

RESEARCH

Open Access



The impact of antimicrobial stewardship interventions on appropriate use of surgical antimicrobial prophylaxis in low- and middle-income countries: a systematic review

Israel Abebrese Sefah^{1,2*} , Sarentha Chetty¹, Peter Yamoah² and Varsha Bangalee¹

Abstract

Background Surgical antimicrobial prophylaxis (SAP) is an effective infection prevention strategy used to reduce postoperative surgical site infection. Inappropriate use of SAP is a concern in low-middle-income countries (LMICs) due to increased mortality risks, adverse reactions, re-admission rates and length of hospital stay. Antimicrobial Stewardship Programs (ASP) have been shown to be effective in improving the appropriate use of antibiotics including the use of SAP. The aim of this review was to evaluate the impact of ASP on the appropriate use of SAP and its implication on patient outcomes in LMICs.

Method The protocol for this review was registered in PROSPERO. Studies published between 1st January 2010 and 31st December 2023 were searched electronically from Medline, Central Cochrane Library, web of science, CINAHL and APA PsychInfo databases. Studies were included if they assessed the impact of ASP interventions on SAP use in low- and middle-income countries (LMICs). Studies were evaluated using the Risk of Bias in Non-Randomized Studies-of Interventions (ROBINS-I) tool for non-randomized and before and after studies as well as the Cochrane Risk of Bias 2 (ROB 2) tool for randomized studies. Findings were summarized in tables.

Results Twenty studies comprising of seventeen before-after studies, two interrupted time series, and one randomized controlled trial were included. Penicillins and cephalosporins were the most commonly used antibiotics for SAP. Most (50%) of the studies were conducted in Asia followed by Africa (45%). While 80% of the studies showed the impact of ASP on compliance to SAP guidelines, only 45% showed an impact on antibiotic utilization. Again, 50% and 60% showed an impact on reducing antibiotic costs and patient length of stay at hospitals respectively. Patient outcomes including rates of surgical site infections and mortality showed no significant change. The studies showed a high risk of bias mainly due to the choice of study designs.

Conclusion ASP interventions in LMICs are effective in improving SAP guideline adherence, antibiotic utilization and their cost. Deliberate effort must be made to improve on the quality of future interventional studies in these settings to guide practice and encourage other LMICs to conduct such studies to assess the influence of different geographical contexts on SAP use.

*Correspondence:

Israel Abebrese Sefah
isefah@uhas.edu.gh

Full list of author information is available at the end of the article



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

Keywords Surgical antimicrobial prophylaxis, Antimicrobial Stewardship Programs, Surgical site infection, Intervention, Antibiotics, Guideline

Introduction

Antimicrobial resistance (AMR) is a global public health problem with an appreciable burden in terms of both morbidity and mortality currently seen in sub-Saharan Africa [1–3]. The World Health Organization (WHO) has responded to this threat through the development of a Global Action Plan to combat AMR in 2015 which has propelled member states to develop their own AMR policy and action plans [4, 5]. It has been estimated that the burden of deaths from AMR could rise to 10 million each year by 2050, along with cost implications, if swift action is not taken to slow or combat AMR [6, 7]. Irrational and excessive use of antimicrobials are known to be key drivers of increasing AMR especially in low- and middle-income countries (LMICs), where poor health outcomes are exacerbated by several factors including poor hygiene, malnutrition and lack of adequate infrastructures [8]. LMICs are countries with income groupings belonging to either low, lower middle or upper middle based on their gross national income (GNI) per capita ranging between 1145 or less and 14,005 as defined by the World Bank [9, 10]. LMICs are known to have higher rates of antibiotic consumption and AMR rates due to the relatively easy access to antibiotics by the public as well as higher rates of utilization of antibiotics in the ‘Watch’ group; which have greater resistance potential [11, 12]. The global consumption of antibiotics increased by 65% between 2000 and 2015, and this has been said to be principally driven by their increased usage in LMICs [13–15]. Therefore a study that assesses the impact of interventions on antimicrobial use in these low healthcare resource settings will provide valuable lessons to guide future policies and practices on the use of cost-effective interventions to reduce AMR rates [16].

One of the major contributors to the inappropriate use of antimicrobials in hospitals is their overuse and misuse as prophylaxis in surgery, which is a problem, especially in LMICs [17–19]. Surgical antimicrobial prophylaxis (SAP) is part of the many effective infection prevention strategies used to reduce postoperative infection at a surgical site [20]. This is performed by administering the appropriate antibiotic at the correct frequency and duration, usually as a single dose for clean, clean-contaminated, and contaminated surgical procedures before incision [21–23]. The efficacy of SAP depends on the choice, dose, timing and duration of administration [23–27]. The inappropriate use of SAP increases mortality risks arising from surgical

site infections (SSIs) as well as increasing adverse reactions, re-admission rates, length of hospital stay, potential colonization and infection with *C. difficile*. It is also associated with increasing costs as well as increasing AMR through increased selective pressure on microorganisms due to misuse and overuse of SAP [28–31]. Several audits and point prevalence surveys in LMIC have also confirmed the inappropriate use of SAP especially due to multiple administrations beyond 24 h following surgery, which can drive increasing AMR rates [21, 28, 32–36]. Studies in LMIC have estimated a high cumulative incidence of SSI arising from all types of surgeries [32, 37–40]. SSIs have also been identified as one of the three most common causes of healthcare-associated infections (HAIs), affecting approximately one-third of patients who have gone through surgery, especially in LMICs. It is said to account for up to 60% of HAIs leading to increased morbidity, mortality and costs globally [41, 42]. There is data to suggest that 60% of SSIs can be prevented by strict adherence to clinical guidelines including their optimal use of SAP [31].

Antimicrobial Stewardship Programs (ASPs) have been identified by the WHO and others as one of the three pillars of an integrated approach to health systems strengthening to reduce inappropriate antibiotic prescribing and associated AMR [43, 44]. The need to optimize antimicrobial use through effective implementation of ASPs in all health facilities is an integral component of one of the five strategic objectives of the Global Action Plan and the National Action Plans of member countries including LMICs [45–49].

ASP interventions such as education/training, prospective audit of antibiotic prescriptions, development of guidelines, computerized decision support, and formulary restriction of last resort antibiotics have shown to be effective in improving the appropriate use of antibiotics including the use of SAP [21, 31, 50, 51]. These interventions have a positive impact on clinical outcomes, economic outcomes and microbiological outcomes [15, 51]. These have been backed by several systematic reviews that have shown the impact of these interventions on antibiotic use though with varying challenges [15, 50–55]. This includes the systematic review by Martinez-Sobalvarro et al. (2022) which suggests that 60% of SSIs can be prevented by strict adherence to clinical guidelines including their optimal use of SAP [31]. Some of these interventions which are persuasive in nature include education of all

key stakeholders, audit with feedback and ward rounds that offer real-time feedback, whereas others that are restrictive in their implementation include formulary restrictions, automatic stop orders and pre-authorization measures for restricted antibiotics [15, 51].

While a considerable number of interventional studies in LMICs have analyzed the impact of ASP interventions on SAP [56–62], the available literature shows that most systematic reviews conducted in this research area are skewed towards reviewing the impact of ASPs on either general patient care and healthcare outcomes or certain specific specialties including critical care and long-term care [10, 15, 44, 51, 52, 63–66]. Though one systematic review has reported on the impact of ASP interventions on SAP use globally [31], there is no identified systematic review that has assessed this in LMICs. Variations in healthcare resources and structure as well as differences in the awareness of ASP among healthcare professionals (HCPs) reflecting their differences in knowledge, attitude and practice, which have been observed in different geographical regions, could lead to varying impacts of ASP interventions on antimicrobial use including SAP [53–55, 67]. Consequently, this systematic review was designed to address this information gap by identifying and assessing the impact of ASP interventions on SAP guideline compliance, clinical, economic and the volume of consumption of antibiotics among surgical patients in LMICs. This will provide robust guidance to LMICs where there are ongoing issues with inappropriate use of SAP driving up AMR.

Method

The review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement [68], and the review protocol (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=515926) was registered on the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42024515926).

Eligibility criteria

Types of participants

The participants included were HCPs who prescribe SAP and surgical inpatients to whom SAP had been prescribed to. The review excluded ASP interventions among surgical patients managed as outpatients.

Types of interventions

We included ASP interventions defined in the Effective Practice and Organization of Care Group (EPOC) under these three categories [51]:

1. Persuasive interventions: audit and feedback, education through dissemination of educational materials or meetings, educational outreach through academic detailing or review of patients, provision of reminders either verbally, on paper, electronically or via posters.
2. Restrictive interventions: completion of compulsory order forms for restricted antibiotics by prescribers, prior authorization or approval by expert, selective reporting of laboratory susceptibilities, formulary restriction, therapeutic substitution, automatic orders
3. Structural interventions: new technology affecting laboratory testing or its turnaround time, a change from paper-based to electronic-based prescribing.

Types of outcomes

The outcome measures for assessing the impact of the ASP interventions were categorized into the following categories adapted from previous studies [31, 51, 52]:

1. SAP protocol compliance outcomes: healthcare professionals' compliance to SAP guidelines/ policies in terms of documentation of indication, the choice, timing and duration of SAP treatment
2. Clinical outcomes: mortality and SSI rates, length of stay
3. Economic outcomes: the cost of antibiotic treatment
4. Antibiotic utilization: the volume of antibiotic consumption measured as days of therapy (DOT) or daily defined dose (DDD)

Types of studies

The included studies were all randomized (RCT) and non-randomized controlled trials (NRCT), controlled and uncontrolled before and after studies and interrupted time series studies.

Inclusion and exclusion criteria

All primary studies, including randomized clinical trials, non-randomized clinical trials, controlled and uncontrolled before and after studies, reporting on the impact of the different types of ASP interventions on the use of SAP among hospitalized patients undergoing surgery were included. In addition, only studies published in English language were included.

