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ABSTRACT

Objective: We sought to characterize and evaluate the effectiveness of pharmacist-led AMS interventions in improving antimicrobial use and subsequent surgical site infections (SSI) in perioperative settings.
Methods: A systematic review and meta-analysis was conducted by searching PubMed, Embase and CINAHL. Two independent reviewers extracted the data using the Descriptive Elements of Pharmacist Intervention Characterization Tool and undertook quality assessment using the Crowe Critical Appraisal. A meta-analysis was conducted using a random-effect model.
Results: Eleven studies were included in this review. Pharmacists were found to have various roles in AMS, including educational sessions, ward rounds, audits and feedback, and guidelines development. The discussion of interventions lacked details on the development. A meta-analysis revealed that pharmacist-led AMS programs in perioperative settings was associated with a significant improvement in antibiotic selection (OR 4.29; 95 % CI 2.52–7.30), administration time (OR 4.93; 95 % CI 2.05–11.84), duration (OR 5.27; 95 % CI 1.58–17.55), and SSI (OR 0.51; 95 % CI 0.34–0.77).
Conclusion: Pharmacist-led AMS programs were effective in improving antimicrobial prescribing while reducing SSI; however most studies were of moderate quality. Studies lacked the utilization of theory to develop interventions, therefore, it is not clear whether theory-derived interventions are more effective than those without a theoretical element. High-quality, multicomponent, theory-derived, interventional studies using appropriate methodology and standardized data collection, are needed.

1. Introduction

Antimicrobial stewardship (AMS) is defined by the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America (IDSA/SHEA) as a coherent set of activities that includes the selection, dose, route, and duration of appropriate antimicrobial therapy.[1–3] These programs aim primarily at optimizing clinical outcomes, while minimizing the undesirable consequences of the antimicrobials use, including toxicity, the selection of pathogenic organisms (such as *Clostridium difficile*) and the emergence of resistance.[4] Additionally, AMS activities go beyond the individual level to also involve system level efficacy parameters. Dyar et al. proposed that antimicrobials should be used in a way “to ensure sustainable access to effective therapy for all who need them”.[3] A plethora of studies advocated for the implementation of AMS strategies across various healthcare settings as they are associated with improved efficacy and safety outcomes, alongside reduced antimicrobial use, expenditure, antimicrobial resistance (AMR) and other nosocomial infection [e.g. surgical site infections (SSIs), postoperative infections, and *Clostridium difficile* (C. difficile) infections].[5–10]

SSIs are serious postoperative complications that has been ranked third among the most common types of nosocomial infections, affecting one-third of patients undergoing surgical procedures[11–13] and leading to an economic loss of up to US$22,130 per patient.[14] It is estimated that up to 60 % of these SSIs can be prevented by using evidence-based guidelines.[15] Infection control and prevention in perioperative settings is therefore assumed to be of an even greater significance.[16] However, adherence to these prevention protocols is often inadequate in around 66 % of cases.[17] For instance, only 5 % of surgical procedures in Brazil are performed in accordance with the protocols recommendations.[18] Similarly, in Ethiopia, over half of the patients used the surgical antibiotic prophylaxis for a duration longer than indicated.[19] Thus, it is essential to adopt AMS programs to promote adherence to surgical antibiotic prophylaxis protocols.

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The American Society of Health-System Pharmacists (ASHP) and the Society of Infectious Disease Pharmacists (SIDP) jointly believe that a pharmacist should be incorporated as a core member of AMS programs.[20] Hence, in recent years, AMS multidisciplinary teams primarily include an infectious disease physician, a medical microbiologist, and a pharmacist.[1] This remodeling of team was in response to the rapidly evolving landscape of healthcare which has called for a parallel change in the scope of pharmacy practice to uptake new roles and responsibilities.[21] Furthermore, many experts advocate for the implementation of pharmacist-led AMS programs as their expertise and clinical knowledge allow them to take a leadership role in AMS teams.[22]

Whilst the implementation of pharmacist-led AMS programs across a variety of healthcare settings is well-established,[10,23–25] there has been no systematic synthesis of the effectiveness of pharmacist-led interventions in perioperative settings. Therefore, the aim of this systematic review and meta-analysis is to evaluate the impact of pharmacist-led AMS interventions on prescribing (compliance rate, timing and duration of antibiotic prophylaxis and antibiotic utilization) and clinical (SSIs rate, postoperative infection rate, C.difficile) outcomes.

2. Methods

This systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.[26] The protocol was published in the International Prospective Register of Systematic Reviews (PROSPERO) [Ref: CRD42023460812].

2.1. Bibliographic search method

A search was conducted of the following library databases, PubMed, Embase, CINAHL, and Google Scholar was used to obtain any relevant grey literature from inception to September 2023. The search terms developed fell into two categories that were related to pharmacy (e.g. pharmacist, pharmacy) and perioperative settings (e.g. perioperative period, perioperative care). The search strategy was kept deliberately broad to capture all outcomes of pharmacist-led interventions, which are antimicrobial stewardship, medication errors, clinically important outcomes, complication, and management of chronic diseases. This review focuses merely on antimicrobial stewardship outcomes. The search was carried out using Medical Subject Headings (MeSH) and other appropriate subject headings and text words. Scoping searches were conducted prior to finalizing the search strategy. Boolean operators such as AND, OR, truncations (*) were used where relevant. The search strategies are included in Supplementary 1 of the electronic supplementary material (ESM).

2.2. Eligibility criteria

Studies were included if they were[1]: randomized controlled trials (RCTs), quasi-experimental, pre-post, prospective, and retrospective cohort[2]; evaluated a pharmacist-led AMS programs[3]; conducted in the perioperative settings[4]; had a control or comparison group (with healthcare professionals other than a pharmacist)[5]; published in a peer-reviewed journal in English or Arabic languages and available in full-text. Case reports, expert opinions, systematic reviews, letters to editors, commentaries, correspondences, news articles, and qualitative studies were excluded from this review, as were conference abstracts if not available in full text. We also excluded studies focusing on pediatric patients.

2.3. Study selection and data extraction

The articles found in the database search were transferred to Rayyan, a web application for systematic reviews, to identify and delete any duplicated articles.[27] The screening and selection procedures involved two phases: screening of titles and abstracts, then full text. Screening of titles/abstracts was conducted by two independent reviewers (LN, SK) with other team members involved in case of discrepancies. Full text screening was conducted by two independent reviewers (LN and SK or BA and MA), with any disagreements resolved by discussion with a third independent reviewer.

The following information was independently extracted from each eligible study by two authors (either LN and SK or BA and MA), who then met to reach consensus:

- Study characteristics: author, year, country, study design, objectives, population, sample size, study duration, and surgical units
- Pharmacist intervention characteristics: recipients, focus of intervention, setting, method of communication, clinical data source, pharmacist action, timing and frequency of action, and materials that support action
- Outcome measures:
  - o Prescribing outcomes: compliance with protocols/procedures, antimicrobial selection, appropriateness of antimicrobial prophylaxis procedures
  - o Clinical findings: surgical site infections (SSI), postoperative infections, *Clostridium difficile* (C.difficile) infection

The intervention characteristics part of the data extraction form was developed in accordance with the DEPICT-2 (Descriptive Elements of Pharmacist Intervention Characterization Tool), which is a validated instrument utilized to assist researchers in accurately describing and characterizing the details of pharmacist interventions.[28] For all investigated endpoints, we did not adopt any particular definition, instead we captured the definitions provided by authors.

2.4. Quality assessment

Quality assessment was conducted by LN and SK or BA and MA independently, and ambiguous studies were discussed with the research team to reach a consensus. All included studies were assessed using the Crowe Critical Appraisal Tool (CCAT) v1.4, a validated and unique tool for appraising different types of study designs.[29] The CCAT covers eight domains: preliminary, introduction, design, sampling, data collection, ethical matters, results, and discussion. Each domain is scored out of five providing an overall score of 40 points. Studies with scores between 36 and 40 indicated high-quality studies, a score between 30 and 35 as moderate and a score below 30 as low quality. This was based on a consensus reached by the reviewers to group studies by quartiles, a similar approach has been adopted by Donnelly et al. and El-Awaisi et al.[30,31] The author of the CCAT tool was also contacted to ensure that this method of interpretation was valid.

2.5. Meta-analysis

The effect of the interventions on the four most commonly measured outcomes in the included trials,[1] appropriateness of antibiotic selection,[2] appropriateness of timeframe,[3] appropriateness of duration, and[4] SSI was analyzed. Where adequate data for the meta-analysis were reported, the results were presented as odds ratios (ORs) and their respective 95 % confidence intervals (CIs) for dichotomous data or standard mean differences (SMDs) and 95 % CIs for continuous data.[32] All p-values were set to be < 0.05 to assess statistical significance. A random-effects model was used due to the expected heterogeneity between studies. Heterogeneity was by the degree of inconsistency I^2 statistics and Chi-square test P-value, with $I^2 \geq 50$ % indicating significant heterogeneity.[33,34] Publication bias was tested statistically using funnel plots followed by Egger's test. Analyses were performed using the IBM Statistical Package for Social Sciences (IBM SPSS Statistics, Version 29.0; IBM Corp, Armonk, NY).

