A systematic review and narrative synthesis of pharmacist-led education-based antimicrobial stewardship interventions and their effect on antimicrobial use in hospital inpatients

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Summary

Background: Antimicrobial stewardship (AMS) programmes optimise antimicrobial use and address antimicrobial resistance. Pharmacists are often key agents of these programmes. The effectiveness of hospital-based AMS interventions when they are led by pharmacists, however, has not previously been reported.

Aim: To evaluate the effectiveness of pharmacist-led AMS interventions in improving antimicrobial use for hospital inpatients.

***Methods*:** Standard systematic review methods were used. The search strategies and databases used in a previous Cochrane review were applied. Studies that reported pharmacist-led AMS interventions were included. Narrative synthesis was used to report the findings. PRISMA guidelines were followed.

Findings: From 6,971 records retrieved and screened, 52 full-text articles were included. Most studies were undertaken in teaching hospitals (n=45) and many were conducted in North America (n=27). Most interventions targeted junior or ward physicians and lasted between one and six months. All studies evaluated educational interventions often in combination with other interventions and reported improvements "in compliance with target AMS practice". Greater compliance was achieved with multiple interventions. Pharmacist-led interventions reduced duration of antimicrobial therapy without increasing mortality. No consistency of evidence was achieved in relation to interventions and reduced duration of hospital stay, nor infections due to antimicrobial resistance or occurrence of *Clostridium difficile*.

Conclusion: This is the first systematic review to evaluate the effectiveness of pharmacist-led AMS interventions in hospital inpatients. Education-based interventions were effective in increasing guideline compliance and reducing duration of antimicrobial therapy. Future hospital-based AMS programmes should consider the involvement of pharmacists to deliver and promote AMS interventions and programmes.

Keywords: (1) antimicrobial stewardship (2) antimicrobial prescribing (3) intervention (4) pharmacist (5) hospital inpatients (6) systematic review

Introduction

Antimicrobial stewardship (AMS) programmes are necessary in every healthcare setting [1]. The implementation of these programmes in hospitals has resulted in improved clinical outcomes and safety, as well as reduced antimicrobial use, expenditure, and antimicrobial resistance (AMR) [2]. Globally, countries are at different stages of implementing these programmes. Most evaluation and evidence of AMS effectiveness has been derived from high-income countries [3]. The majority (183 (83%)) of 221 studies in the 2017 Cochrane review of interventions to improve antimicrobial use in hospitals were conducted in North America and Europe [3]. The World Health Organisation (WHO) has called for a global response to tackle AMR [1], prompting greater engagement with AMS across low- and middle-income countries (LMICs) [4]. Successful implementation of AMS programmes requires a range of conditions including adequate human resources and multidisciplinary engagement [5-7].

Core AMS team members often include an infectious disease physician, medical microbiologist, and pharmacist [8]. In LMICs, particularly with small hospitals, low levels of the implementation of AMS programmes are associated with a lack of specialists in infectious diseases and as such, pharmacists have greater potential to develop and lead AMS in these conditions [9, 10]. Pharmacists have been cited as key agents of hospital AMS [8, 11]. Their role includes introducing and delivering interventions to optimise antimicrobial use, as well as monitoring and reporting AMS performance to achieve programme goals [12, 13]. Pharmacists use a range of AMS interventions to improve antimicrobial prescribing in hospitals, including producing evidence-based guidelines, delivering education and training, reviewing antimicrobial regimens for individual patients and providing advice, and auditing antimicrobial prescribing outcomes and providing data feedback for prescribers [14].

Whilst the inclusion of pharmacists in hospital-based AMS programmes is well-established in many countries, including LMICs [13, 15], there has been no systematic synthesis of the effectiveness of pharmacist-led interventions. The 2017 Cochrane review included 221 studies (published up to January 2015), however, only 20 (9%) studies reported pharmacist-led interventions and these were not combined in a subgroup analysis [3]. The aim of this current systematic review, therefore, was to evaluate the effectiveness of pharmacist-led AMS interventions in improving antimicrobial use for hospital inpatients.

Methods

Standard systematic review methods were used and the study is reported in compliance with the PRISMA guidelines (Appendix Table S1) [16]. The review protocol was registered with PROSPERO (CRD42020205374).