Studies that were qualitative or descriptive in design, conference abstracts or review papers were excluded. Studies that were conducted outside LMICs, that had no ASP intervention nor defined outcomes, and those that were conducted among either non-hospitalized patients

or those who had not gone through surgical procedures were also excluded.

Search strategy and databases

We searched for studies published between 1st January 2010 and 31st December 2023 with search terms composed for Medline, Central Cochrane Library, web of science, CINAHL and APA PsychInfo databases. The decision to start the search on 1st January 2010 was based on the review of included studies from similar reviews and our elaborate literature review that guided us to limit the inclusion of studies that may not be useful based on when such ASP interventional studies became popular. All keywords were mapped to index terms (e.g. using their medical subject headings (MeSH) for Medline) and connected by Boolean operators and truncation, where appropriate, as shown in Table 1. Any useful studies that were omitted due to limitations of our search term were compensated for by the search of the reference lists of included studies and similar reviews to identify all additional relevant studies. Titles and abstracts of published studies were screened independently by two researchers (IAS and PY). Duplicates were removed. Studies that did not meet the eligibility criteria were excluded. Full texts of eligible studies were retrieved and assessed for eligibility by two independent reviewers, and any encountered disagreement was resolved by consensus. Detailed search strategy used for all for the various search engines have been compiled in Supplementary Table 1.

Quality and risk of bias assessment

Bias in each of the included studies were independently and critically assessed by two investigators (IAS and

PY) using the Risk of Bias in Non-Randomized Studies-of Interventions (ROBINS-I) assessment tool for non-randomized and before and after studies as well as the Cochrane Risk of Bias 2 (ROB 2) tool for randomized studies [69, 70]. The assessment was based solely on the primary outcome of each of the included studies. The seven domains of biases that are likely to be associated with non-randomized studies assessed in this study using the the ROBINS-I tool included those that were likely to be due to confounding, selection of participants into the study, classification of interventions, deviation from intended interventions, missing data and measurement of outcome and selection of the reported outcome. The risk of bias for each of the non-randomized studies was determined and documented as either low, moderate and serious for all seven domains, and an overall risk of bias (low, moderate or serious) was assigned to each study. The five domains used for the assessment of the primary outcome of each of the randomized studies included biases arising from the randomization process, deviation from intended interventions, missing outcome data, measurement of the outcome and from the selection of the reported primary result. A risk-of-bias judgment is then assigned as either low risk, some concerns or high risk based on responses to the signaling questions for each domain. The RoB 2 tool for assessment of the risk of bias associated with the primary outcome of a randomized study was based on five domains including biases arising from the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome and lastly due to selection of the reported result.

Table 1 Keywords and index terms used in the search strategy

| SN | Search Terms connected by Boolean Operators and truncation |
|-----|---|
| S1 | Impact OR Effect OR Implementation OR Implication OR Evaluation |
| S2 | Antimicrobial stewardship intervention OR Antimicrobial stewardship OR Antibiotic stewardship intervention OR Antimicrobial stewardship program ^a OR Antibiotic stewardship program ^a |
| S3 | Guideline adherence OR Protocol adherence OR Protocol Compliance OR Guideline Compliance OR Institutional Adherence OR Institutional Compliance |
| S4 | Surgical site infection OR Length of hospital stay OR Mortality OR Comorbidities |
| S5 | Antimicrobial resistance rate OR incidence of 'hospital-acquired infection' OR 'clostridium difficile colonization' OR Antibiotic resistance |
| S6 | Cost of antibiotic treatment OR Cost of antibiotic therapy OR Cost of chemotherapy OR Healthcare cost OR Pharmacy cost OR Hospital cost |
| S7 | Antibiotic utilization OR Antibiotic consumption OR Antimicrobial consumption OR Antimicrobial utilization |
| S8 | Surgical antibiotic prophylaxis OR Surgical antimicrobial prophylaxis OR Perioperative ^a antimicrobial prophylaxis OR Perioperative ^a antibiotic prophylaxis |
| S9 | S3 OR S4 OR S5 OR S6 OR S7 OR S8 |
| S10 | S1 AND S2 AND S9 |

SN refers to serial numbers employed

'OR' and 'AND', Boolean operators

^a End-truncations applied to some terms

Data extraction and management

A standard data collection tool was designed with the following information: author, year of publication, country and region, study design, study setting, study population, study duration, type of intervention and outcome measures based on the format of other similar reviews [31, 52]. Two independent reviewers (IAS and PY) conducted the data extraction from the eligible studies into the pre-tested data collection form.

Data synthesis

The characteristics of the included studies were compiled in a summary table (Table 2). General characteristics of the studies included study design and setting, type and function of intervention, study duration, size and subject. Table 3 presents the impact of the ASP interventions on outcome indicators. These included guideline compliance, cost of antibiotics, volume of antibiotics utilized, duration of hospitalization, SSI rate and mortality rate. We reported mainly on the outcome of the impact of the interventions that were statistical to simplify the reading of the results while providing the detailed results in supplementary tables for easy reference.

A quantitative synthesis was not employed in this study for three principle reasons. These included the overall perceived high risk of bias assessed from the included studies, the predominant use of descriptive statistics (frequency and percentages) by most of the uncontrolled before-after studies. Lastly, there is evidence that pre-post effect sizes should be avoided in meta-analyses as they result in biased outcomes due to natural processes and characteristics of the patients and study settings [84].

Results

Results of the search

The search from the databases and references retrieved 5341 studies. The details of screening and review of full articles for inclusion based on the eligibility criteria are described in the study flow diagram (Fig. 1).

Included studies (size, duration, design, outcome measured and year of publication)

A total of 20 studies [21, 56–61, 71–81, 83] out of 86 full-text articles were included in the review. The remaining 66 studies were excluded for a variety of reasons (Table 5). Nineteen (90%) [21, 56, 57, 59–61, 71–81, 83] employed uncontrolled before-after study design with two being an ITS design [71, 82] and single open-labelled RCT [58] (Supplementary Table 1S). The total study population among the 20 included studies was 40,589 patients, with the lowest and highest in each study for both the pre-intervention and post-intervention phases being 108 to 24,206 respectively. The duration of the

studies lasted between 6 months to 5 years plus 5 months (Table 1). The years of publication for the 20 studies were between 2013 and 2023 (Table 2). Sixteen (80%) [21, 56, 57, 59–61, 71–73, 75–79, 81, 83] of the studies measured guideline compliance, while 45% ($n=9$) [21, 56, 58, 61, 71, 72, 79, 82, 83] measured the volume of antibiotic consumption either measured in daily defined doses (DDD) or days of therapy (DOT). Other outcome indicators measured included the cost of antibiotics prescribed and/or hospitalization [21, 56–58, 71, 73, 74, 77–81], SSI rate [21, 56–60, 71, 74], mortality rate [58, 74] and length of hospital stay [21, 57, 58, 61, 72, 74, 76, 77, 79–81, 83].

Excluded studies

Out of a total of 5334 studies retrieved, 86 full-text studies were assessed for their eligibility. Sixty-six studies (Fig. 1—Supplementary Table S2) were subsequently excluded due to reasons such as no intervention ($n=21$), the study being conducted outside LMICs ($n=35$), the studies not related to surgical prophylaxis ($n=6$), the study used an outcome indicator outside the review objectives ($n=1$), a review paper ($n=1$) or a study protocol ($n=1$).

Geographical location of study

Ten (50%) [56–58, 77–83] of the included studies were conducted in Asia, nine (45%) [21, 59–61, 71–75] in Africa and one (5%) [76] in Europe. Three ($n=3/9$) [72, 74, 75] of the studies conducted in Africa were performed in Egypt, two ($n=2/9$) [59, 61] were undertaken in South Africa and one each in Nigeria [21], Uganda [60], Kenya [71] and Sudan [73]. Six ($n=6/10$) [56–58, 77–83] of the studies in Asia were conducted in China, and one each in India [82], Malaysia [56], Vietnam [81] and Pakistan [83]. The only study conducted in Europe [76] was in Turkey.

Type of antibiotics

Seven (35%) [21, 56, 60, 61, 71, 81, 83] of the included studies used the penicillin class of antibiotics either alone or in combination with other antibiotics such as metronidazole as the choice of SAP. The penicillins included ampicillin with/ without cloxacillin, co-amoxiclav and piperacillin with tazobactam. The other common class of antibiotic used as SAP were the cephalosporins [56, 57, 59, 60, 73, 77–81, 83] which included cefazolin, ceftriaxone and cefuroxime. Other SAP antibiotics included ciprofloxacin, levofloxacin, moxifloxacin, vancomycin and clindamycin (Table 2).