3. Results

3.1. Identification and selection of studies

A total of 6,816 studies were identified from databases and 8 studies were identified from citation searching (Fig. 1). After removing 1,871 duplicates and 4,755 records through title/abstract screening due to irrelevance, 190 studies were sought for retrieval. Out of the 123 retrieved reports, 11 studies were included in the current review.

3.2. Study characteristics

Characteristics of included studies are presented in Table 1. Included studies comprised of five pre-post studies,[35–38] three quasi-experimental studies,[39–41] two retrospective cohort studies,[42,43] one randomized controlled trial,[44] and one prospective audit and feedback study.[45] Five studies were from China,[37,38,41–43] two from USA,[36,40] and one each from Pakistan,[39] Sudan,[44] South Africa,[45] and Nigeria.[35] Included studies varied in terms of the surgical units of interest, with most studies (n = 4) including multiple surgical departments,[36,39,44,45] followed by cardiothoracic (n = 2),[40,41] orthopedic (n = 2)[38,43] and one each for obstetrics and gynecology,[35] transplant,[42] and urology.[37]

3.3. Quality of studies

Total scores ranged between 28 and 35, with a median score of 32.45. The majority of studies (n = 8) were of moderate quality, while three showed low quality. As noted in Fig. 2, the main defects leading to lower quality amongst included studies were related to the sampling methods and data collection techniques.

3.4. Overview of pharmacist-led AMS programs

Detailed description of pharmacist-led AMS interventions according to DEPICT-2 tool is reported in Table 2 and Fig. 3. The presentation of findings in this section is as follows: (1) recipients and setting, (2) method of communication, (3) pharmacist actions.

3.4.1. Recipients of the intervention and setting where it took place

The medical staff (including surgeons, physicians, anesthesiologist, and nurses) were the main target of the various AMS activities undertaken by pharmacists in all included studies.[35–45] In addition to the health care professionals, five studies also incorporated pharmacist-provided services directly to patients.[38,40–43]

All interventions took place in hospital settings with the majority being educational sessions, protocol development or ensuring adherence to therapeutic guidelines within the hospital premises.[35–37,39,40,44,45] Some studies reported that, in addition to the latter, pharmacist delivered AMS services at hospital bedside[38,41–43] or hospital-based clinic.[43] Kwiatkowski et al. (2021), reported that part of the intervention was conducted at the patient's house through telephone interviews.[40]

3.4.2. Communication with recipients

Ten studies has described the method of communication as face-to-face interactions,[35,37–45] with two studies reporting additional methods including teleconferencing[45] and telephone calls.[40] The sole method of communication in the study by Lessard et al. was a messaging feature in the electronic medical records (EMR) system.[36]

Seven out of eleven included studies reported a continuous provision of the pharmacist input during the perioperative period.[37,38,40–44] In the studies by Abubakar et al. (2019) and Butt et al. (2019), contact was made with the recipient only twice as the interventions were focused on protocol development[35] and educational sessions to healthcare professionals,[39] respectively. The study by Brink et al. (2017) reported a frequency of once every 8–10 weeks interval, and then as needed in the process of implementation.[45] Interaction was done only once between surgeons and pharmacists in the study by Lessard et al.[36]

Mode of contact to deliver the interventions was primarily (n = 9)

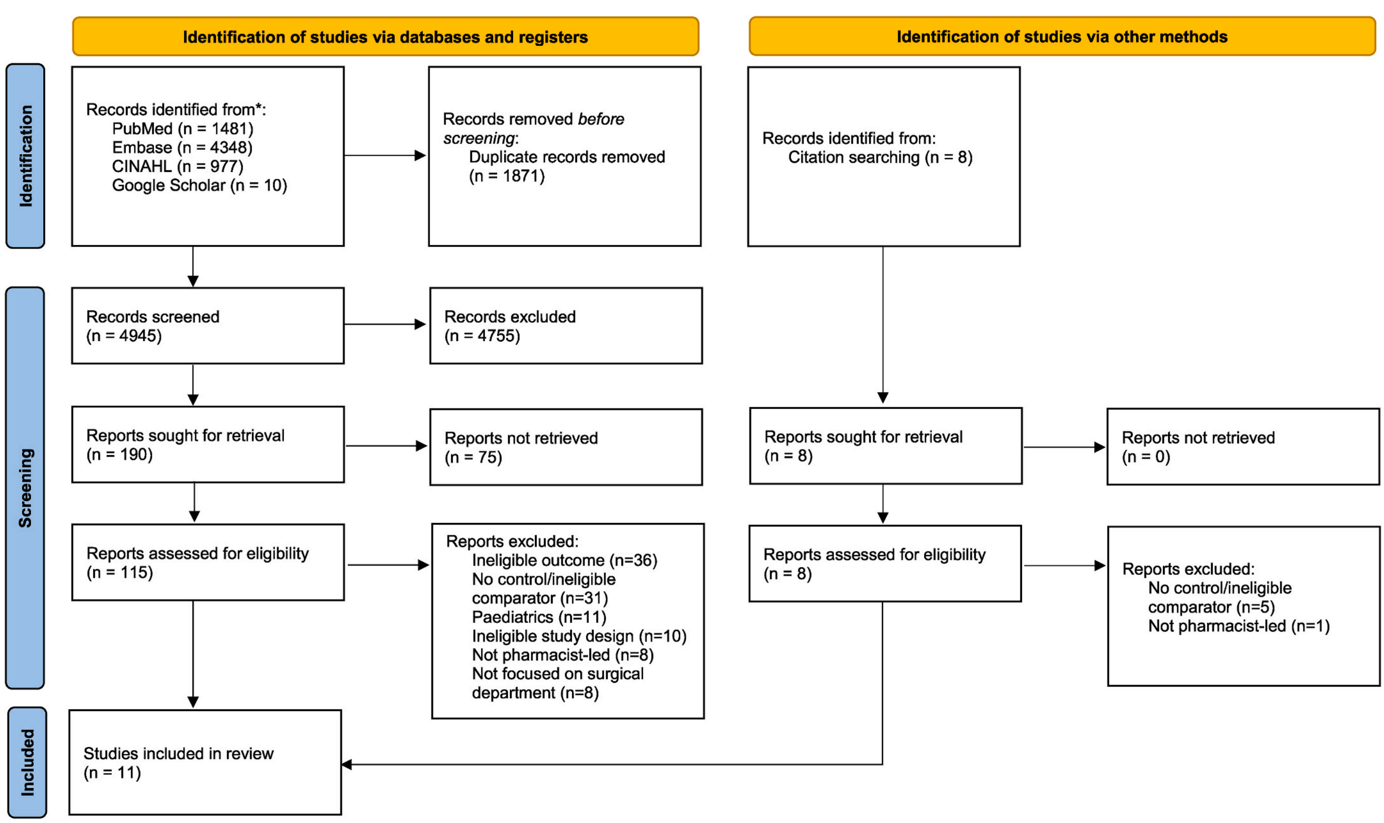

Fig. 1. PRISMA flow diagram.

Table 1
Characteristics of included studies.