Search strategy and selection criteria

We included articles that identified pharmacist-led interventions in improving antimicrobial use (search terms also included antibiotic, antibacterial, and anti-infective) in hospital inpatient settings. We applied the comprehensive search strategies used in the original 2017 Cochrane review [3] to identify recent primary articles, published between February 2015 and July 2020. The search period for the original Cochrane review [3] was from inception to January 2015. The electronic databases searched were: MEDLINE (OvidSP®), Embase (OvidSP®), and the Cochrane Central Register of Controlled Trials (CENTRAL). Reference lists of retrieved articles were also searched and screened. The search was limited to articles published in English. The search terms and results from each database are shown in Appendix Table S2.

Our review included randomised controlled trials (RCTs) and non-randomised studies (NRS) (controlled before-and-after studies, interrupted-time-series studies, and before-and-after studies). Any population of inpatients admitted in any type of hospital was included. We excluded studies that were undertaken in ambulatory care, accident and emergency departments, or urgent care. We also excluded studies that did not compare interventions with usual care or standard practice.

Type of outcome measures

A variety of outcomes are often reported across studies to evaluate the effectiveness of AMS interventions. There is no consensus regarding which "prescribing outcomes" are the most relevant to illustrate the effectiveness of the programmes [8]. To demonstrate the effectiveness of pharmacist-led AMS interventions, we examined primary outcomes on "compliance with target practice" and "duration of antimicrobial treatment". These are commonly used across AMS studies [3, 17] and represent the common metrics to measure quality of antimicrobial use in acute care settings [18].

Compliance with target practice was assessed using a variety of measures. These included the proportion of antimicrobial prescriptions (drug selection (indication), dose, route of administration, or duration), or proportion of physicians' responses that adhered to antimicrobial guidelines, antimicrobial policies, or recommended practices. The proportion of patients treated in accordance with antimicrobial guidelines or policies was also included.

Secondary outcomes included clinical (mortality and length of hospital stay) and microbiological (infections due to antimicrobial-resistant organisms or *Clostridium difficile*) outcomes.

Data collection and analysis

Data management and selection of studies

Covidence® reference software was used for data management. All search results (including their titles, abstracts, and full texts) were uploaded to Covidence. Duplicate articles across databases were removed before screening. Two authors (TM and NA) independently screened and reviewed titles and abstracts of retrieved articles from the searches and reference lists. Full text articles were then evaluated against eligibility criteria. Discrepancies were resolved by discussion between TM and NA.

Data extraction

Duplicate (TM and NA), independent data abstraction was performed using a bespoke data extraction sheet developed by all authors. The extraction sheet included year of publication, setting, study design, type of hospital, AMS characteristics, participants, type of AMS interventions, intervention recipient, antimicrobial target for interventions, intervention materials, intervention duration, presence of controls, outcomes, and results. Discrepancies were resolved by a discussion.

Risk of bias assessment

We assessed the risk of bias for RCTs using the Cochrane risk of bias tool with six assessment criteria [19]. Studies were scored low risk if all criteria were scored as low, medium risk if one or two criteria were scored unclear or high, and high risk if more than two criteria were scored as unclear or high [3]. We applied the ROBINS-I risk assessment tool to assess the risk of bias for NRS using seven criteria [20]. Duplicate, independent risk of bias assessment was performed, and discrepancies were also resolved by discussion.

Data synthesis

A narrative synthesis was used to report the findings due to the heterogeneity of the included studies in terms of design, types of interventions, and outcomes. We applied PICO (participants, interventions, comparator, and outcomes) elements to report the findings of our review.

Explanation of terms used to describe pharmacist-led interventions

We classified intervention components in accordance with the Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy [21]. Five intervention components were considered relevant with pharmacist interventions in AMS including: educational outreach involving individual patient review and recommendations for change; dissemination of educational materials using group meetings; academic detailing; audit and feedback; and reminders. We also included *'restriction'* as outlined in the Cochrane review [3], when pharmacists used pre-authorisation (expert approval) or antimicrobial formulary restriction for their interventions.

In our review, we classified interventions as *'audit and feedback'* only if they provided a summary of clinical performance to healthcare professionals over a specified period of time [21]. For studies that met our definition, we recorded feedback frequency, format (verbal, written, or both), and whether it was delivered to only prescriber groups or any other healthcare professionals across the hospital (Appendix Table S3).

We further grouped intervention components according to their intervention function as outlined in the Cochrane review [3], to help manage a variety of interventions used across all included studies and to help understand how they were used to change prescribing behaviour. We classified any intervention component as *'education'* if studies used educational outreach, distribution of educational materials, academic detailing, or a combination of these. As a result, we divided intervention components from all included studies into five clusters: education; education plus audit and feedback; education plus reminders; education plus restriction; and education plus audit and feedback plus reminders.