Intervention type and function

All of the 20 studies adopted persuasive or enabling interventions for their ASP intervention with no study using a restrictive intervention (Table 1). Eighteen (90%)

Table 2 General characteristics of included studies

| S/N | Study | Country and setting | Study design | Antibiotics | Intervention type | Intervention function | Study duration | Study size and subjects | Outcome measured |
|-----|-----------------------------|---|---|--|---|-----------------------|----------------|-------------------------|---|
| 1 | Abubakar et al., 2019 [21] | Nigeria, obstetrics and gynaecology wards of 2 tertiary hospitals | Uncontrolled before-after | Ampicillin, cloxacillin + metronidazole (Hospital A) and Co-amoxiclav (Hospital B) | Guideline development, education, audit and feedback, posters | Persuasive | 8 months | 486 patients | Guideline compliance, antibiotic consumption, cost and SSI rate |
| 2 | Aiken et al., 2013 [71] | Kenya, general, obstetric and gynaecological, orthopaedic and neurological surgical ward in a 300-bed capacity Hospital | Before-after with interrupted time series | Ampicillin + metronidazole | Guideline development, education, training, audit and personalized feedback | Persuasive | 18 months | 3343 patients | Guideline compliance, antibiotic utilization, cost and mortality |
| 3 | Brink et al., 2017 [59] | South Africa, surgical wards of 34 private hospitals | Uncontrolled before-after | Cefazolin, Gentamycin, Vancomycin | Prospective audit and feedback, education | Persuasive | 2.5 years | 24,206 patients | Guideline compliance, SSI rate and mortality |
| 4 | Ngonzi et al., 2021 [59] | Uganda, obstetrics and gynaecology ward of a teaching hospital | Uncontrolled before-after | Ampicillin, ampicillin + cloxacillin, ceftriaxone, benzylpenicillin | Education and audit and feedback | Persuasive | 6 months | 678 patients | Guideline compliance, antibiotic prescription rate, SSI rate |
| 5 | Saied et al., 2015 [72] | Egypt, surgical wards of 5 tertiary hospital | Uncontrolled before-after | | Education, poster reminder, audit and feedback | Persuasive | 1 year | 1303 patients | Guideline compliance, antibiotic consumption |
| 6 | Suliman et al., 2020 [73] | Sudan, obstetrics and gynaecology ward | Uncontrolled before-after | Cefuroxime | Guideline development, verbal contact with prescribers | Persuasive | 3 months | 195 patients | Guideline compliance, cost, SSI rate |
| 7 | Bashar et al., 2021 [61] | South Africa, vascular, general, gastroenterology surgical ward of teaching hospital | Uncontrolled before-after | Co-amoxiclav, Piperacillin / tazobactam | Weekly ASP ward round | Persuasive | 8 months | 476 patients | Guideline compliance, cost, antibiotic consumption |
| 8 | Bassiouny et al., 2020 [74] | Egypt, neonatal surgical ward in Specialized Pediatric Hospital | Uncontrolled before-after | | Guideline distribution to staff, Pharmacist ward rounds, audit and feedback | Persuasive | 9 months | 210 neonates | Guideline compliance, antibiotic utilization (DOT/1000 patient days), drug cost, length of stay, SSI rate, rate of MRSA in admitted patients, rate of MRSA colonization |

Table 2 (continued)

| S/N | Study | Country and setting | Study design | Antibiotics | Intervention type | Intervention function | Study duration | Study size and subjects | Outcome measured |
|-----|------------------------------|--|---------------------------|--|---|-----------------------|--|-------------------------|--|
| 9 | Abelgawaad et al., 2021 [75] | Egypt, orthopedic and trauma surgery in a University Hospital | Uncontrolled before-after | | Guideline development and distribution to concerned staff, audit and feedback, poster reminder | Persuasive | 10 months | 108 patients | Guideline compliance, SSI rate |
| 10 | Karaali et al., 2019 [76] | Turkey, general surgical clinic of tertiary hospital | Uncontrolled before-after | | Guideline update, appointment of ASP leaders, training of surgical team, prospective audit with feedback | Persuasive | 5 years and 5 months | 3771 patients | Guideline compliance (choice, timing, duration), length of stay |
| 11 | Wang et al., 2015 [77] | China, caesarean sections in obstetric and gynaecology ward of tertiary hospital | Uncontrolled before-after | Cefazolin, cefradine, cefoxitin, cefuroxime, clindamycin | Education of obstetricians, prospective audit and feedback to obstetrician | Persuasive | 6 months | 410 patients | Length of stay, duration of prophylaxis, costs of hospitalization and antibiotic |
| 12 | Zhang et al., 2014 [78] | China, urological surgery department of a tertiary hospital | Uncontrolled before-after | Ceftizoxime, ceftoxitin, cefotiam, aztreonam, levofloxacin, cefamandole ester | Audit with feedback | Persuasive | 12 months (6 months pre-intervention and 6 months post-intervention) | 370 patients | Guideline compliance (timing, duration, choice), cost of hospitalization and antibiotic cost |
| 13 | Zhou et al., 2015 [79] | China, urology department of a tertiary hospital | Uncontrolled before-after | Ceftoxime, ornidazole, piperacillin sulbactam, moxifloxacin, ciprofloxacin, cefotiam | Establishment of AMS team, audit with feedback, Guideline development, Poster development, Pharmacist ward rounds | Persuasive | 12 months (3 months each for 4 years—2020–2013) | 112 patients | Guideline compliance (timing and duration), cost, length of stay and volume of consumption |
| 14 | Zhou et al., 2021 [80] | China, orthopaedic department of University Hospital | Uncontrolled before-after | Vancomycin, clindamycin, levofloxacin, cephalosporin | Pharmacist participation in ward rounds, Medication reconciliation, allergy history assessment by pharmacist, Education | Persuasive | 6 months (3 months each for pre-intervention and post-intervention) | 873 patients | Length of stay, Cost of total drug and antimicrobial used, rate of consumption |

Table 2 (continued)

| S/N | Study | Country and setting | Study design | Antibiotics | Intervention type | Intervention function | Study duration | Study size and subjects | Outcome measured |
|-----|--------------------------|--|---|---|--|-----------------------|---------------------------------------|-------------------------|--|
| 15 | Zhou et al., 2016 [57] | China, cardiothoracic surgical ward of tertiary hospital | Uncontrolled before-after | Cefuroxime, cefonicid, clindamycin, cefepime, ciprofloxacin, vancomycin, ceftriaxone, imipenem, ceftazidime and sulbactam | Pharmacist participation in ward rounds, audit and feedback, educational sessions, supplying guideline as hand-out to team | Persuasive | 3 years and 6 months | 412 patients | SSI rate, length of stay, antibiotic cost, guideline compliance (timing, duration, choice) |
| 16 | Phan et al., 2016 [81] | Vietnam, 6 surgical departments (including trauma, orthopaedic, thoracic vascular, gastroenterology, hepatobiliary, urology and request-based) | Uncontrolled before-after | Co-amoxiclav, cephalothin, cefazolin, cefaclor, cefepime/sulbactam, ciprofloxacin, moxifloxacin, fosfomycin | Educational meetings, audit with feedback | Persuasive | 48 months (4 years from 2017 to 2020) | 354 patients | Guideline compliance, length of stay and cost of antimicrobials |
| 17 | Yuan et al., 2023 [58] | China, cardiovascular specialized tertiary hospital | open-label, cluster-randomized controlled trial | Not stated | Guideline development, audit and feedback | Persuasive | 6 months | 2470 patients | Antimicrobial consumption (measure in DOT and DDD), Length of stay, SSI rate, mortality rate, Cost of hospitalisation |
| 18 | Wattal et al., 2020 [82] | India, tertiary hospital in New Delhi | Interrupted time series | | Audit and feedback | Persuasive | 24 months | Not stated | Antimicrobial consumption |
| 19 | Ahmed et al., 2022 [82] | Malaysia, gastrointestinal surgery ward of a military hospital | Uncontrolled before-after | Ceftriaxone, cefuroxime, meropenem, ciprofloxacin, co-amoxiclav, Trimethoprim/ sulfamethoxazole, cefprozil | Guideline development, education, audit and feedback | Persuasive | 14 months | 362 patients | Compliance of choice, dose, timing and duration, SSI rate, cost of antibiotics consumed, Antimicrobial consumption (measured in DDD) |

Table 2 (continued)

| S/N | Study | Country and setting | Study design | Antibiotics | Intervention type | Intervention function | Study duration | Study size and subjects | Outcome measured |
|-----|------------------------|---|---------------------------|---|--|-----------------------|----------------|-------------------------|--|
| 20 | Butt et al., 2019 [83] | Pakistan, 3 surgical departments (orthopaedic, gynaecologic and general surgery wards) of a tertiary hospital | Uncontrolled before-after | Cefazoline, cefradine, cefuroxime, ceftriaxone, cefixime, cefaxidime, ceoperazone/ sulabactam, co-amoxiclav, piperacillin/ tazobactam, amikacin, metronidazole, ciprofloxacin, moxifloxacin, vancomycin | Education and training, audit and feedback | Persuasive | 6 months | 450 patients | Guideline compliance, cost of antibiotic use and hospitalization |

Table 3 Impact of ASP interventions on reported study outcome(s)

| First author (year) | Type of surgery | Type of wounds | Impact on compliance | Impact on antibiotic utilization | Impact on antibiotic cost | Impact on length of stay | Impact on SSI | Impact on mortality rate |
|----------------------------|---|---|--|--|---|---|---|--------------------------|
| Abubakar et al., 2019 [21] | Elective and emergency obstetric and gynaecologic surgeries | Clean, clean-contaminated, contaminated | Timing: 14.2% to 43.3% ($p < 0.001$) Duration: 0 to 21.8% ($p < 0.001$) | 16.6 ± 3.6 DDD/procedure to 12.8 ± 6.8 DDD/procedure ($p < 0.001$) | Mean cost reduced from 16.2 ± 3.2 to 12.0 ± 6.5 USD ($p < 0.001$) | 6.4 ± 2.8 days to 6.1 ± 2.6 ($p = 0.288$) | SSI rate from 4 to 3.4% ($p < 0.722$) | |
| Alken et al., 2013 [71] | Elective and emergency caesarean section, orthopaedic/ neurosurgery, gynaecology and general surgeries | Clean, clean-contaminated, contaminated | Pre-operative compliance from 60 to 98% ($p < 0.0001$) Post-operative antibiotic use fell from 40 to 10% ($p = 0.001$) | 739.30 to 564.93 DDD /1000 patient days ($p = 0.038$) | Total cost reduced from 617.22 USD to 364.16 USD | | SSI risk for clean and clean-contaminated surgery for superficial wound RR = 0.66 CI 0.49–0.91, $p = 0.01$ Deep wound RR = 0.66 CI 0.49–0.91, $p = 0.01$ SSI risk for contaminated and dirty surgery superficial wound RR = 0.17 CI 0.04–0.74, $p = 0.01$ Deep wound RR = 0.66 CI 0.49–0.91, $p = 0.006$ Change in risk of deep or organ-space SSI were non-significant SSI rate from 2.46 to 1.97% ($p = 0.0029$) | |
| Brink et al., 2017 [59] | Obstetric and gynaecological, orthopaedic, cardiothoracic, vascular, gastrointestinal and plastic surgeries | Clean and clean-contaminated | Choice: 81.2% to 95.9% ($p = 0.0004$) Duration: 80.8 to 93.9% ($p = 0.0005$) Timing: 34.7 to 56.4% ($p < 0.001$) Dose: 70.5 to 87.0 ($p = 0.0002$) Overall: 66.8 to 83.3% ($p < 0.0001$) | | | | | |