Author	Country	Objective	Study design	Sample size	Study duration	Surgical unit	Included patient characteristics
Abubakar et al, 2019	Nigeria	To evaluate the impact of antibiotic stewardship interventions on compliance with surgical antibiotic prophylaxis practice	Prospective pre and post intervention	464 patients (226 pre intervention; 238 post intervention)	6 months	Obstetrics and gynecology	Women who had elective and emergency obstetric and gynecologic surgeries (clean, clean-contaminated and contaminated wounds)
Brink et al, 2017	South Africa	To implement an improvement model for PAP to achieve a reduction in SSIs	Prospective audit and feedback strategy	24206 surgical cases	2.5 years	Obstetric and gynaecology, orthopedic, cardiovascular, thoracic and other vascular surgery, neurosurgery, gastrointestinal, plastic surgery, and urology	Adult patients who had indications for intravenous PAP
Butt et al, 2019	Pakistan	To evaluate the impact and cost-benefit value of pharmacist's educational intervention for antibiotic use in post-surgical prophylaxis	Prospective quasi experimental study	450 patients (225 control; 225 intervention)	Not reported	General, orthopedic, and gynecological	Patients with clean/clean contaminated surgeries from general, orthopedic and gynecology wards on surgical prophylaxis and without systemic disease
Elnour et al, 2022	Sudan	To test the clinical pharmacist's impact on faciliating the implementation of SAP protocol	Randomized controlled trial	226 patients (113 control; 113 intervention)	Not reported	Hernia repair, thyroidectomy, appendectomy and cholecystectomy	Patients of both genders above 18 years and less than 65 years undergoing elective surgery
Kwiatkowski et al, 2021	USA	To implement and evaluate a pharmacist-led BLA clarification interview service in the preoperative setting	Quasi-experimental	87 patients (50 control; 37 intervention)	5 months	Cardiothoracic	Patients with BLA, perioperative clinic appointment, and surgery requiring betalactam as prophylaxis
Lessard et al, 2023	USA	To detail antimicrobial stewardship pharmacist-led efforts working with an interdisciplinary team to optimize preoperative antimicrobials in patients with PAL	Before - After	1572 patients	2 years	Otolaryngology, general surgery, gynecology, neurosurgery, obstetrics, ophthalmology, orthopedics, podiatry, and urology	Patients with PAL
Yang et al, 2019	China	To comprehensively assess the impact of pharmacistled post-transplant medication management for kidney transplant recipients	Retrospective cohort study	204 patients (84 pre intervention; 120 post intervention)	2 years	Transplant	Patients receiving living-donor or deceased-donor kidney transplants
Zhang et al, 2014	China	To evaluate the impact and cost-benefit value of pharmacist interventions for prophylactic antibiotic use	Before - After	370 patients (174 pre intervention; 196 post intervention)	18 months	Urology	Patients undergoing clean or clean-contaminated urologic procedures
Zhou et al, 2016	China	To study the impact of multifaceted pharmacist interventions on antibiotic prophylaxis in perioperatively	Pre-post quasi-experimental study	963 patients (412 baseline; 551 intervention)	2 years	Cardiothoracic	Patients undergoing clean or clean-contaminated cardiothoracic surgery
Zhou et al, 2021	China	To assess the impact of the pharmacist-led standardization of the cephalosporin intradermal skin test on perioperative antibiotic prophylaxis	Pre-post intervention study	873 patients (425 pre intervention; 448 post intervention)	3 months	Orthopedic	All patients admitted for orthopedic surgeries except surgeries related to facial bones
Zhou et al, 2023	China	To evaluate the clinical effects and cost-effectiveness of pharmacist-led intervention in the perioperative anti-infection prophylaxis	Retrospective observational study	472 (236 control; 236 intervention)	1 year	Orthopedic	Patients with elective internal fixation surgery and with a wound class categorized as clean

PAP: perioperative antibiotic prophylaxis; SSIs: surgical site infections; SAP: surgical antimicrobial prophylaxis; BLA: beta-lactam allergy; PAL: penicillin allergy labeling.

through contact with group with the medical staff (including surgeons, physicians, anesthesiologist, and nurses).[35,38–45] In the study by Kwiatkowski et al. an initial meeting including stakeholders and the surgery team took place to approve the intervention material.[40] A one-on-one contact with patients was also described in four studies[38,40,42,43] and with physicians in three studies.[36,37,41]

3.4.3. Pharmacists AMS interventions

All studies, except for one,[39] conducted a multifaceted pharmacist-led AMS intervention (Fig. 3 and Table 2). The most frequently (n = 8) identified intervention was pharmacist-delivered educational and training sessions for healthcare providers.[35,38–41,43–45] All included studies delivered informative didactic lectures to facilitate the dissemination of protocols or to educate staff on various AMS-related topics. Educational activities provided to other healthcare providers focused on antibiotic pharmacotherapy, pharmacokinetics and dynamics, spectrum of antibiotics, local resistance data, or disease-specific guidelines. Four studies also reported that supportive educational

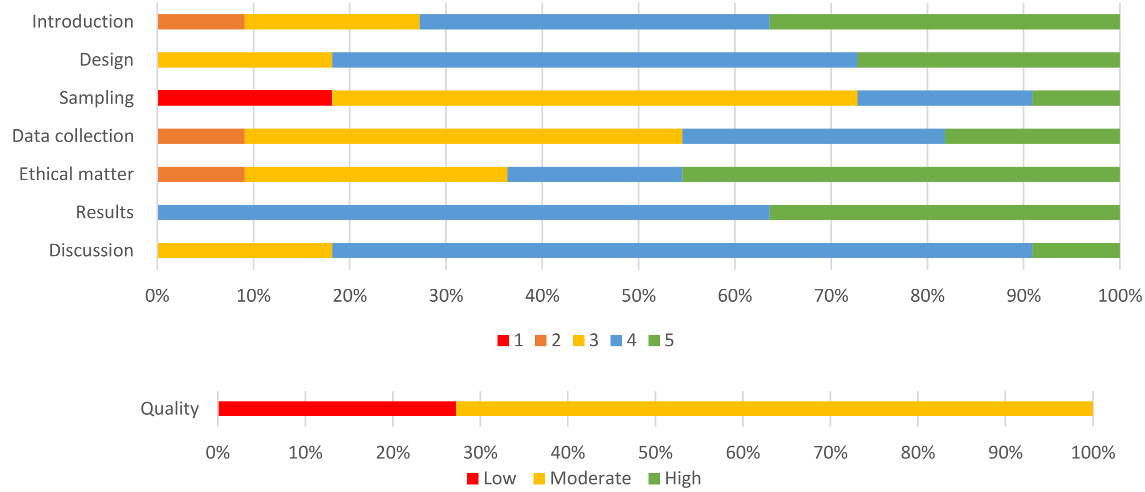

Fig. 2. Stacked bar chart showing results of the quality assessment.

materials were utilized as part of the educational initiative including posters,[35] mobile messages,[45] and handouts/brochures.[41,43]

Additionally, auditing and feedback were part of the pharmacist's duties in five studies.[35,37,41,43,45] History review and medication reconciliation (n = 5),[36–38,40,42] modification of treatment plans (n = 5),[37,40–43] and participation in daily rounds (n = 4)[38,41,43,44] were also described. Pharmacists also had active roles in the development[35,44] and approval[40] of surgical prophylaxis institutional protocols and materials.

Nine out of the eleven included studies furnished information on the basis for the implemented intervention. The development of the pharmacist-led AMS interventions was predominantly based on clinical guidelines[29,39,40,45,52] and institutional protocols[33,36,37,49,51]; however no further details were provided on the structure and process of these interventions.

3.5. Outcomes related to adherence to AMS protocols

This section presents findings related to the adherence to adopted AMS protocols or institutional procedures. The section is divided into the following[1]: Adherence to AMS protocols and procedures,[2] Antibiotic selection,[3] Appropriateness of AMS procedures. The latter is further divided into timeframe, duration, and dose. In this section, we also report the findings of the meta-analysis for antibiotic selection, appropriateness of timeframe, and appropriateness of duration.

3.5.1. Adherence to AMS protocols and procedures

Three studies reported on the adherence to developed protocols or followed procedures, with all three studies showing significant improvement (Table 3).[39,44,45] Meta-analysis was not feasible due to the discrepancies in the reported data. Brink et al. (2017) reported on the overall mean rate of compliance to perioperative antibiotic prophylaxis (PAP), which was significantly higher ($P < 0.0001$) in the intervention group as compared to control group with 83.3 % (95 % CI 80.8–85.8) and 16.5 % (66.8 % (95 % CI 64.8–68.7), respectively.[45] Butt et al. (2019) reported the composite endpoint of correct choice, dose, frequency, and duration, which increased from 1.3 % in the usual care arm to 2.4 % in the intervention arm ($P = 0.0005$).[39] Lastly, Elnour et al. (2022) reported on the adherence to the developed surgical antibiotic prophylaxis (SAP) protocol, indicating a significantly higher compliance rate in the intervention group (43.6 % vs 56.7 %; $P < 0.001$).[44]

3.5.2. Antibiotic selection

All studies have reported on the selection of antibiotic agents. Appropriateness of antibiotic choice was reported in nine out of the eleven included studies,[36–41,43–45] of which seven were pooled in a meta-analysis (Fig. 4A).[37–41,43,44] These studies (n = 3441 patients; 1635 control vs 1806 intervention) reported an overall OR of 4.29 favoring the intervention group (95 % CI 2.52–7.30, $P < 0.001$) with a high heterogeneity level ($I^2 = 83$ %). Amongst studies included in the meta-analysis, Zhou et al. (2023) was the only one to show non-significance in the rate of appropriate antibiotic selection between the two groups.[43]

Both studies that were not included in the meta-analysis also showed statistically significant improvement in the selection of appropriate antibiotics (Table 3). Brink et al. (2017) reported a significant overall mean rate favoring the pharmacist-led AMS intervention (81.2 % (95 % CI 78.5–83.8) vs 95.9 % (95 % CI 89.9–100); $P = 0.0004$ Similarly, Lessard et al. (2023) reported the outcome in days of therapy/1000 patient days (DOT/1000 PD) and showed a statistical significance favoring the intervention arm (81.3 (86 %) vs 90.6 (96.3 %); $P < 0.001$).

