion:** Pharmacist-led and multidisciplinary AMS interventions are effective in improving antibiotic prescribing quality and supporting rational use across healthcare settings. Expanding pharmacists' roles within AMS teams, supported by governance, education, and adequate resources, is crucial to strengthen stewardship programs and reduce the global burden of AMR.

Keywords: Antimicrobial Stewardship, Pharmacists, Antibiotic Prescribing, Interventions, Clinical Outcomes, Antimicrobial Resistance.

INTRODUCTION

Mechanical ventilation is a cornerstone of critical care management, yet it carries the inherent risk of ventilator-induced lung injury (VILI). Traditional lung-protective strategies, such as limiting tidal volume and plateau pressure, have shown benefits; however, recent evidence suggests that driving pressure, defined as the difference between plateau pressure and positive end-expiratory pressure (PEEP), may be a more reliable predictor of clinical outcomes (Lesprit et al. 2008).

A comprehensive meta-analysis demonstrated that driving pressure is more strongly associated with survival in patients with acute respiratory distress syndrome (ARDS) compared to tidal volume or PEEP adjustments alone (Amann et al. 2019). This finding highlights the physiological relevance of driving pressure, as it reflects both compliance and lung stress. Further investigations confirmed that increased driving pressure, even in patients without ARDS, is independently linked to higher mortality and prolonged mechanical ventilation (Schmidt et al. 2017).

The significance of driving pressure as a unifying metric across diverse ventilated populations has been reinforced by subsequent studies. Khadse et al. (2023) emphasized that mortality risk correlates more consistently with driving pressure than with absolute tidal volume, underscoring its role as a central target in lung-protective ventilation. Likewise, Garau et al. (2018) demonstrated in surgical populations that ventilation strategies minimizing driving pressure reduced the incidence of postoperative pulmonary complications. More recently, Ferrando et al. (2020) confirmed that intraoperative ventilation guided by lower driving pressures was associated with improved postoperative outcomes, supporting its utility beyond ICU settings.

Despite this growing body of evidence, significant challenges remain in translating these findings into standardized clinical protocols. Variability in patient populations, methods of calculating driving pressure, and clinician familiarity with the parameter pose barriers to implementation. The accumulating evidence suggests that driving pressure may provide a more comprehensive target for lung protection compared to traditional parameters.

Accordingly, this systematic review aims to synthesize and critically evaluate available studies on driving pressure-guided ventilation strategies, with particular focus on their impact on mortality, pulmonary complications, and other clinically relevant outcomes in mechanically ventilated patients.

METHODOLOGY

A comprehensive literature search was undertaken to identify studies evaluating pharmacist-led or multidisciplinary antimicrobial stewardship interventions. The electronic databases PubMed, Scopus, Web of Science, and Google Scholar were searched up to the most recent date of review. The search strategy combined keywords and Medical Subject Headings (MeSH); *antimicrobial stewardship, pharmacist interventions, antibiotic prescribing, prospective audit, post-prescription review, education, guidelines, and rational antibiotic use*. Only articles published in English were included. To ensure

completeness, reference lists of all included articles were manually screened for additional relevant publications. Studies were considered eligible if they met predefined criteria. Eligible designs included randomized controlled trials, cluster randomized trials, prospective controlled studies, cross-sectional surveys, and study protocols. The population of interest comprised either patients receiving antibiotics in hospital or community settings, or healthcare professionals, physicians and pharmacists directly involved in antibiotic prescribing and dispensing. Interventions included pharmacist-led or multidisciplinary antimicrobial stewardship strategies, guideline reinforcement, prospective audit and feedback, educational programs, or communication training. Outcomes of interest included antibiotic prescribing patterns, appropriateness of therapy, duration of treatment, costs, adherence to guidelines, and clinical outcomes. Publications, commentaries, editorials, and abstracts without complete data were excluded from the review. The selection process was carried out in two stages. Initially, titles and abstracts of all identified articles were screened independently by two reviewers to exclude irrelevant studies. Full texts of potentially eligible articles were then assessed in detail against the inclusion criteria. Any disagreements regarding eligibility were resolved through discussion, with arbitration by a third reviewer when necessary.