Table 3 (continued)

| First author (year) | Type of surgery | Type of wounds | Impact on compliance | Impact on antibiotic utilization | Impact on antibiotic cost | Impact on length of stay | Impact on SSI | Impact on mortality rate |
|-------------------------------|---|------------------------|--|---|--|--|--|-------------------------------|
| Ngonzi et al., 2021 [60] | Elective and emergency caesarean section | Clean | Timing: 18.0 to 90.4% ($p < 0.0001$) Guideline checklist: 6.5 to 91.7% ($p < 0.0001$) | | | | SSI rate from 14.5% (pre-intervention) to 7.4% ($p = 0.017$) (intervention) to 10.5% (post-intervention) ($p = 0.198$) | |
| Saied et al., 2015 [72] | General, orthopaedic, obstetrics and gynaecological surgeries | Clean and contaminated | Timing: 37.6 to 41.6% ($p = 0.49$) Duration: 3.0 to 28.7 ($p < 0.0001$) | Average for the 5 Hospitals is 780.8 to 513.2 DOT/ 1000 patient days | | From 4.3 \pm 5.0 to 5.1 \pm 5.6 | | |
| Suliman et al., 2019 | Caesarean section | Clean | Inappropriate choice reduced from 69.1 at pre-intervention to 0% after intervention | | From 735 Sudanese pounds to 505 Sudanese pounds ($p < 0.0001$) | | | |
| Bashar et al., 2021 [61] | Vascular, general and gynaecological surgery | Clean and contaminated | Overall compliance: 36 to 41 Choice: 35 to 38% Duration: 92.3 to 93.4% | From 739.30 DDD/ 1000 patient days (35%) to 564.93 DDD/ 1000 patient days (0.038) | | 8.33 \pm 7.58 to 13.44 \pm 11.83 ($p = 0.001$) | | |
| Bassiouny et al., 2020 [74] | General surgery | Clean-contaminated | | | 4838.4 \pm 3063.85 to 3652.43 \pm 2258 ($p = 0.714$) | 15.15 \pm 11.38 to 11.94 \pm 10.71 ($p = 0.027$) | SSI rate: 54.2 to 20.0% | Mortality rate: 33.3 to 20.7% |
| Abdelgawaad et al., 2021 [75] | Lumbar spinal surgery | Clean and contaminated | Mean duration of SAP use from 2.63 to only 1.00 | | | 3.33 \pm to 2.04 | | |

Table 3 (continued)

| First author (year) | Type of surgery | Type of wounds | Impact on compliance | Impact on antibiotic utilization | Impact on antibiotic cost | Impact on length of stay | Impact on SSI | Impact on mortality rate |
|---------------------------|---|------------------------------|---|----------------------------------|--|--|---------------|--------------------------|
| Karaali et al., 2019 [76] | Breast, Thyroid, Hernia repair, Gas-tric and Colorectal surgeries | Clean and clean-contaminated | Mean duration from 1.54±2.19 to 0.69±1.7 (year 1) and to 0.3±1.2 (year 3) Compliance with choice: 55.6 to 62.1% (year 1) and 64.5% (year 3) Compliance with timing: 81.9 to 82.4% (year 1) and 83.7% (year 3) Compliance with duration: 60.2 to 19.7% (year 1) to 7.5 (year 3) | | | 1.94±1.95 to 2.15±1.91 (year 1) and 1.82±1.63 (year 2) | | |
| Wang et al., 2015 [77] | Elective caesarean section | Clean | Choice: 4.06 to 94.42% Choice and dose: 3.55 to 93.91% Choice, dose and timing: 2.54 to 92.39% Compliance to choice, dose, duration and timing: 0 to 19.29 | | Mean antibiotic cost: 363.93 to 18.63 (USD) (p<0.001) Mean hospitalization cost: 1903.26 USD to 1529.35 USD (p<0.001) | 6.21 to 6.25 (p=0.536) | | |

Table 3 (continued)

| First author (year) | Type of surgery | Type of wounds | Impact on compliance | Impact on antibiotic utilization | Impact on antibiotic cost | Impact on length of stay | Impact on SSI | Impact on mortality rate |
|-------------------------|--|------------------------------|---|---|--|--|--------------------------------------|--------------------------|
| Zhang et al., 2014 [78] | Urological surgery (adrenalectomy, nephrectomy, varicocele ligation) | Clean and clean-contaminated | Choice: 22.72 to 68.75% ($p < 0.001$) Correct choice and dose: 6.82 to 7.50% ($p > 0.005$) Correct choice, dose, time: 6.82 to 7.50% ($p > 0.005$) Correct choice, dose, timing and duration: 0.0 to 0.0% Mean duration of prophylaxis 7.58 to 2.91 ($p < 0.001$) | 98.39 DDD /100 patient days in 2010 to 40.48 DDD /100 patient days in 2013 Antibiotic use rate of 94.91% in 2010 to 89.44% in 2013 | Hospitalization cost: 4141.26 USD to 4134.24 Antibiotic cost: 338.59 USD to 98.95 USD ($p < 0.001$) | From mean of 11.95 days in 2010 to 8.58 days in 2013 | | |
| Zhou et al., 2015 [79] | Urological surgery | Clean and clean-contaminated | Choice: 22% in 2010 to 80% in 2013 Timing from 19% in 2010 to 60% in 2013 Duration reduced from 3.92 ± 1.59 in 2010 to 2.00 ± 1.41 in 2013 | 98.39 DDD /100 patient days in 2010 to 40.48 DDD /100 patient days in 2013 Antibiotic use rate of 94.91% in 2010 to 89.44% in 2013 | Mean antibiotic cost from 338 USD in 2010 to 91.06 USD in 2013 ($p = 0.024$) | From mean of 11.95 days in 2010 to 8.58 days in 2013 | | |
| Zhou et al., 2021 [80] | Orthopedic surgery | Clean | | | Cost % of 16.8 to 13.8% ($p < 0.001$) Antimicrobial per patient from 49.7 USD to 44.2 USD ($p = 0.024$) | Mean of 11.47 to 11.01 ($p = 0.293$) | | |
| Zhou et al., 2016 [57] | Cardiothoracic surgery | Clean and clean-contaminated | Choice: 42.1 to 95.1% ($p < 0.001$) Duration (>48 h): 96.5 to 64.0% ($p < 0.001$) Timing: 45.9 to 97.6% ($p < 0.001$) | | Mean cost 232.1 ± 199.0 to 64.7 ± 44.4 ($p < 0.001$) | 64.7 ± 44.4 to 67.2 ± 52.6 ($p < 0.67$) | SSI rate: 1.2 to 1.4% ($p > 0.99$) | |

Table 3 (continued)

| First author (year) | Type of surgery | Type of wounds | Impact on compliance | Impact on antibiotic utilization | Impact on antibiotic cost | Impact on length of stay | Impact on SSI | Impact on mortality rate |
|--------------------------|---|------------------------------|--|---|--|--|--|--|
| Phan et al., 2016 [81] | Trauma, orthopaedic, thoracic vascular, gastroenterology, hepatobiliary, urology and request-based surgeries | Clean and clean-contaminated | Timing: 34.4 ± 2.6 pre-intervention to 40.7 ± 3.8 intervention phase to 38.5 ± 3.7 post-intervention phase (p = 9.29) Choice: 17.85 to 36.4% to 55.9% (p < 0.001) Timing: 57.6% to 52.5% to 66.1% (p = 0.102) Duration: 39.8% to 39.0% to 74.6% (p < 0.001) Overall: 12.7% to 12.7% to 39.0% (p < 0.001) | Mean for intervention 6.8 ± 5.3 and control of 8.0 ± 4.8 DDD/admission Median reduction from 190.68 DDD/100 bed days to 185.88 DDD/100 bed days (3-month post-intervention) and 187 DDD/100 bed days (6-month post-intervention) | Cost of antimicrobial (median) 56.1 USD to 190 USD (p < 0.001) | Length of stay (median) 5.6 to 5.0 (0.082) | SSI rate of 2.8% (2.0–3.9) for intervention group and 2.9% (2.0–4.0) for control group | Mortality: 0.4% (0.1–0.9) for intervention group and 0.5 (0.2–1.1) for control group |
| Yuan et al., 2023 [58] | Open-chest Cardiovascular surgeries | Clean and clean-contaminated | | | Median antimicrobial cost for intervention group and 188.64 USD (139.04–290.4) for control group | Median length of stay 14 (12–17) for intervention group and 14 (12–16) for control group | | |
| Wattal et al., 2020 [82] | Cardiac, obstetric and gynecological, urological, plastic and cosmetic, orthopaedic, neurosurgery, ophthalmological, thoracic, vascular and general surgeries | Clean and clean-contaminated | | | | | | |
| Ahmed et al., 2022 [56] | Appendectomy, bile duct/ gall bladder surgery, colorectal surgery and other types of gastrointestinal surgeries | Clean-contaminated | Choice: 51.23 to 53.05% Dose: 32.72 to 53.66% Timing: 64.81 to 74.39% Duration: 14.20 to 19.51% | 920.36 (pre-intervention) to 788.56 (post-intervention) DDD/100 surgeries | 9513.92 to 7730.11 giving a reduction difference of 1783.81 Saudi Riyal (equal to 475.39 USD) (p < 0.05) | | SSI rate: 0.41 to 0.04% | |