Four studies have investigated the use of vancomycin as a prophylactic agent in the perioperative settings,[36,38–40] two of which showed a significant decreased utilization the intervention group, Lessard et al. (2023): 3.2 % vs 0.4 % DOT/1000 PD, $P < 0.001$; Zhou et al. (2021): 8.5 % vs 1.6 %; $P < 0.001$).[36,38] Whilst Butt et al. (2019) showed a comparable vancomycin use between groups with (7.6 % vs 4.9 %; $P = 0.329$),[39] Kwiatkowski et al. (2021) demonstrated a significant increase in the intervention group from (38 %) to (59 %, 0.047).[40]

Lessard et al. (2023) and Zhou et al. (2021) explored the use of clindamycin for surgical prophylaxis, both of which showed a significant decrease ($P < 0.001$) of use in the intervention group.[36,38]

3.5.3. Appropriateness of AMS procedures

3.5.3.1. Appropriate timeframe. Six studies reported on the timely administration of antibiotics relative to the procedure,[35,38,40,43–45] whereof four were eligible for the meta-analysis.[35,38,43,44] The pooled effect through all interventions (n = 2125 patients, 987 control; 1138 intervention) indicates that the group with pharmacist-led AMS program has 4.9 times the odd of having the antibiotic administered in an appropriate timeframe as compared to the control group (OR 4.93; 95 % CI 2.05–11.84, $P = 0.0003$; $I^2 = 92$ %) (Fig. 4B).

The two studies that were not included in the meta-analysis also showed significant improvement in the timely administration of the antibiotic (Table 3). Brink et al. (2017) reported a significant increase in the mean rate of timely administration in the intervention group [34.7 %

Table 2
Description of pharmacist interventions.

Study	Pharmacist action(s)	Recipient, Setting, (Mode of Contact)	Methods of communication	Clinical data sources	Source of guide for intervention	Timings of action	Frequency of contacts	Supportive materials
Abubakar et al., 2019	1 Development and dissemination of departmental protocol for surgical antibiotic prophylaxis 2 Educational meeting with the obstetricians and gynecologists 3 Audit and feedback using baseline data and reminder in the form of wall mounted posters	Obstetrics/gynecology doctors, Hospital, (contact with group)	Face to face	EMR, anesthesia, nursing and medication records	Departmental protocol for SAP	N/A	Twice	Wall mounted posters
Brink et al., 2017	1 Initial training sessions detailing the Netcare PAP guideline and the core measures and improvement indicators to pharmacists and pharmacy managers 2 This group enrolled and trained multidisciplinary antibiotic management teams consisting of surgeons, anesthetists, hospital, nursing and theatre managers, and peri-operative and surgical ward nurses 3 Each pharmacist was required to undertake a stepwise implementation process in their hospital by auditing	Medical staff, Hospital, (contact with group)	Face to face and teleconference	Not reported	Netcare adaptation of the Institute for Healthcare Improvement (IHI) Model	N/A	8–10 week intervals, then as needed	Written or mobile phone messages
Butt et al., 2019	Delivered two educational and training sessions for doctors and nurses to brief and discuss the standard treatment guidelines regarding the use of antibiotics for surgical prophylaxis (duration 10–15 days)	Medical staff, Hospital, (contact with group)	Face to face	EMR	ASHSP guidelines for antimicrobial prophylaxis	N/A	Twice	None
Elnour et al., 2022	1 Develop SAP protocol 2 Accompany surgeons while prescribing 3 Provide educational activities to medical staff 4 Ensure strict adherence to the protocol	Surgeon, Hospital, (contact with group)	Face to face	EMR	Not reported	On or during patient admission	Continuous	None
Kwiatkowski et al., 2021	1 Meet with stakeholders and surgery team for input and approval of intervention material 2 Deliver thorough education to the medical team 3 Telephone interviews with patients before admission 4 Update allergy status on the system 5 Notify the surgeons of any necessary considerations before procedures	Patients, medical staff and stakeholders, Hospital and recipient home, (one-on-one, contact with groups)	Face to face, telephone	EMR	Institutional guidelines	1 week before clinic visit, then during patient admission	Continuous	None
Lessard et al., 2023	1 Review preoperative orders, in most cases 24 h in advance 2 Independently adjust preoperative orders for nonpreferred preoperative antimicrobials, such as clindamycin and	Surgeons, Hospital, (one-on-one)	Messaging system in the EMR	Patient registry	CPA criteria	Before procedure	Once	None

(continued on next page)

Table 2 (*continued*)

Study	Pharmacist action(s)	Recipient, Setting, (Mode of Contact)	Methods of communication	Clinical data sources	Source of guide for intervention	Timings of action	Frequency of contacts	Supportive materials
	vancomycin, to preoperative cefazolin							
Yang et al., 2019	1 Direct patient care during hospitalization 2 Reviewing medication regimens 3 Resolving medication-related problems 4 Medication reconciliation 5 Answering drug information questions 6 Therapeutic drug monitoring (TDM) 7 Making therapeutic recommendations 8 Patient education	Patients and physicians, Hospital bedside, (one-on-one, contact with group)	Face to face	Not reported	Not reported	On or during patient admission	Continuous	None
Zhang et al., 2014	1 Collect patient information from EMR 2 Judge the appropriateness of prophylactic antibiotics 3 Communicate with surgeons offering suggestions 4 Feedback to hospital administrators 5 Continuous monitoring 6 Summarize and report findings to hospital administration	Physicians, Hospital, (one-on-one)	Face to face	Medication chart	Hospital guidelines	Pre-operative	Continuous	None
Zhou et al., 2016	1 Participate in ward rounds and making drug treatment plans 2 Communicate with surgeons when irrational antibiotics were prescribed 3 Provide educational sessions and handouts about antibiotic prophylaxis for medical teams 4 Extract the medical records and assessing using an auditing system 5 Report the categorized data on irrational use of prophylactic antibiotics every week	Medical staff, Hospital bedside and hospital, (one-on-one, contact with group)	Face to face	EMR	STSP and NHFPC guidelines	On or during patient admission	Continuous	Post educational session handouts
Zhou et al., 2021	1 Join the treatment team in ward rounds 2 Conduct medication reconciliation 3 Inquire/reassess the patient's allergy history 4 Provide a standard concentration of skin test solution 5 Provide training to all the medical staff	Patients and medical staff, Hospital bedside and hospital, (one-on-one, contact with group)	Face to face	EMR	Approved hospital protocol	On or during patient admission	Continuous	Written action plan
Zhou et al., 2023	1 Participate in daily rounds 2 Discuss with physicians to formulate perioperative antibiotic prophylaxis norms 3 Instruct the implementation of anti-infection plan by nurses 4 Distribute of brochures on antibacterial drugs for health care providers 5 Provide special lectures on rational use of antibiotics every quarter	Patients and medical staff, Hospital bedside (rounds, clinic) and hospital, (one-on-one, contact with group)	Face to face	EMR, outpatient clinic revisit records, telephone follow-up data	NHFPC Guidelines, published official documents	During admission	Continuous	Brochures

(*continued on next page*)

Table 2 (*continued*)

Study	Pharmacist action(s)	Recipient, Setting, (Mode of Contact)	Methods of communication	Clinical data sources	Source of guide for intervention	Timings of action	Frequency of contacts	Supportive materials
	6 Follow up the infection complications and readmission of patients at 6 months postoperatively							

EMR: electronic medical record; N/A: not applicable; SAP: surgical antibiotic prophylaxis; ASHSP: American Society of Health-System Pharmacist; CPA: collaborative practice agreement; STSP: Society of Thoracic Surgeons Practice; NHFPC: National Health and Family Planning Commission of the People's Republic of China.

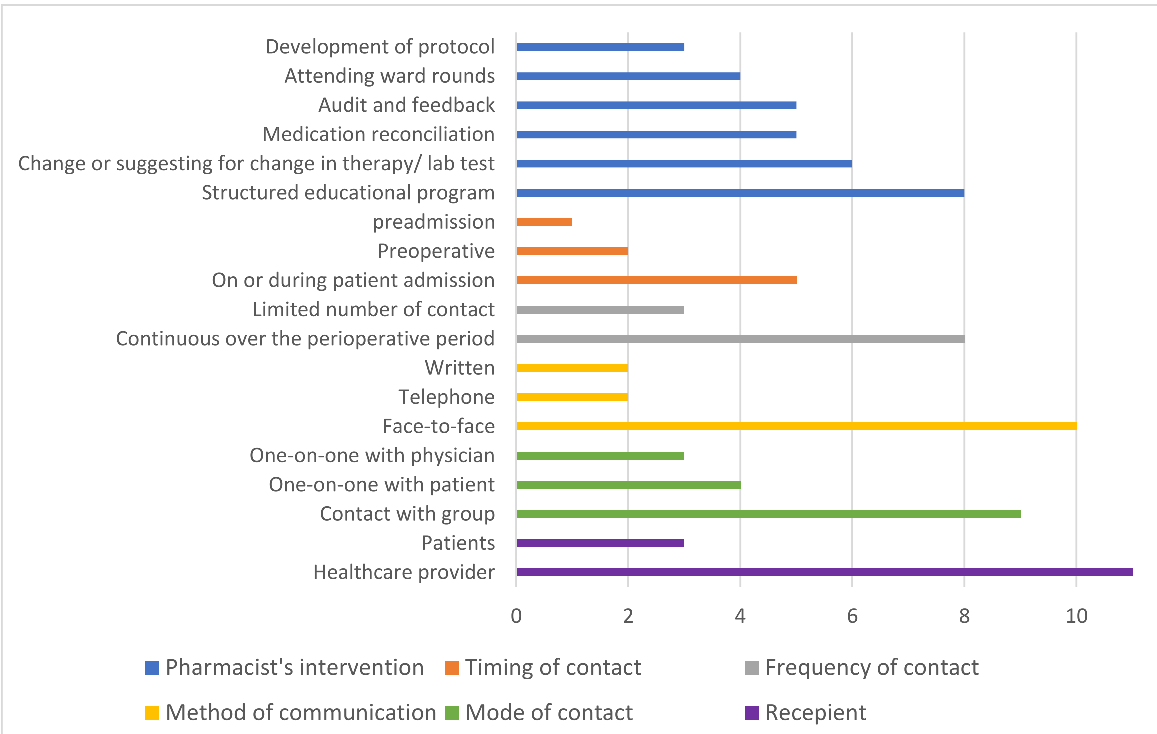

Fig. 3. Summary of the pharmacist-led AMS programs characteristics using DEPICT-2 tool.