Results

Search results

Twenty studies from the original Cochrane review [3] which reported pharmacist-led AMS interventions in hospital inpatients were included in this current systematic review. A total of 6,918 articles were identified by the database searches and 33 additional articles were identified from reference lists of retrieved articles. A total of 52 studies were included in the final analysis [22-73] (Figure 1).

Characteristics of studies

Summary characteristics of included studies are shown in Table I. Details of data extracted from all 52 studies classified by their design are also described in Table II to V and are fully presented in Appendix Table S3. The majority of studies were NRS (n=46). Most studies were undertaken in North America (n=27) and Asian countries (n=17) (15/17 were categorised as LMICs) [74]. Most studies were undertaken in a one hospital (n=39) and most sites were teaching hospitals (n=45). Interventions were mainly targeted at antimicrobial treatment (n=41) which included: empirical (antimicrobial is prescribed before causative pathogen is known); definitive (antimicrobial is prescribed when causative pathogen becomes available); and switch therapy (switching from an intravenous to an oral antimicrobial agent when patient condition is clinically improved and stable). The remaining nine studies targeted antimicrobial prophylaxis for the prevention of surgical site infections. The intervention period varied from one to over 12 months and for most studies (n=27) ranged between one and six months.

Risk of bias of included studies

The risk of bias assessments of individual studies are fully presented in Appendix Table S4 and S5. Of six RCTs, common reasons for high risk of bias were related to study design which included lack of blinding participants (patients and intervention recipients) and outcome assessors (Figure 2). Most RCTs (n=3) clearly indicated that their studies were not blinded. The high proportion of studies with an unclear risk of bias was due to a lack of description of data or method used to conceal the allocation sequence. Low risk of bias was found in relation to the completeness of reporting outcomes and data, as well as random allocation method. There was one study which randomised patients based upon physician judgement.

Among non-randomised studies, common reasons for medium to serious risk of bias were related to selection bias which included selections of setting and participants, as well as type of outcomes to evaluate the intervention effects (Figure 3). All hospitals included in this review had AMS in place and medical wards where AMS had been established were often included to test the interventions. When overall risk of bias assessed from seven criteria in each study was scored, serious risk of bias was more likely to be found in studies published before 2016 (Appendix Table S5). Lack of rigor in controlling confounding factors was a frequent limitation. Most NRS included in this review were before-and-after studies. Confounding factors from most before-and-after studies included a lack of sample size calculation, non-random convenience sampling, and a lack of the utilisation of identical time periods between pre- and post-intervention to eliminate any potential seasonal influences.

Study findings

The following sections provide a detailed description of elements and effectiveness of pharmacist-led interventions in improving antimicrobial use for hospital inpatients.

(1) Who were participants or targets of pharmacist interventions?

Participants in this review referred to patients and prescribers. We focused on prescribers who prescribed antimicrobial agents and thus were targeted by pharmacist interventions. Of the 52 studies, interventions were targeted at or delivered to junior or ward physicians (n=42) [23-31, 34-36, 38-41, 44-49, 51, 53-66, 68-72], specialist physicians (paediatricians, obstetricians, gynaecologists, anaesthetists, or surgeons) (n=12) [22, 23, 32, 33, 37, 42, 43, 50, 52, 64, 67, 73], and nurses (n=5) [29, 43, 50, 52, 67]. The number of patients reviewed by pharmacists was clearly reported in 46 studies [22-33, 35-51, 54, 55, 57-60, 62-68, 70-73]. These represented a total of 14,552 patients, of which 7,319 and 7,233 were from intervention and control groups, respectively.

(2) Who delivered the interventions? Were they trained to deliver interventions?

All 52 studies involved hospitals that had AMS programmes in place, with a variety of pharmacist-led AMS interventions. The other healthcare professionals involved in AMS teams varied across studies; most (n=42) comprised at least one physician (non-specialist physician or specialist in infectious diseases) who acted as a leader and one pharmacist who operated, facilitated, and delivered interventions [22-26, 30-42, 44, 46, 47, 49-53, 55-66, 69-71, 73]. Ten studies reported that AMS programmes were operated and led by pharmacists [27-29, 43, 45, 48, 54, 67, 68, 72].

Interventions were facilitated and delivered by "clinical" pharmacists (n=37) [22-38, 40-45, 47, 48, 50-52, 55, 58, 61, 63, 64, 67, 70, 72, 73], infectious disease pharmacists (n=9) [39, 49, 53, 54, 57, 60, 62, 65, 71], and "clinical" pharmacists together with infectious disease pharmacists (n=6) [46, 56, 59, 66, 68, 69].