Table 3 (continued)

| First author (year) | Type of surgery | Type of wounds | Impact on compliance | Impact on antibiotic utilization | Impact on antibiotic cost | Impact on length of stay | Impact on SSI | Impact on mortality rate |
|------------------------|--|------------------------------|--|--|--|--|---------------|--------------------------|
| Butt et al., 2019 [83] | Cholecystectomy, appendectomy, caesarean section, hysterectomy, hernia procedure | Clean and clean-contaminated | Choice: 11.6 to 28% ($p < 0.001$) Choice and dose: 11.1 to 28% ($p < 0.001$) Choice, dose and frequency: 10.7 to 27% ($p < 0.001$) Choice, dose, frequency and duration: 1.3 to 12.4% ($p < 0.001$) | Average number of antibiotic use from 2.090 ± .902 to 1.86 ± 0.859 ($p = 0.006$) | Antibiotic cost from 2463.17 ± 3546.42 to 1829 ± 256.32 ($p = 0.03$) | 5.4 ± 4.8 to 4.5 ± 3.4 ($p = 0.023$) | | |

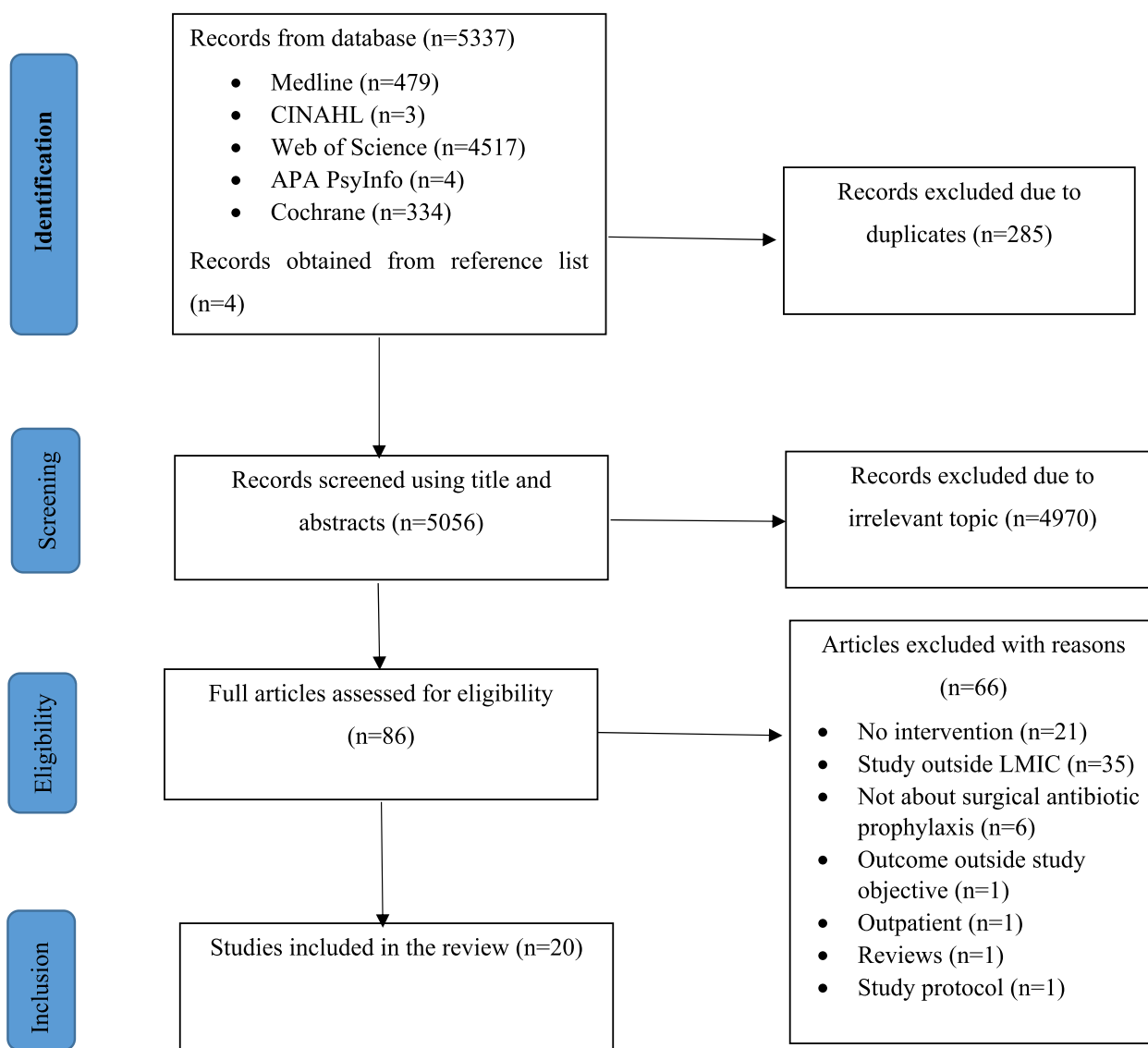


Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram

[21, 56–61, 71–75, 77–81, 83] of the studies had a combination of two or more interventions tested. Seventeen (85%) [21, 56–60, 71, 72, 74–79, 81–83] of the studies used the audit and feedback intervention; twelve studies (60%) [21, 56, 57, 59, 60, 71, 72, 76, 77, 80, 81, 83] tested an education and training intervention; and seven (35%) [21, 56, 71, 73, 75, 76, 79] studies tested the development and/or update of a SAP guideline intervention. Other interventions included pharmacist-led ward rounds and the use of reminders in the workplace (Table 2).

Number of hospitals and type of wards

A total of seventeen studies (90%) [56–58, 60, 61, 71, 73–83] out of the twenty were conducted in one hospital,

with a study (one each) conducted in two hospitals [21], five [72] and 34 [59] hospitals. The majority ($n = 13/20$) of the studies were conducted in a tertiary/ teaching hospital [21, 57, 58, 60, 61, 72, 75–80, 82, 83]. Most of the studies ($n = 6/20$) [21, 60, 71, 73, 77, 83] were conducted in an obstetrics and gynaecology ward followed by those in a general surgical ward ($n = 4/20$) [59, 71, 72, 76]. Other specialized study sites included orthopaedic, trauma, cardiovascular, urological and gastrointestinal wards (Table 2).

Type of surgeries and wounds

Elective and emergency caesarean sections were the commonest ($n = 6/20$) [21, 60, 71, 73, 77, 83] surgical

procedures performed across the studies. All of the 20 studies involved SAP use in clean wounds, sixteen (80%) studies [21, 56–59, 61, 71, 72, 74–76, 78, 79, 81–83] involved clean-contaminated wounds, while contaminated wounds were observed in only two (10%) studies [21, 71].

Impact of stewardship interventions on SAP guidelines compliance

Sixteen (80%) [21, 56, 57, 59–61, 71–73, 75–79, 81, 83] of the 20 studies reported on the impact of ASP on compliance to SAP guidelines. All twelve studies compared pre-intervention compliance with post-intervention compliance (Table 3). Eleven [21, 56, 57, 59, 60, 72, 76–79, 81] out of the twelve studies assessed the impact of intervention on the timing of administration of SAP, and four [21, 57, 59, 60] of them reported statistically significant improvement of this outcome indicator. Ten [56, 57, 59, 73, 76–79, 81, 83] of the twelve studies reported on the compliance to SAP guideline based on the choice, of which five [57, 59, 78, 81, 83] of them showed statistically significant improvement. Nine [21, 47, 57, 59, 61, 72, 76–79, 81, 83] of the twelve studies reported on compliance to guidelines due to the duration of SAP used in practice, and six [21, 57, 59, 72, 78, 81] of them showed statistically significant increase in compliance after the ASP intervention. Five [59, 61, 77, 81, 83] of the studies reported on overall compliance to SAP guidelines based on choice, timing, duration and/or dose of which three [59, 81, 83] showed a statistically significant improvement (Table 3).

Impact of stewardship interventions on antibiotic utilization

Nine [21, 47, 58, 61, 71, 72, 79, 82, 83] studies reported the impact of ASP intervention on antibiotic utilization out of which four studies [21, 61, 71, 83] showed a statistically significant reduction after the intervention. Of the nine [21, 56, 58, 61, 71, 79, 82] studies that reported on antibiotic utilization, seven [21, 56, 58, 61, 71, 79, 82] reported utilization using DDDs, one [72] reported as DOT and one [83] as the number of antibiotics used. Of the four studies that showed a significant reduction, all were measured in DDDs, and the ASP interventions employed were all persuasive. While two [21, 71] out of the four studies employed a combination of three interventions namely guideline development, education of clinicians and audit and feedback, one study [61] employed weekly AMS team ward rounds, and one study [83] employed a combination of education on guidelines and audit and feedback meetings (Table 3).

Impact of stewardship interventions on antibiotic cost

Ten [21, 56, 57, 71, 73, 74, 77, 78, 80, 81] studies reported the impact of the ASP intervention on the cost of antibiotics. Seven [21, 56, 57, 73, 77, 80, 81] of these studies reported a statistically significant reduction of antibiotic cost after the introduction of the ASP. These studies utilized a persuasive ASP intervention. All of the seven studies utilized a combination of interventions namely guideline development, education of clinicians and audit with feedback to the surgical team [21, 56]; education and audit with feedback [77, 81]; pharmacist participation in ward rounds, education and audit with feedback [57, 80]; and guideline development and verbal contact with prescribers [73] (Table 3).

Impact of stewardship interventions on length of stay

Twelve [21, 57, 58, 61, 72, 74–77, 80, 81, 83] studies reported on the impact of ASP interventions on the length of hospital stay, of which four [21, 61, 74, 83] studies reported a statistically significant reduction. Of these four studies, one [61] study utilized a single intervention namely a weekly AMS team ward round, while three [21, 74, 75, 83] studies utilized a combination of interventions including guideline development, education, audit with feedback and pharmacist-led ward rounds (Table 3).

Impact of stewardship interventions on the surgical site infection rate

Eight [21, 56–60, 71, 74] studies reported on the impact of the ASP on the SSI rate. Out of these, two [59, 71] studies reported a statistically significant reduction. While the study by Brink et al. [59] reported a significant reduction through the use of education and audit with feedback, Aiken et al. [71] utilized a combination of guideline development, education and audit with feedback (Table 3).