(95%CI 31.7–37.7) vs 56.4 % (95 % CI 53.1–59.6); P < 0.0001],[45] while Kwiatkowski et al. (2021) reported a non-significant decrease in time to incision by 8 min in the intervention as compared to the control group (P = 0.848).[40]

3.5.3.2. Appropriate duration. Seven studies looked into the appropriate duration of antimicrobial prophylaxis duration between groups,[35,39,41–45] of which five have been pooled into a meta-analysis.[35,39,41,43,44] The pooled OR was 5.27 (95 % CI 1.58–17.55, P = 0.007; I^2 = 96 %) favoring the intervention group (n = 2575 patients, 1212 control; 1363 intervention) (Fig. 4C).

The two studies that were not included in the meta-analysis also showed a significant improvement in the adherence to the appropriate duration of use. Brink et al. (2017) reported a significant improvement in the adherence to duration of antimicrobial prophylaxis in the intervention group [80.8 % (95 % CI 79.0–82.5) vs 93.9 % (95 % CI 88.1–99.6); P < 0.0001].[45] Likewise, Yang et al. (2019) reported a mean duration of 6 days in the intervention group versus 13.41 days in the control group.[42]

3.5.3.3. Appropriate dose. Appropriateness of dose was only examined in two studies.[43,45] Brink et al. (2017) demonstrated a higher rate of 87.0 % (95 % CI 81.3–92.8) in the intervention group for prescribing the recommended dose as compared to 70.5 % (95 % CI 67.1–73.9) in the control group (P = 0.0002).[45] Zhou et al. (2023) also reported a significantly more appropriate dosage in the intervention group (96.6 %) as compared to usual care (83.9 %; P < 0.001).[43]

3.6. Outcomes related to infections

In this section, we report findings in relation to infection outcomes as follows[1]: SSI,[2] postoperative infections,[3] *Clostridium difficile* infection. We conducted a meta-analysis for the impact of pharmacist-led AMS programs on SSI, which is also presented in this section.

3.6.1. Surgical site infection (SSI)

Of the 11 included studies, six reported outcomes related to the impact of pharmacist-led AMS strategies on SSI.[35,40–45] Three of these studies aligned with the Centers for Disease Control and Prevention (CDC) definition of SSI which recommend measuring SSI rate at 30 days postoperatively[35,40,45]; however Abubakr et al. (2019) indicated that they only followed patients for the duration of hospitalization. Elnour et al. provided their own operational definition which was consistent with the CDC one at measured the SSI at 30-day.[44] A China-based study adopted a national definition which also recommend evaluating SSI after 30 days of the surgery.[41] Zhou et al. (2023) was the only study that did not provide a definition or a timepoint for which the outcome was assessed.[43]

Five of the six studies were included in the meta-analysis intervention as outcome rates were already reported or were calculable using

Table 3
Outcomes of pharmacist-led AMS programs.

Study	Follow up duration	Compliance to protocol/ procedure	Antibiotic selection	Appropriateness of AMS procedures	Infection-related outcomes
Abubakar et al., 2019 rowhead	Duration of hospitalization	Not reported	- Prescription of 3rd generation cephalosporin 29.2 % vs 20.6 %, P = 0.032 - Rate of redundant antibiotic prescription: 70.8 % vs 51.7 %, P < 0.001 - DDD of surgical antibiotic prophylaxis/procedure: 16.6 ± 3.6 vs 12.8 ± 6.8 P < 0.001	- Compliance with timing: 32 (14.2 %) vs 103 (43.3 %), P < 0.001 - Compliance with duration: 0 (0 %) vs 52 (21.8 %), P < 0.001	- SSI: 4 % vs 3.4 %; P = 0.722
Brink et al, 2017	30–90 days	Overall mean % compliance rate 66.8 % (95 % CI 64.8–68.7) vs 83.3 % (95 % CI 80.8–85.8), P < 0.0001	- Antibiotic choice consistent with the guideline: 81.2 % (95 % CI 78.5–83.8) vs 95.9 % (95 % CI 89.9–100); P = 0.0004	- Timely administration: 34.7 % (95% CI 31.7–37.7) vs 56.4 % (95 % CI 53.1–59.6); P < 0.0001 - Prescribe the recommended dose: 70.5 % (95 % CI 67.1–73.9) vs 87.0 % (95 % CI 81.3–92.8); P = 0.0002 - Prescribe the recommended duration: 80.8 % (95 % CI 79.0–82.5) vs 93.9 % (95 % CI 88.1–99.6); P = 0.0005	- SSI rate: 2.46 (95 % CI 2.18–2.73) vs 1.97 (95 % CI 1.79–2.15), 19.7 % decrease; P = 0.0029
Butt et al, 2019	Not reported	Correct choice, dose, frequency & duration: 3 (1.3 %) vs 28 (12.4 %), P = 0.0005	- Average number of antibiotics used: 2.09 ± 0.902 vs 1.86 ± 0.859, P = 0.006 - Appropriate drug choice: 26 (11.6 %) vs 63 (28 %), P = 0.0005 - First generation cephalosporin (cefazolin): 34 (15.1 %) vs 53 (23.6 %), P = 0.031 - Vancomycin: 17 (7.6 %) vs 11 (4.9 %), P = 0.329)	- Duration of antibiotic use: 66.01 ± 41.01 h vs 55.20 ± 36.21 h, P = 0.003 - Duration of antibiotic usage (12–60 h): 128 (57.1 %) vs 150 (67 %), P = 0.032	Not reported
Elnour et al, 2022	14 days	Adherence to SAP protocol: 43.6 % vs 56.7 %, P < 0.001	- Adherence to first generation cephalosporin (cefazolin): 59 (52.2 %) vs 78 (69 %), P < 0.001	- Prescribed at the time of anesthesia induction or at 1 h before operation:75 (66.4 %) vs 87 (77 %), P < 0.001 - The recommended duration of SAP: 46 (44.2 %) vs 71 (62.8 %), P < 0.001	- SSI: intervention: 42.5 %–25.7 %, control: 57.5 %–44.2 %; P = 0.001
Kwiatkowski et al, 2021	30 days	Not reported	- Cefazolin use: 14/50 (28 %) vs 24/ 37 (65 %); P = 0.001 - Vancomycin use: 19 (38 %) vs 22 (59 %); P = 0.047	- Time to incision decreased by a median of 8 min; P = 0.848	- SSI: 5 (10 %) vs 0 (0 %); P = 0.051 - *C. difficile*: 1 2 % vs 0 (0 %); P = 0.387
Lessard et al, 2023	Duration of hospitalization	Not reported	- Preferred preoperative antimicrobial prophylaxis utilization (DOT/1000 PD): cefazolin: 81.3 (86 %) vs 90.6 (96.3 %), P < 0.001 - Nonpreferred preoperative antibiotics prophylaxis utilization (DOT/1000 PD): clindamycin: 1.9 (2.1 %) vs 0.2 (0.2 %), P < 0.001; vancomycin: 2.7 (3.2 %) vs 0.5 (0.4 %), P < 0.001	Not reported	Not reported
Yang et al, 2019	30 days	Not reported	- AUD: 68.42 vs 52.37	- Mean duration: 13.41 vs 6.02 days	- Postoperative infections: 7.1 % vs 7.5 %; P = 0.57 - *C. difficile*: 3.33 % vs 5.95 %; P = 0.49
Zhang et al, 2014	Duration of hospitalization	Not reported	- Correct antibiotic choice rate: 20 (22.72 %) vs 55 (68.75 %); P < 0.001 - Unnecessary prophylaxis: 83 (48.54 %) vs 68 (35.23 %), P < 0.001 - Rate of using 2nd-generation cephalosporins: 5 (1.7 %) vs 129 (65.8 %), P < 0.001 - Rate of using 3rd & 4th generation cephalosporin: 106 (36.05 %) vs. 30 (15.31 %), P < 0.001	Not reported	Not reported
Zhou et al, 2016	Not reported	Not reported	- Patients receiving rational prophylactic antibiotic selection: 144 (42.1 %) vs 483 (95.1 %), P < 0.001	- Proportion of patients receiving antibiotic prophylaxis for <48 h: 12 (3.5 %) vs 183 (36.0 %), P < 0.001	- SSI rate: 12 (3.5 %) vs 6 (1.2 %); P = 0.02