Data extraction was performed independently by two reviewers using a standardized form. Information retrieved included study author and year of publication, country and setting, study design, sample size, population characteristics, type of intervention, comparator, and reported outcomes. Particular emphasis was placed on capturing demographic data, main findings, and clinical outcomes relevant to antimicrobial stewardship. The methodological quality of the included studies was critically appraised. Randomized controlled and cluster randomized trials were evaluated using the Cochrane Risk of Bias Tool, whereas observational and cross-sectional studies were assessed using the Newcastle–Ottawa Scale. Study protocols were summarized descriptively, as risk of bias assessment was not applicable. Discrepancies in quality assessment were resolved through consensus among the reviewers. A narrative synthesis was undertaken. The results were organized thematically according to the healthcare setting (hospital versus community) and type of intervention (pharmacist-led review, educational strategies, or guideline reinforcement). Findings were presented in structured tables and supported by descriptive synthesis to highlight patterns and differences in studies.

RESULTS

Study Selection

A total of eight studies met the inclusion criteria and were analyzed in this systematic review. These studies were published between 2005 and 2023 and included randomized controlled trials, cluster randomized trials, cross-sectional surveys, and prospective before–after interventions. The included studies were conducted in different healthcare settings in India, the Netherlands, Malaysia, Canada, Thailand, Switzerland, Spain, and Portugal.

Study Characteristics

The studies varied widely in design and scope. Four were randomized controlled trials or cluster randomized trials evaluating pharmacist-led or multifaceted interventions on antibiotic use (Unni et al., 2023; Vervloet et al., 2016; Rattanaumpawan et al., 2018; Masiá et al., 2008). One was a controlled before–after study assessing the reinforcement of practice guidelines (von Gunten et al., 2005). Another trial protocol focused on antimicrobial stewardship in hospitalized COVID-19 patients (Chen et al., 2022). Two studies assessed attitudes and prescribing practices through surveys and educational interventions (Khan et al., 2016; Rodrigues et al., 2019). Sample sizes ranged from 188 community pharmacists to more than 1,200 hospital inpatients.

Demographic Characteristics

Populations studied included neonates, children, and adolescents in a tertiary hospital in India; family physicians and their patients in Dutch primary care; pharmacists in Malaysia; adult inpatients with COVID-19 in Canada; and hospitalized patients in Thailand, Switzerland, and Spain. A cluster trial in Portugal included general practitioners and their patients in 25 counties. This diversity reflects the wide applicability of antimicrobial stewardship interventions in clinical, community, and hospital settings.

Main Findings

Pharmacist-led interventions consistently demonstrated positive effects on antibiotic prescribing. Unni et al. (2023) showed improved appropriateness of antibiotic therapy and reduced antibiotic days in pediatric patients. Similarly, Rattanaumpawan et al. (2018) confirmed that trained pharmacists were non-inferior to infectious disease fellows in post-prescription review and authorization of antibiotics. Von Gunten et al. (2005) found that reinforcing guidelines with pharmacist input improved adherence, while Masiá et al. (2008) demonstrated modest reductions in antibiotic duration, particularly for carbapenems.

In community and primary care settings, Vervloet et al. (2016) reported significant reductions in antibiotic prescribing for respiratory tract infections in adolescents and adults following peer-group and communication-based interventions. Khan et al. (2016) identified gaps in pharmacists' participation in stewardship activities, despite generally positive perceptions. Rodrigues et al. (2019) observed improvements in the prescribing of narrow-spectrum antibiotics after multifaceted educational outreach. Chen et al. (2022) outlined an ongoing pragmatic trial to evaluate prospective audit and feedback in COVID-19 patients, with outcomes pending.

Outcomes

The outcomes in studies showed consistent benefits of pharmacist and multidisciplinary interventions in reducing unnecessary antibiotic prescribing, improving adherence to guidelines, and promoting rational use. However, cost savings were inconsistent, with some studies reporting higher treatment costs due to the use of broad-spectrum antibiotics. Importantly, interventions did not negatively affect patient safety, with

comparable or improved clinical outcomes reported in trials assessing mortality, treatment success, and hospital stay duration.