Impact of stewardship interventions on mortality rate

Two studies reported on the impact of the ASP on mortality; however, neither of them showed a statistically significant reduction in mortality following the ASP. The Bassiouny et al. [74] study utilized a combination of guideline distribution to clinicians, pharmacist ward rounds and audit with feedback, while Yuan et al. [58] utilized a combination of guideline-based decision tools, audit and feedback integrated with a physician order entry system (Table 3).

Risk of bias in included studies

All seventeen before-after studies and two ITS studies (Table 2) assessed for risk of bias using the ROBINS-I

Table 4 Risk of bias assessment for before-after studies and interrupted time series studies

| Study | Bias due to confounding | Bias in selection of participants into the study | Bias in classification of intervention | Bias due to deviations from intended intervention | Bias due to missing data | Bias in measurement of outcomes | Bias in selection of reported results | Overall risk of bias judgment |
|-------------------------------|-------------------------|--|--|---|--------------------------|---------------------------------|---------------------------------------|-------------------------------|
| Abubakar et al., 2019 [21] | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |
| Aiken et al., 2013 [71] | Serious | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Serious |
| Brink et al., 2017 [59] | Serious | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Serious |
| Ngonzi et al., 2021 [60] | Serious | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Serious |
| Saied et al., 2015 [72] | Serious | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Serious |
| Suliman et al., 2020 [73] | Serious | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Serious |
| Bashar et al., 2021 [61] | Serious | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Serious |
| Bassiouny et al., 2020 [74] | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |
| Abdelgawaad et al., 2021 [75] | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |
| Karaali et al., 2019 [76] | Serious | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Serious |
| Wang et al., 2015 [77] | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |
| Zhang et al., 2014 [78] | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |
| Zhou et al., 2015 [79] | Serious | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Serious |
| Zhou et al., 2021 [80] | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |
| Zhou et al., 2016 [57] | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |
| Phan et al., 2016 [81] | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |
| Wattal et al., 2020 [82] | Serious | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |
| Ahmed et al., 2022 [56] | Serious | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |
| Butt et al., 2019 [83] | Moderate | Moderate | Moderate | Moderate | Moderate | Moderate | Low | Moderate |

tool had an overall serious risk of bias (Table 4). A moderate risk of bias was observed in eleven ($n = 17$, 65%) of the before-after studies. These were due to biases likely to have occurred in five domains namely bias due to the selection of participants into the study, bias introduced by either differential or non-differential misclassification of interventions, bias due to deviations from intended interventions bias due to missing data and bias in the measurement of outcomes. All seventeen before-after studies and two ITS studies had a low risk of bias due to the likely of selective reporting of results in a way that depends on favourable findings.

A serious risk of bias was also observed in six ($n = 17$, 39%) of the before-after studies and the two ITS studies [71, 82]. The serious risk of bias was assigned mainly due to bias due to confounding as a result of failure to control for key confounders by assessing and adjusting for them. The only RCT study [58], which was assessed for risk of bias using the RoB 2 tool, showed an overall high risk of bias due to serious concerns of deviation from the intended interventions. Two domains (D1 and D4) were assigned the risk level of having some concerns, and they included biases due to the randomization process and measurement of the primary outcome.

Table 5 Risk of bias chart using the Revised Cochrane Risk of Bias Tool for Randomized Trial (RoB 2)

| Study ID | Experimental arm | Comparator arm | Outcome | Risk domains (D 1–5) and level of risk assigned | Overall risk | Keys to each domain risk level assigned | | | | | |
|---|---|-----------------|---|--|--------------|---|--------------|-------------|-----------|-------|--------------------|
| EPIC trial | Guideline-based decision support tool and weekly feedback | No intervention | Antibiotic consumption, length of stay, mortality rate, cost of hospitalization | <table border="1"> <tr> <td>D1—β</td> <td>D2—μ</td> <td>D3—α</td> <td>D4—β</td> <td>D5—μ</td> </tr> </table> | D1— β | D2— μ | D3— α | D4— β | D5— μ | μ | α —Low risk |
| D1— β | D2— μ | D3— α | D4— β | D5— μ | | | | | | | |
| <p>β—Some concerns</p> <p>μ—High risk</p> <p>Details of Risk Domains</p> <p>D1—Randomization process</p> <p>D2—Deviations from the intended interventions</p> <p>D3—Missing outcome data</p> <p>D4—Measurement of the outcome</p> <p>D5—Selection of the reported result</p> | | | | | | | | | | | |

Two domains (D2 and D5) were also assigned high risk of bias, and they included biases due to deviation from intended interventions and selective reporting of favourable results. The only domain that was assessed as having low risk of bias was that due to missing outcome. The overall risk of bias for this study using the RoB 2 tool was assessed to be high (Table 5).

Discussion

We believe this is the first systematic review to investigate the impact of ASPs on the appropriate use of SAP together with clinical and economic benefits in LMICs to provide a robust guide for countries still struggling to improve antibiotic use for SAP. The review included 20 studies published between 2010 and 2023 and a total sample size of 40,589 with the lowest and highest being 108 and 24,206 patients, respectively. The total duration for each study lasted between 6 months to 5 years and 5 months. Overall, this review, which was limited to LMICs, included more studies and number of patients than a similar review that also evaluated the impact of ASPs on SAP use [31].

Almost an equal number of studies in this review were conducted in Asia and Africa, reflecting concerns in both continents of increasing inappropriate use of antibiotics [85–89]. Nevertheless, this is a positive observation demonstrating that countries in Africa with much limited healthcare resources have not been left behind in implementing AMS Programs to reduce unnecessary use of antibiotics as surgical prophylaxis. This is similar to other areas of antibiotic use in LMICs where ASP interventions have shown positive impact though more effort must be made to increase leadership commitment [15, 52, 90]. This is also important because current point prevalence surveys in Africa and other LMICs have shown high unnecessary use of antibiotics administered as SAP [28, 29, 33–36].

The findings from this review show that while antibiotics in the penicillin class, including co-amoxiclav and ampicillin, and the first-generation cephalosporin such as cefazolin were being used as SAP, there was a high usage of antibiotics in the ‘Watch’ group in some settings. This was mostly due to the prescribing of second- and third-generation cephalosporin including cefuroxime and ceftriaxone respectively for SAP, which have a higher risk of causing AMR and therefore should be avoided where possible [12, 23]. Other antibiotics that may pose a challenge by driving up AMR development include the use of the quinolone class such as ciprofloxacin and levofloxacin. These concerns have also been observed in several point prevalence surveys conducted in LMICs [28, 29, 33–35, 91–93].

Most of the ASP interventions that were employed in the studies included in this review were a combination of two or more persuasive interventions including audit and feedback, clinician education and the use of reminders. This is similar to other reviews on the impact on ASP interventions [15, 31, 51, 52, 94]. While restrictive interventions including formulary restrictions and expert approval have been shown to produce an immediate impact than persuasive and structural interventions [50], a combination of persuasive interventions has rather proven to give a more sustainable impact due to the positive behavioural change consequences they have on clinicians attitude and practice beyond knowledge influence [31, 51, 94].

Most of the studies in this review evaluated the impact of AMS interventions on SAP use, which was similar to the study by Joselin et al. (2022) [31]. The main outcomes measured under this indicator included the timing of administration as well as the choice and duration of use of the SAP. The indicator that showed a greater proportion of significant improvements after the intervention implementation was the duration of use (67%), followed by the choice of antibiotics (50%) and lastly by the timing of administration 36%). While fewer studies reported on the impact of intervention based on a combination of two or more of these parameters, a greater number (60%) recorded a significant change. The increase in adherence to SAP following the implementation of AMS interventions was also observed by Joselin et al. (2022) [31]. One study identified some potential barriers to SAP guideline adherence as poor knowledge of local guidelines, lack of agreement of local guideline content by key stakeholders, workload and time constraints on adherence to the timing of administration, poor communication, unclear roles among surgical team members and the fear of repercussion arising from scanty use of SAP to prevent SSIs [94]. These specific challenges need to be identified in individual settings through a qualitative study and appropriate behaviour change intervention adopted as part of a broader AMS quality improvement project to address the poor adherence behaviour to improve future use. Successful ASPs undertaken in LMICs can also provide examples going forward. This review showed that AMS interventions resulted in overall reduction in SAP utilization in most of the included studies. Most of these studies utilized DDD as compared to DOT in measuring the volume of consumption of antibiotics. These findings agree with several reviews that have shown that AMS interventions are associated with improved antibiotic utilization [15, 52, 65, 88]. This finding is relevant as increased and unnecessary use of antibiotics, including SAP, are known to

be the main drivers of AMR, increase in adverse reactions and high healthcare costs, re-admission rates, length of hospital stay and potential colonization and infection with *C. difficile* [15, 28–30].

Encouragingly, our review showed that the implementation of ASPs in 70% of the included studies resulted in a reduction in antibiotic costs. This observation is most likely a consequence of the reduction in the utilization of SAP by cutting down on the duration of its use. Since all the included studies involved SAP use in clean wound surgeries, and 80% of them involved clean-contaminated wounds, it follows that an improvement in guideline adherence will naturally lead to a reduction in both indicators. This is because current guidelines recommend a single dose of the effective antibiotics to be administered 1 or 2 h before incision except when the duration of surgery is twice its half-life or greater volume of blood is lost during surgery while suggesting a limited duration of use to 24 h for procedures where evidence is lacking [21–23, 28, 95, 96].

Few of the included studies in our review reported a significant impact of ASPs on patients' length of hospitalization after surgery, the risk of SSI rate and mortality rate. This may imply that though guideline compliance with SAP use was reported to have improved in most studies leading to a reduction in the cost and utilization of antibiotic, this did not translate into a significant impact on these indicators. This is perhaps not surprising since the use of SAP reduces the chance of infection at the surgical site and any associated morbidity and mortality. In addition, the findings can be interpreted that an appreciable reduction in antibiotic use, especially the length used post-operatively, through the ASP did not result in any negative consequences including the rate of mortality and SSI rates and their length of hospital stay indicating greater morbidity. However, compared to the other indicators, these three clinical indicators were less often measured in the included studies.