(*continued on next page*)

Table 3 (*continued*)

Study	Follow up duration	Compliance to protocol/ procedure	Antibiotic selection	Appropriateness of AMS procedures	Infection-related outcomes
			- Unnecessary changes of prophylactic antibiotics: 60 (17.5 %) vs 33 (6.5 %), P < 0.001	- First prophylactic antibiotic dose in appropriate time frame: 157 (45.9 %) vs 496 (97.6 %), P < 0.001	
Zhou et al, 2021	Duration of hospitalization	- Number of patients receiving intradermal skin tests: 407 (95.8 %) vs 74 (16.5 %); P < 0.001	- Use of cephalosporin for perioperative antibacterial prophylaxis: 355 (83.5 %) vs 433 (96.6 %); P < 0.001 - Clindamycin: 28 (6.6 %) vs 4 (0.9 %), P < 0.001 - Vancomycin: 36 (8.5 %) vs 7 (1.6 %); P < 0.001	Not reported	Not reported
Zhou et al, 2023	6 months	Not reported	- Appropriate antibiotic selection: 230 (97.5 %) vs 234 (99.2 %), P = 0.285 - Medication prevention: 236 (100 %) vs 228 (96.6 %), P = 0.007 - Medication selection: irrational use of post OP cefonicid 34 (14.4 %) vs 0 (0 %), P < 0.001; 1st/2nd generation cephalosporin: 230 (97.5 %) vs 223 (94.5 %), P = 0.101	- Timing of administration: (within 0.5–1hr before surgery) 181(76.7 %) 210(92.1 %), P < 0.001; (less than 0.5h before surgery) 42 (17.8 %) vs 8 (3.5 %), P < 0.001 - Timely administration:185 (78.4 %) vs 223 (94.5 %), P < 0.001 - Medication duration (<24hr): 89 (37.7 %) vs 144 (63.2 %), P < 0.001; (24–48): 62 (26.3 %) vs 48 (21.1 %), P = 0.186; (>48hr): 85 (36.0 %) vs 36 (15.8 %), P < 0.001 - Duration appropriateness: 89 (37.7 %) vs 152 (64.4 %), P < 0.001 - Dosage appropriateness: 198 (83.9 %) vs 228 (96.6 %), P < 0.001	- Postoperative infections: 3.8 % vs 2.5 %; P = 0.431 - Incision-related infections: 3.0 % vs 1.3 %; P = 0.201

AMS: antimicrobial stewardship; SAP: surgical antibiotic prophylaxis; DOT/1000 PD: Days of therapy/1000 patient days; AUD: antibiotic use density.

raw numerator and denominator data.[35,40,41,43,44] Compared with the before period of usual care, pooled analysis of all interventions reduced the risk of SSI by (OR 0.51; 95 % CI 0.34–0.77, P = 0.001; $I^2 = 0$) (Fig. 4D).

Brink et al. (2017) was the only study that was not included in the meta-analysis, and it reported SSI at 30 or 30–90 days for superficial incisional or deep incisional procedures, respectively; however only a composite SSI rate (not specified) was reported. Findings showed a statistically significant reduction in SSI rate from a mean group rate of 2.46 (95 % CI 2.18–2.73) pre-intervention to 1.97 postintervention (95 % CI 1.79–2.15; P = 0.0029).[45]

3.6.2. *Postoperative infections*

Three studies investigated the rates of postoperative infections, all of which did not favor the pharmacist intervention group. Zhang et al. (2014) and Zhou et al. (2023) demonstrated insignificant reductions in the incidence of all-cause postoperative infections of [3 (1.72 %) to 3 (1.53 %); P = 0.883] and [9 (3.8 %) to 6 (2.5 %); P = 0.431], respectively.[37,43] Yang et al. (2019) also revealed a non-significant difference in the incidence of infection between arms (7.1 % vs 7.5 %, P = 0.57). It is noteworthy that none of the studies reported a definition or the timepoint at which the outcome was measured.

3.6.3. *Clostridium difficile (C.difficile) infection*

Only two studies compared the incidence of *C. difficile* between both groups and neither showed an association between pharmacist interventions and the decline in C.difficile incidence. Kwiatkowski et al. (2021) adopted the IDSA definition and showed a non-significant difference in the incidence of C.difficile between groups [1 (%2) vs 0; 0.387).[40] Similarly, Yang et al. showed a slight reduction in the incidence of C.difficile, yet insignificant (5.95 % vs 3.33 %; P = 0.49).[42] The latter did not provide a definition for this outcome.

3.7. *Publication bias*

Potential publication bias was evaluated by constructing funnel plots and using Egger's test (Fig. 4). There was some indication of asymmetry in the funnel plot for the antibiotic selection appropriateness, implicating some publication bias as evidenced by Egger's (P = 0.029) (Fig. 5A). No significant publication bias was noted with the duration, timeframe, and SSI outcomes (P = 0.11, P = 0.505, P = 0.592, respectively) (Fig. 5B, C, 5D).

4. Discussion

4.1. *Statement of principle findings*

To our knowledge, this is the first systematic review and meta-analysis to investigate pharmacist roles in AMS and the impact of pharmacist-led AMS programs on antibiotic prescribing and subsequent clinical findings in perioperative setting. Pharmacist interventions were multifactorial and consisted of four main elements: education and training; daily clinical duties (e.g. medicines optimization and medication management); audits and feedback; and protocol development. Nevertheless, none of the included studies reported on the development of the implemented interventions. The meta-analyses showed that pharmacist-led AMS interventions are associated with improved surgical antibiotic prophylaxis prescribing; appropriate antibiotic (OR 4.29, 95 % CI 2.52–7.30; P < 0.001), appropriate timeframe (OR 4.93, 95 % CI 2.05–11.84, P = 0.0003), and appropriate duration (OR 5.27, 95 % CI 1.58–17.55, P = 0.007). The analysis also showed a significant reduction in SSI in perioperative settings (OR 0.51; 95 % CI 0.34–0.77, P = 0.001).

4.2. *Characteristics of pharmacist interventions*

All studies, except for one, reported the implementation of multifaceted interventions which included a wide range of pharmacist-led AMS activities (such as education, direct patient care, audits and feedback, protocol development). Our findings concur with previously published systematic reviews on pharmacist-led AMS in various settings which also identified multifaceted interventions as a common occurrence.[10,23,24] There is a growing body of evidence supporting multitargeted interventions as they are more likely to enhance the compliance with target AMS practice, and to ensure the sustainability of the