Most studies (n=48) reported how pharmacists were trained to facilitate and deliver the interventions to be evaluated. Pharmacists received specific training in 39 studies [22-38, 40-48, 50-52, 55, 58, 61, 63, 64, 66, 67, 70, 72, 73]. Pharmacists were trained in relevant courses which varied depending on the type of interventions tested. Training sessions were mainly provided by members of an AMS team and focused on education components regarding infection management and antimicrobial utilisation. These often included criteria to assess patient response to antimicrobials, definition of appropriate antimicrobial use, evaluation of adherence according to guidelines, as well as how recommendations and clinical advice should be made and delivered to prescribers when antimicrobials were not prescribed in accordance with guidelines.

Of the nine studies which did not provide specific training, all involved infectious disease pharmacists with postgraduate degrees in infection management or who held a specialised residency in infectious diseases [39, 49, 53, 54, 57, 60, 62, 65, 71].

(3) What interventions did pharmacists use to improve antimicrobial prescribing? How were they delivered?

The details of intervention components and materials are fully described in Appendix Table S6. Education was used in all studies (n=52) and educational outreach based upon the review of individual cases was the most common intervention component (n=45) [23-25, 27, 28, 30-39, 41-62, 65, 66, 68-73]. Pharmacist recommendations were mainly derived and tailored from international or local guidelines, protocols agreed by Pharmacy and Therapeutics Committees, or clinical decision support triggered by microbiology results or therapeutic drug monitoring of antimicrobial agents. The majority (n=39) of studies described the mode for providing pharmacist recommendations, 30 of which used verbal communication (face-to-face contact,

interaction during ward round, or by mobile phone) [23, 24, 27, 30-33, 36-39, 41-44, 46, 50, 51, 53-55, 57, 59, 60, 62, 66, 69-71, 73]. Nine additional studies used non-verbal (written recommendations in medical charts or electronic medical records) (n=5) [25, 35, 45, 56, 65] and both verbal and non-verbal communication (n=4) [28, 52, 58, 72].

Dissemination of educational materials (local guidelines, switch therapy criteria, or protocols developed by interdisciplinary teams) was reported in 19 studies [22, 25, 26, 28, 29, 31, 39, 40, 43, 44, 50, 54, 60, 62-64, 66-68]. Educational materials were disseminated by pharmacists through several routes which included prescriber meetings, intra-organisational networks, or medical charts.

Academic detailing was evaluated in 12 studies [22, 38, 40, 42, 43, 48, 49, 58, 64, 67, 69, 70]. A variety of intervention materials were used by pharmacists, including key messages from guidelines, scientific evidence, problem-based case studies, or local resistance data. These were delivered through lectures or training sessions.

Of 16 studies that reported "audit and feedback" as an intervention, five did not meet the definition in our review [34, 53, 55, 56, 72], even though they described their intervention as "audit and feedback" in the title or the methods. The intervention in these five studies was educational outreach using review cases with the provision of recommendations for change. Audit and feedback was assessed in 11 studies [22, 29, 37, 42, 43, 50, 52, 58, 60, 64, 69], all of which involved feedback directly delivered to prescriber groups. Three studies reported that feedback was also provided to other healthcare professionals, including hospital administrative boards [37, 42, 58]. All studies reported the use of direct communication to deliver feedback which included presentations during group meetings or journal club discussions. One study reported the dissemination of their audit through an intra-organisational network [58].

Reminders were reported in eight studies and combined with education [22, 25, 29, 31, 38, 39, 63, 64]. Reminders acted as an intervention to remind physicians to optimise antimicrobial use, and included the use of manual reminders (pocket size guidelines, posters summarising key messages from guidelines, or stickers printed on medical charts) and computer systems (alert messages integrated in prescribing processes). Studies seldom evaluated 'restriction' as an intervention used by pharmacists (n=3). When restriction was reported, it included pre-authorisation using expert approval (n=2) [30, 59] and antimicrobial formulary restriction (n=1) [54] and these were always combined with education.

(4) Can pharmacist-led interventions improve antimicrobial use for hospital inpatients?
A range of outcomes were reported, including prescribing outcomes (compliance with target practice and duration of antimicrobial therapy), clinical outcomes (mortality and length of

hospital stay), and microbiological outcome. The effect size information of pharmacist-led AMS interventions from individual studies which are classified by their design and presented in hierarchical order in terms of levels of evidence, are fully described in Table II to V.