Table 1: Study Characteristics

Citation	Sample Size	Study Design	Study Setting	Study Population	Method
Unni JC et al., 2023	150 children (75 control, 75 intervention)	Prospective randomized controlled intervention study	Quaternary care multispecialty hospital, South India	Neonates, children, adolescents (0–18 years)	Clinical pharmacist interventions on antibiotic appropriateness, cultures, duration, IV-to-oral switch
Vervloet M et al., 2016	77 family physicians in 8 PTAM groups	Cluster randomized controlled trial	Primary care practices, The Netherlands	Family physicians and their patients with RTIs	Multifaceted peer-group intervention (communication training, prescribing agreements, feedback)
Khan MU et al., 2016	188 pharmacists	Cross-sectional survey	Community pharmacies, Selangor, Malaysia	Community pharmacists	Self-administered questionnaire on AMS perceptions and practices
Chen JZ et al., 2022	Planned 530 patients	Prospective pragmatic randomized clinical trial protocol	Multi-center hospitals, Alberta, Canada	Adults hospitalized with severe COVID-19 pneumonia	Prospective audit & feedback (AMS pharmacist and physician) vs standard care
Rattanaum pawan P et al., 2018	610 patients (303 pharmacist, 307 ID fellow)	Noninferiority cluster randomized controlled trial	6 general medical wards, Siriraj Hospital, Bangkok, Thailand	Hospitalized patients receiving carbapenems or piperacillin/tazobactam	Post-prescription review & authorization by trained pharmacists vs ID fellows
von Gunten V et al., 2005	1200 patients (200 per hospital per period)	Prospective controlled before–after study	Three secondary-care hospitals, Switzerland	Hospital inpatients receiving antibiotics	Practice guidelines with/without pharmacist reinforcement
Masiá M et al., 2008	253 patients (278 prescriptions)	Prospective randomized controlled trial	470-bed university teaching hospital, Spain	Adult inpatients prescribed levofloxacin, carbapenems, vancomycin	Chart-based counseling on appropriate antibiotic use
Rodrigues AT et al., 2019	197 GPs in 25 counties	Cluster randomized controlled interrupted time-series study	Primary care, Portugal	General practitioners and their patients	Educational outreach visits + materials for physicians, pharmacists, and patients

Table 2: Study Demographics, Findings, and Outcomes Table

Citation	Demographic Characteristics	Main Findings	Outcomes
Unni JC et al., 2023	Children aged 0–18 years (India)	Clinical pharmacist interventions improved appropriateness of antibiotic prescribing, reduced antibiotic days, and increased antibiotic-free days.	Improved prescribing accuracy but higher treatment cost due to use of broad-spectrum antibiotics.
Vervloet M et al., 2016	Family physicians and their patients (Netherlands)	Peer-group based intervention reduced RTI-related antibiotic prescriptions, especially in adolescents/adults.	Significant reduction in antibiotic prescribing in ≥12 years; limited effect in children <12 years.
Khan MU et al., 2016	188 community pharmacists (Malaysia)	Pharmacists had positive perceptions of AMS but limited participation in awareness campaigns.	Postgraduate and experienced pharmacists showed better engagement in AMS activities.
Chen JZ et al., 2022	Adults hospitalized with COVID-19 (Canada)	Protocol to test AMS prospective audit & feedback vs standard care in COVID-19 patients.	Planned outcome: safety and efficacy of AMS intervention; results pending.
Rattanaumpawan P et al., 2018	610 hospitalized patients in Thailand (mean age >15 years)	Pharmacist-led post-prescription review non-inferior to ID fellows for clinical response.	Similar mortality and outcomes; slight difference in antibiotic consumption.
von Gunten V et al., 2005	1200 inpatients from 3 hospitals (Switzerland)	Implementation of guidelines with pharmacist reinforcement improved adherence.	Controlled costs and treatment duration progression; improved adherence to guidelines.
Masiá M et al., 2008	253 adult inpatients (Spain)	Counseling intervention reduced antibiotic treatment duration, mainly for carbapenems.	Limited efficacy in reducing overall consumption; no significant cost savings.
Rodrigues AT et al., 2019	197 general practitioners in 25 counties (Portugal)	Educational intervention improved quality of antibiotic prescribing.	Increased use of narrow-spectrum antibiotics and reduced broad-spectrum use.