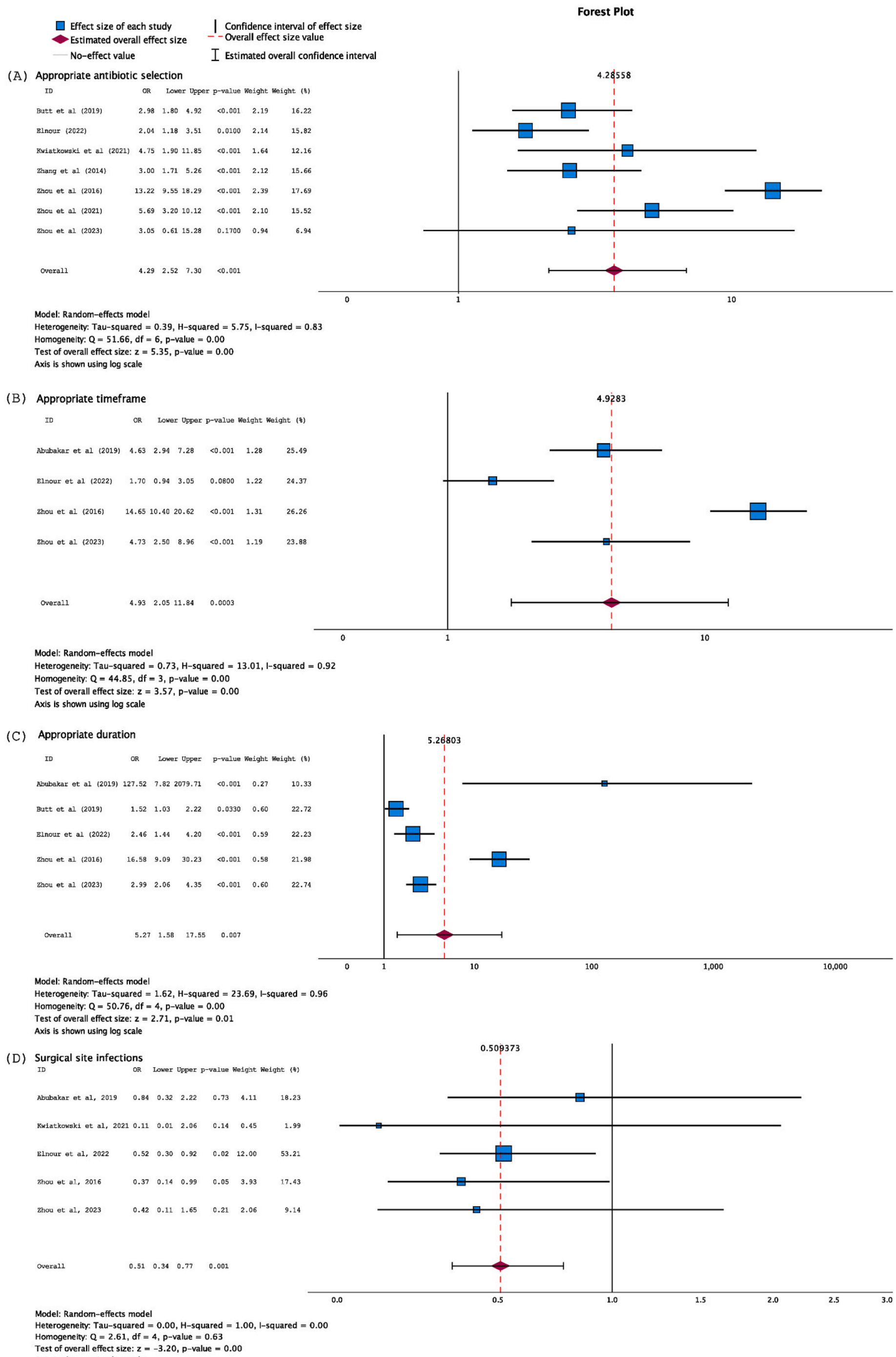

Fig. 4. Forest plots displaying the effect of the intervention on (A): appropriate antibiotic selection; (B): appropriate timeframe; (C): appropriate duration; (D) surgical site infection.

behavior change induced by the interventions.[1,5,10,46]

Education delivered to other healthcare professionals was the major intervention used by pharmacists to improve antimicrobial prescribing in perioperative settings. There is wealth of evidence about the effectiveness of educational interventions in influencing the prescribing behaviors and optimizing prescribing attitudes.[5,10,47–53] For instance, a meta-analysis by Saha et al. showed that education provided to general practitioners including dedicated lectures, academic detailing, and workshops have resulted in a significant increase in antibiotic prescribing adherence rates (OR 1.96, 95 % CI 1.56–2.45).[50] Additionally, dissemination of educational information through brochures, handouts, written plans, or posters can serve as an important mean to improving antibiotics use and sustaining the modified behavior of prescribing.[1] A cross-sectional study by Landgren et al. targeting the perioperative antibiotic prophylaxis through an educational campaign reported an initial improvement in prescribing behavior; however this effect was unsustainable over the 12 months follow-up period.[48] A Cochrane review on the other hand noted that the dissemination of educational materials was associated with improved sustainability of appropriate antibiotic use, as opposed to education alone.[5] Only four of the included studies in this review reported the dissemination of supportive materials; whether the positive effect on antibiotics use was maintained in any of the included studies cannot be fathomed due to the short follow-up durations.

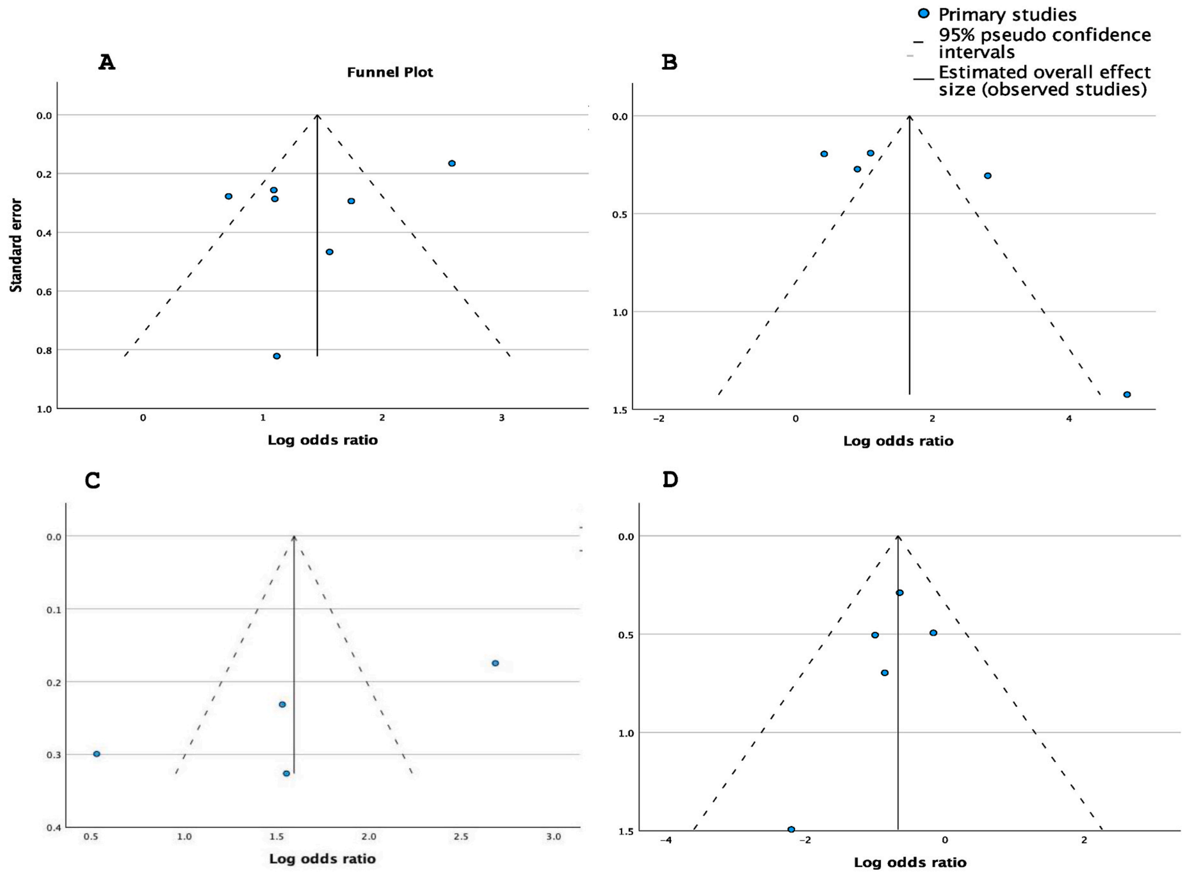

Fig. 5. Funnel plots to assess the publication bias for studies assessing pharmacist-led antimicrobial stewardship programs on (A): appropriate antibiotic selection; (B): appropriate timeframe; (C): appropriate duration; (D) surgical site infection.

Prospective audits and feedback technique is one of two core elements recommended by the IDSA and CDC for effective AMS implementation.[1,54] The goal of this technique is to improve the use of antibiotics while reducing undesired consequences (e.g. antimicrobial resistance, adverse events) in real time. The process involves assessing appropriateness of antibiotics prescriptions with regards to indication, drug choice, dose, route, and duration.[1,55] Once a thorough assessment is done, suggestions of change in regimens and feedback are communicated to the primary team. This process is typically carried on by a clinical pharmacist with AMS training.[55] Audits and feedback have been repeatedly proposed as an effective strategy in encouraging sustainable practice change.[5,10,56] It is associated with improving antimicrobial use in various settings (including community hospitals, pediatric care, intensive care units, and oncology wards) without negative effects on other clinical outcomes.[1,10] Despite its well-established role, audits and feedback have been described in only five out of the eleven included studies, indicating a room for improvement in terms of engaging pharmacists in hospital auditing and feedback activities in the perioperative settings.