We are aware of some limitations of this study. Firstly, our findings in this review are limited because most of the studies included were non-randomized (mostly uncontrolled before-after studies) resulting in a high risk of bias due to failure to control for confounders, maturation effects and cyclical trends [52, 97, 98]. We could not estimate the true effect of ASP interventions on clinical outcomes due to the predominant use of descriptive statistics including proportions and frequencies to demonstrate impact instead of assessing for risk and odd ratios. In addition, the results must be interpreted in the context of the use of surgical antibiotic prophylaxis in the hospital settings in LMICs. We also included only studies published in the English language in the database search which may introduce publication bias. Despite these limitations, we believe our findings

are robust providing policy and intervention guidance for appropriate use of ASP in LMICs.

Conclusion

The review showed that ASP interventions implemented in LMICs are effective in improving SAP guideline adherence, antibiotic utilization and their cost with no significant negative impact on patient outcomes among surgical patients. This review will help provide guidance on the selection of effective ASP interventions to implement that will result in a significant and sustainable positive impact on the above outcomes and the type of indicators to measure to monitor such improvements in hospital settings in low-resource settings, especially in African countries. It is recommended that governments, healthcare managers and researchers in other LMICs should support more of such research that measure the impact of ASP interventions on SAP use to guide future policies and practices on antibiotic use in this area.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13643-024-02731-w>.

Additional file 1. Search strategy.

Additional file 2. Excluded studies and reasons.

Authors' contributions

Protocol development: IAS, SC, PY, VB; conceptualization: IAS, SC, VB; methodology: IAS, SC, VB; data search: IAS; screening of retrieved studies: IAS, PY; data collection: IAS, SC, PY, VB; data analysis: IS, PY, SC, VB; risk of bias assessment: IAS, PY; data curation: IAS, VB; writing—original draft preparation: IAS, SC, PY, VB; writing—all authors; visualization: IAS, PY, SC, VB; supervision: IAS, SC, PY, VB. All authors have read and agreed to the published version of the manuscript.

Funding

This research received no external funding.

Data availability

The data that support the findings of this study are available from the corresponding author, [IAS], upon reasonable request.

Declarations

Competing interests

The authors declare that they have no competing interests.

Author details

¹Discipline of Pharmaceutical Sciences, School of Health Sciences, University of KwaZulu-Natal, Durban, South Africa. ²Pharmacy Practice Department, School of Pharmacy, University of Health and Allied Sciences, PMB 31, Ho, Volta Region, Ghana.

Received: 17 April 2024 Accepted: 29 November 2024

Published online: 19 December 2024

References

- Gelband H, et al. The state of the world's antibiotics 2015. *Wound healing Southern Africa*. 2015;8(2):30–4.
- WHO. Sixty-seventh World Health Assembly. WHO 67th World Health Assembly Webpage. 2014. <https://iris.who.int/handle/10665/260211>. Accessed 30 Jan 2024.
- Sartorius B, et al. The burden of bacterial antimicrobial resistance in the WHO African region in 2019: a cross-country systematic analysis. *Lancet Glob Health*. 2024;12(2):e201–16.
- WHO. Sixty-eighth World Health Assembly. WHO 68th World Health Assembly Webpage. 2015. https://apps.who.int/gb/ebwha/pdf_files/wha68-rec1/a68_r1_rec1-en.pdf. Accessed 30 Jan 2025.
- Charani E, et al. An analysis of existing national action plans for antimicrobial resistance—gaps and opportunities in strategies optimising antibiotic use in human populations. *Lancet Glob Health*. 2023;11(3):e466–74.
- Dadgostar P. Antimicrobial resistance: implications and costs. *Infect Drug Resist*. 2019;12:3903–10.
- Hofer U. The cost of antimicrobial resistance. *Nat Rev Microbiol*. 2019;17(1):3–3.
- Collignon P, et al. Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis. *The Lancet Planetary Health*. 2018;2(9):e398–405.
- World Bank Country and Lending Groups: country classification; 2024, 2024 via <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups>. Accessed on the 30th January.
- Van Dijk C, Vlieghe E, Cox JA. Antibiotic stewardship interventions in hospitals in low-and middle-income countries: a systematic review. *Bull World Health Organ*. 2018;96(4):266.
- Klein EY, et al. Assessment of WHO antibiotic consumption and access targets in 76 countries, 2000–15: an analysis of pharmaceutical sales data. *Lancet Infect Dis*. 2021;21(1):107–15.
- Sulis G, et al. Exposure to World Health Organization's AWaRe antibiotics and isolation of multidrug resistant bacteria: a systematic review and meta-analysis. *Clin Microbiol Infect*. 2022;28(9):1193–202.
- Antoñanzas F, Goossens H. The economics of antibiotic resistance: a claim for personalized treatments. *Eur J Health Econ*. 2019;20:483–5.
- Klein EY, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci*. 2018;115(15):E3463–70.
- Akpan MR, et al. Implementation of antimicrobial stewardship programmes in African countries: a systematic literature review. *J Glob Antimicrob Resist*. 2020;22:317–24.
- Sartelli M, et al. Antibiotic use in low and middle-income countries and the challenges of antimicrobial resistance in surgery. *Antibiotics*. 2020;9(8):497.
- Bozkurt F, et al. Analysis of antimicrobial consumption and cost in a teaching hospital. *J Infect Public Health*. 2014;7(2):161–9.
- Santana RS, et al. The cost of excessive postoperative use of antimicrobials: the context of a public hospital. *Rev Col Bras Cir*. 2014;41:149–54.
- Abula T, Kedir M. The pattern of antibiotic usage in surgical in-patients of a teaching hospital, northwest Ethiopia. *Ethiop J Health Dev*. 2004;18(1):35–8.
- Mwita JC, et al. Key issues surrounding appropriate antibiotic use for prevention of surgical site infections in low-and middle-income countries: a narrative review and the implications. *Int J Gen Med*. 2021;14:515–30.
- Abubakar U, Syed Sulaiman S, Adesiyun A. Utilization of surgical antibiotic prophylaxis for obstetrics and gynaecology surgeries in Northern Nigeria. *Int J Clin Pharm*. 2018;40:1037–43.
- Small FM, Grivell RM. Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section. *Cochrane Database Syst Rev*. 2014;2014(10):CD007482.
- World Health Organization, The WHO AWaRe (access, watch, reserve) antibiotic book. 2022.
- Ng RS, Chong CP. Surgeons' adherence to guidelines for surgical antimicrobial prophylaxis—a review. *Australas Med J*. 2012;5(10):534.
- Misra AK, et al. Antibiotic prophylaxis for surgical site infection: need of time. *Health*. 2015;3(3):1–7.
- Weber WP, et al. Timing of surgical antimicrobial prophylaxis: a phase 3 randomised controlled trial. *Lancet Infect Dis*. 2017;17(6):605–14.
- Bratzler DW, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Surg Infect*. 2013;14(1):73–156.
- Sefah IA, et al. Appropriateness of surgical antimicrobial prophylaxis in a teaching hospital in Ghana: findings and implications. *JAC-Antimicrob Resist*. 2022;4(5):dlac102.
- Oshikoya KA, et al. Surgical antimicrobial prophylaxis and its dose appropriateness among paediatric patients in a Nigerian teaching hospital. *J Chemother*. 2019;31(6):329–42.
- Tiri B, et al. Impact of antimicrobial stewardship interventions on appropriateness of surgical antibiotic prophylaxis: how to improve. *Antibiotics*. 2020;9(4):168.
- Martinez-Sobalvarro JV, et al. Antimicrobial stewardship for surgical antibiotic prophylaxis and surgical site infections: a systematic review. *Int J Clin Pharm*. 2022;44(2):301–19.
- Cooper L, et al. Supporting global antimicrobial stewardship: antibiotic prophylaxis for the prevention of surgical site infection in low-and middle-income countries (LMICs): a scoping review and meta-analysis. *JAC-Antimicrob Resist*. 2020;2(3):dlaa070.
- Saleem Z, et al. A multicenter point prevalence survey of antibiotic use in Punjab, Pakistan: findings and implications. *Expert Rev Anti Infect Ther*. 2019;17(4):285–93.
- Al Matar M, et al. Point prevalence survey of antibiotic use in 26 Saudi hospitals in 2016. *J Infect Public Health*. 2019;12(1):77–82.
- Anand Paramadhas BD, et al. Point prevalence study of antimicrobial use among hospitals across Botswana; findings and implications. *Expert Rev Anti Infect Ther*. 2019;17(7):535–46.
- Afriye DK, et al. Antimicrobial point prevalence surveys in two Ghanaian hospitals: opportunities for antimicrobial stewardship. *JAC-Antimicrob Resist*. 2020;2(1):dlaa001.
- Rickard J, et al. Surgical infections in low-and middle-income countries: a global assessment of the burden and management needs. *Surg Infect*. 2020;21(6):478–94.
- Sway A, et al. Burden of surgical site infection following cesarean section in sub-Saharan Africa: a narrative review. *Int J Women's Health*. 2019;11:309–18.
- Rojas-Gutierrez E, Vilar-Compte D. An overview of surgical site infection in low-and middle-income countries: the role of recent guidelines, limitations, and possible solutions. *Curr Treat Options Infect Dis*. 2019;11:300–16.
- Monahan M, et al. Surgical site infection and costs in low-and middle-income countries: a systematic review of the economic burden. *PLoS One*. 2020;15(6):e0232960.
- Diaz V, Newman J. Surgical site infection and prevention guidelines: a primer for Certified Registered Nurse Anesthetists. *AAANA J*. 2015;83(1):63–8.
- Poolman JT, Anderson AS. *Escherichia coli* and *Staphylococcus aureus*: leading bacterial pathogens of healthcare associated infections and bacteremia in older-age populations. *Expert Rev Vaccines*. 2018;17(7):607–18.
- World Health Organization (WHO). Antimicrobial stewardship programmes in health-care facilities in low-and middle-income countries: a WHO practical toolkit. 2019. <https://iris.who.int/bitstream/handle/10665/329404/9789241515481-eng.pdf?sequence=1>. Accessed 30 Jan 2024.
- Nathwani D, et al. Value of hospital antimicrobial stewardship programs (ASPs): a systematic review. *Antimicrob Resist Infect Control*. 2019;8:1–13.
- Ministry of Health. Ghana National Action Plan on antimicrobial resistance (2017–2021). https://www.moh.gov.gh/wp-content/uploads/2018/04/NAP_FINAL_PDF_A4_19.03.2018-SIGNED-1.pdf. Accessed 30 Jan 2024.
- Fuller WL, et al. National action plan on antimicrobial resistance: an evaluation of implementation in the World Health Organization Africa region. *J Public Health Afr*. 2022;13(2):2000.
- Ahmed SM, et al. The Implementation of National Action Plan (NAP) on Antimicrobial Resistance (AMR) in Bangladesh: challenges and lessons learned from a cross-sectional qualitative study. *Antibiotics*. 2022;11(5):690.
- Harant A. Assessing transparency and accountability of national action plans on antimicrobial resistance in 15 African countries. *Antimicrob Resist Infect Control*. 2022;11(1):1–15.