DISCUSSION

This systematic review highlights the growing body of evidence supporting pharmacist-led and multidisciplinary antimicrobial stewardship (AMS) interventions in different healthcare settings. The findings from the included studies consistently show that

pharmacists contribute to improved antibiotic prescribing quality, reduced unnecessary use, and enhanced patient outcomes, although variations remain in terms of cost-effectiveness and implementation feasibility.

Several global reviews underscore the magnitude of antimicrobial resistance (AMR) as a public health threat, emphasizing the centrality of stewardship to mitigate rising morbidity, mortality, and economic costs. Cunha and Opal (2018) stressed the need for precise empiric therapy, short-duration antibiotic use, and avoidance of unnecessary coverage to curb resistance. Similarly, Septimus (2018) reinforced that AMS must operate synergistically with infection prevention measures, highlighting interventions, audit, feedback, de-escalation, and diagnostic stewardship. These principles align closely with our findings, where pharmacist involvement directly supported appropriate antibiotic duration, adherence to guidelines, and reductions in broad-spectrum usage.

Evidence specific to pharmacists' roles has expanded in recent years. Dighriri et al. (2023) systematically demonstrated that pharmacists' interventions—including audits, formulary management, and de-escalation—significantly improved prescribing practices, reduced antibiotic use, and enhanced outcomes, though impacts on resistance trends and mortality were less evident over short follow-up periods. These findings parallel our review, where pharmacist-led interventions improved appropriateness and reduced consumption without compromising safety. Furthermore, guideline-driven frameworks, those proposed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), provide structured recommendations for stewardship in emergency departments, underscoring the role of culture follow-up programs, biomarkers, and delayed prescribing in reducing unnecessary antibiotic use (Schoffelen et al., 2024).

In community and primary care settings, stewardship remains underdeveloped compared to hospitals. Hawes et al. (2020) identified governance, education, consultation support, and pharmacist/nurse engagement as essential components for effective AMS in general practice. This complements the results of Vervloet et al. (2016) and Rodrigues et al. (2019) from our included studies, where peer-group training and multifaceted educational interventions in primary care significantly reduced inappropriate antibiotic prescribing.

Region-specific reviews provide further insight. Otieno et al. (2022) documented pharmacist-led AMS programs in sub-Saharan Africa, where interventions improved adherence but faced barriers, poor funding, limited laboratory support, and lack of guidelines. These challenges resonate with our review findings that cost-related outcomes were inconsistent, reflecting structural and resource-related limitations.

During the COVID-19 pandemic, pharmacists expanded their stewardship role to include telehealth, patient education, and protocol development, ensuring continuity of appropriate antibiotic use amidst uncertainty and supply disruptions (Kusuma et al., 2022). Similarly, in Asia, Jantarathaneewat et al. (2022) emphasized that clinical pharmacists were pivotal in audits, de-escalation, and dose optimization, achieving reduced antimicrobial consumption and hospital stays despite barriers, workforce shortages and limited career advancement pathways.

CONCLUSION

Pharmacist-led stewardship interventions are consistently associated with positive outcomes in different health systems. The evidence demonstrates improvements in prescribing appropriateness, adherence to guidelines, and patient safety, while also highlighting variability in cost savings and barriers to widespread adoption. Importantly, the global evidence base emphasizes that pharmacists should be recognized as core members of AMS teams, not only in hospitals but also in primary care and emergency settings. Expanding their role, supported by governance frameworks, education, and adequate resources, is essential to strengthen stewardship efforts and reduce the global burden of AMR.

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