Three studies described the pharmacist's involvement in the development of institutional protocols targeting perioperative antimicrobial use. Additionally, four studies reported institutional guidelines to be their main source of guidance for the intervention. Utilizing a facility-specific therapeutic guideline that is tailored to the hospital's needs and resources have been emphasized by the IDSA and the CDC as one of the prioritized and recommended actions for a seamless integration of AMS in hospital settings.[1,54] Implementing facility-specific pathways consistently yielded positive effects in the utilization of antibiotics; specifically, appropriate choice of initial therapy, selecting a narrower-spectrum antibiotic, shortening duration of use, and early intravenous-to-oral switch.[1]

There is a dearth of data on the development of the implemented interventions in terms of structure and processes. Whilst it was noted that most reviews relied on local or international guidelines as the scientific basis for the intervention, no further details were provided. Additionally, none of the embedded studies explicitly mentioned an underlying theory in their development of the interventions. With an explicit theoretical rationale, interventions could be more effective and better replicated in other contexts if the mechanism of action was better understood.[57–60] The absence of reporting of the theoretical underpinnings of the included interventions prevented us from drawing any conclusions in regard to the impact of theory-informed interventions in this area. Michie et al. elucidated that even if the theory-driven intervention does not yield a favorable findings in favor of the intervention, it helps to identify, from a huge array, the intervention components that might work.[61]

Multiple resources have emphasized on the need for a direct and verbal communication between the provider of interventions and prescribers when sharing insights related to AMS, as it has been proven to be more effective and even an integral part in some cases.[1,10,54,56] Direct communication was one of the four main pharmacist-reported facilitators to the implementation of sustainable AMS programs in hospital settings; it was perceived as an enabler for an interactive discussion between pharmacists and prescriber that would lead to greater acceptance and engagement with AMS activities.[56] In a systematic review of 52 studies to evaluate the impact of pharmacist-led education-based AMS interventions, 30 studies demonstrated a positive impact for the use of verbal communication with prescribers across diverse settings.[10] In the current review, most studies utilized direct face-to-face interactions, reflecting the effectiveness of this mode of contact on antimicrobial use.

4.3. Surgical antimicrobial prophylaxis prescribing

This review revealed a significant increase in guideline compliance and reducing duration of antimicrobial therapy. Similar findings have been described by two other systematic reviews and meta-analyses. Monmaturapoj et al. included nine studies assessing the effectiveness of educational-based interventions on the practice of antimicrobial prophylaxis.[10] Eight of these studies have incorporated multicomponent interventions of education and audit and feedback, which demonstrated significant improvements in AMS practices, including appropriate antimicrobial agent selection, timing of first dose prior to surgery, and duration of prophylaxis. Similarly, Saha et al. reported a significant reduction in antibiotic prescribing rate (OR 0.86, 95 % CI 0.78–0.95) and improvement of antibiotic prescribing adherence rate (OR 1.96, 95 % CI 1.56–2.45) at 6 months follow-up after the implementation of the pharmacist intervention.[50]

Three studies included in this review have discussed the pharmacist role in perioperative settings in patients with penicillin allergies.[36,40,43] Interventions included reassessment of allergy status and referral to allergy specialist if needed. Two of these studies have reported a significantly increased use of the preferred antibiotic prophylaxis agent (cefazolin),[36,40] whereas one reported a comparable use of cephalosporins in both groups.[43] The IDSA recommends the promotion of allergy assessments in patients with beta-lactam allergy, when appropriate, as it could potentially improve AMS practices through selection of antibiotic choice, inflation in adherence to guidelines, and reducing length of hospital stay and costs.[1] In a prospective observational study, a collaborative work between pharmacists and allergists led to a significant increase in beta-lactam prescriptions in patients with documented allergy (26 % vs 66 %; $P < 0.0001$).[62] This reinforces the emerging evidence that proposes potential additional roles for pharmacists in perioperative settings.

4.4. Infection-related outcomes

Antimicrobial prophylaxis is the single most effective intervention to reduce the risk of SSI; however, prescribing practices should be aligned with accepted SAP regimens to be effective.[63–65] In fact, a study that examined surveillance data for 144,075 surgical procedures concluded that there is an association between the risk of SSI and failure to comply with the protocols in relation to the selection and timing of administration of the antimicrobial agent.[66] Therefore, and in compliance with the IDSA recommendations, we investigated the impact of pharmacist-led AMS strategies on infection-related outcomes including SSI, postoperative infections, and C.difficile infections.[1] Our findings showed that pharmacist-led AMS practices are effective in reducing the incidence of 30-day SSI in perioperative settings. A previous systematic review of fourteen studies with a bundle of interventions showed that 28.5 % of included studies led to a reduction in surgical site infection rate.[9] Nonetheless, this study did not focus on pharmacist interventions nor pooled the data from included study.

We also looked into the impact of pharmacist AMS interventions on postoperative infections and *C. difficile* infections. However, these outcomes were seldom examined in the literature and the current evidence is of poor quality which resulted in conflicting findings. Additionally, the studies lacked a description for the adopted definition and for the timepoint at which it was measured. Hence, we could not draw any conclusions in relation to these outcomes.

4.5. Strengths and limitations

This study goes beyond the traditional method of exploring the impact of AMS practices, which usually focuses on procedural aspects and adherence to appropriate AMS practices, to also investigate if this improved adherence reflects improvement in clinical findings (i.e. SSI). It is noteworthy that, to our knowledge, our study is the first to examine the impact of pharmacist-led AMS strategies on both prescribing and clinical findings across all healthcare settings and patient subsets. This is pivotal as it complies with the IDSA recommendations which indicated that SSI should be explored to ensure that improved adherence will be translated into patient-related findings.[1] The DEPICT-2 tool was used for systematic extraction and analysis of the intervention's core components amongst included studies, which eliminated the rater effect and, hence, provided more consistency to our results.[28] The reporting of this systematic review followed PRISMA guidelines[67] and the protocol was registered on PROSPERO.

There are a number of limitations to our study. First, high heterogeneity was noted with performed analyses, which could be attributed by the diversity of surgical units included in the studies as well as the varied interventions carried out by pharmacists in each study. Second, the sample size of included studies was relatively small and reflected in the total number of events in the pooled data; however, statistical significance was reached in all performed analyses, indicating that current sample sizes provided adequate power. Third, the included studies had a relatively short duration of follow-up (i.e. less than 12 months), which raises questions regarding the sustainability of the interventions. Fourth, although findings on SSI were promising; this evidence is generally of moderate quality and insufficient volume.

4.6. Impact of the findings on research, practice, and policy

Findings from our review highlighted the effectiveness of multi-component pharmacist-led AMS programs in perioperative settings, which includes education, audits and feedback, daily clinical duties (i.e. direct patient care such as medication reconciliation, treatment optimization, and attending daily rounds), and protocol development. Therefore, we encourage policy makers to consider the implementation of pharmacist-led AMS interventions in these settings. We also recommend the dissemination of educational materials (e.g. handouts/brochures) as part of any educational initiative, as it serves as a reminder for healthcare providers which could potentially improve the sustainability of the favorable effects. Moreover, we recommend educational sessions that are based on structured needs assessment as they are expected to improve outcomes.[68] Additionally, we advise that future interventions incorporating pharmacists in the auditing and feedback procedures.

There was a lack of consideration of behavioral theories in intervention development. Prescribing decisions of physicians is a complex process that is influenced by multiple interacting factors.[69] Despite the available literature on opinions and predictions of the physician's prescribing-decisions and behaviors, no single hypothesis can explain or encompass all factors associated with this process. Thus, complex theoretical frameworks [such as the theory of planned behavior (TPB),[70] theoretical domains framework (TDF)[71] and behavior change taxonomy (BCT)[72]] have been designed to enhance our understanding of how several factors can simultaneously influence the prescribing behaviors.[69] Additionally, the use of theoretical constructs is more likely to yield positive and sustainable results compared to pragmatic approaches.[57–59] Additionally, the gathering of more gold standard evidence such as RCTs is essential to enable measuring the impact of pharmacists AMS intervention in perioperative settings. There is therefore a need for a well-designed, systematic and comprehensive study of a theory-derived pharmacist-led intervention aiming to target different factors influencing the prescribing behavior.

A high variation in the methods of describing the interventions has been observed amongst included studies. Additionally, many studies reported insufficient information regarding the intervention which could hinder its reproducibility. Therefore, we endorse the use of the DEPICT-2 tool as it can standardize the process of reporting, collecting, and synthesizing data pertaining to pharmacist interventions.[28,73]

Whilst the current evidence from this review supports the positive impact of pharmacist-led practices on reducing SSI; this evidence is generally of moderate quality and insufficient volume. Hence, we encourage future researchers who are interested in investigating AMS practices to also assess the impact of these practices on SSI.

5. Conclusion

Pharmacist-led AMS programs were effective in enhancing the appropriateness of antibiotic selection, timely administration, reducing duration of antimicrobial therapy, and reducing SSI; however most studies were of moderate quality. The most common pharmacists-provided services were educational sessions, multidisciplinary ward rounds, audits and feedback, and development of institutional guidelines. The discussion of interventions lacked details on the development. Studies lacked the utilization of theory to develop interventions, therefore, it is not clear whether theory-derived interventions are more effective than those without a theoretical element. High-quality, multicomponent, theory-derived, interventional studies using appropriate methodology and standardized data collection, are needed.

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Ethical approval

Not required.

Availability of data

All data generated or analyzed in this systematic review are included in this article and/or its figures. Further inquiries can be directed to the corresponding author.

CRediT authorship contribution statement

Lina Naseralallah: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Somaya Koraysh:** Writing – original draft, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Bodoor Aboujabal:** Writing – review & editing, Project administration, Methodology, Data curation. **May Alasmar:** Writing – review & editing, Project administration, Methodology, Data curation.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sapharm.2024.08.006.

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