49. Ranjalkar J, Chandy SJ. India's National Action Plan for antimicrobial resistance—an overview of the context, status, and way ahead. *J Fam Med Prim Care*. 2019;8(6):1828.
50. Davey P, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Syst Rev*. 2013;(4):CD003543. <https://doi.org/10.1002/14651858.CD003543.pub3>.
51. Davey P, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev*. 2017;2(2):CD003543.
52. Siachalinga L, Mufwambi W. Impact of antimicrobial stewardship interventions to improve antibiotic prescribing for hospital inpatients in Africa: a systematic review and meta-analysis. *J Hosp Infect*. 2022;129:124–43.
53. Cox JA, et al. Antibiotic stewardship in low-and middle-income countries: the same but different? *Clin Microbiol Infect*. 2017;23(11):812–8.
54. El-Sokkary R, Asaad A. Hospital antibiotic stewardship interventions in low and middle income countries: a systematic review and meta-analysis. *Microb Infect Dis*. 2020;1(3):153–67.
55. Galindo-Fraga A, Villanueva-Reza M, Ochoa-Hein E. Current challenges in antibiotic stewardship in low-and middle-income countries. *Curr Treat Options Infect Dis*. 2018;10:421–9.
56. Ahmed NJ, et al. Implementing an antimicrobial stewardship programme to improve adherence to a perioperative prophylaxis guideline. *Healthcare*. 2022;10(3):464. MDPI.
57. Zhou L, et al. Optimizing prophylactic antibiotic practice for cardiothoracic surgery by pharmacists' effects. *Medicine*. 2016;95(9):e2753.
58. Yuan X, et al. Evaluation of the effectiveness and safety of a multi-faceted computerized antimicrobial stewardship intervention in surgical settings: a single-centre cluster-randomized controlled trial. *Int J Antimicrob Agents*. 2023;61(5):106787.
59. Brink AJ, et al. From guidelines to practice: a pharmacist-driven prospective audit and feedback improvement model for peri-operative antibiotic prophylaxis in 34 South African hospitals. *J Antimicrob Chemother*. 2017;72(4):1227–34.
60. Ngonzi J, et al. Impact of an educational intervention on WHO surgical safety checklist and pre-operative antibiotic use at a referral hospital in southwestern Uganda. *Int J Qual Health Care*. 2021;33(3):mzab089.
61. Bashar MA, et al. Impact of an antibiotic stewardship programme in a surgical setting. *S Afr J Infect Dis*. 2021;36(11):307.
62. Liu J, et al. Impact of the antibiotic stewardship program on prevention and control of surgical site infection during peri-operative clean surgery. *Surg Infect*. 2018;19(3):326–33.
63. Falcone M, et al. Antimicrobial consumption and impact of antimicrobial stewardship programmes in long-term care facilities. *Clin Microbiol Infect*. 2019;25(5):562–9.
64. Huebner C, Flessa S, Huebner N. The economic impact of antimicrobial stewardship programmes in hospitals: a systematic literature review. *J Hosp Infect*. 2019;102(4):369–76.
65. Lee CF, et al. Impact of antibiotic stewardship programmes in Asia: a systematic review and meta-analysis. *J Antimicrob Chemother*. 2018;73(4):844–51.
66. Kaki R, et al. Impact of antimicrobial stewardship in critical care: a systematic review. *J Antimicrob Chemother*. 2011;66(6):1223–30.
67. Zanichelli V, et al. Variation in antibiotic use among and within different settings: a systematic review. *J Antimicrob Chemother*. 2018;6:17–29.
68. Moher D, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg*. 2010;8(5):336–41.
69. Sterne JA, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919.
70. Higgins JP, et al. Assessing risk of bias in a randomized trial. *Cochrane handbook for systematic reviews of interventions*. 2019: p. 205–228.
71. Aiken AM, et al. Changing use of surgical antibiotic prophylaxis in Thika Hospital, Kenya: a quality improvement intervention with an interrupted time series design. *PLoS One*. 2013;8(11):e78942.
72. Saied T, et al. Antimicrobial stewardship to optimize the use of antimicrobials for surgical prophylaxis in Egypt: a multicenter pilot intervention study. *Am J Infect Control*. 2015;43(11):e67–71.
73. Suliman SM, Yousef BA, Hamadelnil AA. Impact of guidelines implementation for the rational use of prophylactic antibiotics in elective cesarean sections at Elqutainah Teaching Hospital. *J Family Med Prim Care*. 2020;9(1):162.
74. Bassiouny DM, et al. Establishment of an antimicrobial stewardship strategy on the surgical NICU at Cairo University specialized pediatric hospital. *J Pediatr Surg*. 2020;55(9):1959–64.
75. Abdelgawaad AS, et al. Perioperative antibiotic prophylaxis in spinal surgery. *Sicot-J*. 2021;7:31.
76. Karaali C, et al. A new antibiotic stewardship program approach is effective on inappropriate surgical prophylaxis and discharge prescription. *J Infect Dev Countries*. 2019;13(11):961–7.
77. Wang J, et al. Impact of pharmacist interventions on rational prophylactic antibiotic use and cost saving in elective cesarean section. *Int J Clin Pharmacol Ther*. 2015;53(8):605–15.
78. Zhang HaiXia ZH, et al. Pharmacist interventions for prophylactic antibiotic use in urological inpatients undergoing clean or clean-contaminated operations in a Chinese hospital. 2014.
79. Zhou Y, et al. Impact of pharmacist intervention on antibiotic use and prophylactic antibiotic use in urology clean operations. *J Clin Pharm Ther*. 2015;40(4):404–8.
80. Zhou H, et al. The impact of pharmacist intervention on prophylactic antibiotics use in orthopedic surgery at a hospital in China. *Medicine*. 2021;100(52):e28458.
81. Phan QTN, et al. Impact of antimicrobial stewardship intervention in clean and clean-contaminated surgical procedures at a Vietnamese national hospital. *Trop Med Int Health*. 2022;27(4):454–62.
82. Wattal C, et al. Antimicrobial prescribing patterns of surgical speciality in a tertiary care hospital in India: role of persuasive intervention for changing antibiotic prescription behaviour. *Indian J Med Microbiol*. 2017;35(3):369–75.
83. Butt SZ, et al. Post-surgical antibiotic prophylaxis: impact of pharmacist's educational intervention on appropriate use of antibiotics. *J Infect Public Health*. 2019;12(6):854–60.
84. Cuijpers P, et al. Pre-post effect sizes should be avoided in meta-analyses. *Epidemiol Psychiatr Sci*. 2017;26(4):364–8.
85. Abubakar U, Salman M. Antibiotic use among hospitalized patients in Africa: a systematic review of point prevalence studies. *J Racial Ethn Health Disparities*. 2024;11(3):1308–29. <https://doi.org/10.1007/s40615-023-01610-9>.
86. Acam J, et al. Antimicrobial prescription patterns in East Africa: a systematic review. *Syst Rev*. 2023;12(1):18.
87. Saleem Z, et al. Point prevalence surveys of antimicrobial use: a systematic review and the implications. *Expert Rev Anti Infect Ther*. 2020;18(9):897–910.
88. Honda H, et al. Antimicrobial stewardship in inpatient settings in the Asia Pacific region: a systematic review and meta-analysis. *Clin Infect Dis*. 2017;64(suppl_2):S119–26.
89. Murray JL, et al. Drivers of inappropriate use of antimicrobials in South Asia: a systematic review of qualitative literature. *medRxiv*, 2023.
90. Otieno PA, et al. A systematic review of pharmacist-led antimicrobial stewardship programs in Sub-Saharan Africa. *Int J Clin Pract*. 2022;2022:3639943.
91. Bediako-Bowan AA, et al. Antibiotic use in surgical units of selected hospitals in Ghana: a multi-centre point prevalence survey. *BMC Public Health*. 2019;19(1):1–10.
92. Talaat M, et al. A point prevalence survey of antibiotic use in 18 hospitals in Egypt. *Antibiotics*. 2014;3(3):450–60.
93. Okoth C, et al. Point prevalence survey of antibiotic use and resistance at a referral hospital in Kenya: findings and implications. *Hosp Pract*. 2018;46(3):128–36.
94. Hassan S, et al. Factors that influence adherence to surgical antimicrobial prophylaxis (SAP) guidelines: a systematic review. *Syst Rev*. 2021;10:1–20.
95. Allegranzi B, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis*. 2016;16(12):e276–87.
96. Allegranzi B, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis*. 2016;16(12):e288–303.
97. Harris AD, et al. The use and interpretation of quasi-experimental studies in medical informatics. *J Am Med Inform Assoc*. 2006;13(1):16–23.
98. Eliopoulos GM, et al. The use and interpretation of quasi-experimental studies in infectious diseases. *Clin Infect Dis*. 2004;38(11):1586–91.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.