(4.1) Prescribing outcomes

Compliance with target practice

Compliance was assessed using different metrics, including drug selection (indication), dosage, route of administration, duration of therapy, or de-escalation after interventions were delivered by pharmacists. The intervention effect was an improvement in compliance with target practice estimated by the difference in proportion of compliance between intervention and control groups.

Of the 39 studies (6 RCTs and 33 NRS) that reported this outcome, all reported increased compliance with target practice after intervention delivery. The improvements in compliance varied across studies. Twenty-three studies (4 RCTs and 19 NRS) evaluated an education-only intervention [23, 24, 26-28, 32, 33, 36, 40, 41, 44-46, 48, 49, 55, 62, 65, 67, 70-73], of which 14 (all NRS) reported significant increases in compliance [26, 28, 32, 44-46, 48, 49, 62, 65, 67, 70-72]. Sixteen studies (2 RCTs and 14 NRS) evaluated education plus other interventions and all reported statistically significant improvements in compliance compared with control [22, 25, 29-31, 37-39, 42, 43, 50, 52, 54, 58, 60, 64].

Of the 14 non-randomised studies that reported combined interventions, 10 evaluated education-based interventions plus audit and feedback [22, 29, 37, 42, 43, 50, 52, 58, 60, 64], six of which [29, 37, 43, 50, 60, 64] demonstrated greater improvements when compared with the other four that did not use audit and feedback (three used reminders or one used restriction) [31, 38, 39, 54] and all of the 23 studies using an education-only intervention.

Two interrupted-time-series studies reported increased trends in the proportion of compliance with target AMS practice during intervention delivery [56, 69]. One evaluated education-based interventions plus audit and feedback and the interventions demonstrated a significant increase of trend in compliance during two years of the intervention period [69]. The other study evaluated education-only intervention but did not show a significant increase of trend in improvement in compliance during three years of the intervention delivery [56].

Duration of antimicrobial therapy

In total, 34 studies (3 RCTs and 31 NRS) reported the duration of antimicrobial therapy as an outcome and all reported reduced duration of antimicrobial treatment after intervention delivery. Of these, 25 studies (1 RCT and 24 NRS) demonstrated statistically significant reductions [24, 26, 29, 31, 32, 34-38, 42, 43, 53-60, 63, 66-68, 70]. Reduced duration varied

substantially depending on type of antimicrobial use and type of infections treated. Six studies (1 RCT and 5 NRS) showed consistent evidence that the duration of intravenous antimicrobial therapy before switching to an oral antimicrobial agent was significantly shorter following pharmacist interventions, and ranged between 1.0 to 1.7 days [24, 26, 29, 31, 35, 63].

(4.2) Clinical outcomes

A total of 19 studies (2 RCTs and 17 NRS) reported mortality as an outcome. Interventions were not associated with increased mortality in any study [24, 38, 39, 44, 48, 51, 53, 55, 57, 59, 60, 62, 65, 66, 68, 70-73]. Three studies (all NRS) reported significant reductions in mortality [55, 62, 70].

Overall duration of hospitalisation due to infection was reported by 34 studies (1 RCT and 33 NRS), the majority of which (n=29) (all NRS) demonstrated reduced length of stay, which was statistically significant in 13 studies [29, 33-35, 38, 49-51, 56, 59, 63, 67, 70]. Reduced length of stay differed widely depending on type of infections and type of s treated and ranged between 0.6 and 10 days. Contradictory results were also reported from five studies (1 RCT and 4 NRS) that interventions increased length of stay but did not show a significant difference compared with control group [24, 28, 32, 48, 71].

(4.3) Microbiological outcomes

Ten studies (1 RCT and 9 NRS) reported microbiological outcomes in terms of infections due to antimicrobial-resistant organisms or *Clostridium difficile*. Most studies (1 RCT and 6 NRS) did not show a statistically significant difference after pharmacist interventions had been delivered [26, 48, 50, 53, 60, 65, 73]. Of the remaining, one study reported a significant reduction in infections due to multi-drug resistant organisms from 31.7% to 23.8% [55]. Another study reported a significant decrease in the annual *Clostridium difficile* infection rate from 4.0 to 2.2 cases per month per 10,000 patient-days [54]. In addition, one interrupted-time-series study highlighted a drop in the annual rate of two common pathogens causing hospital-acquired infections of levofloxacin-resistant *Escherichia coli* and *Klebsiella pneumoniae*, of 1.6% and 3.0% respectively [69]. Nevertheless, contradictory results were also reported with these two pathogens which showed an increased trend of an annual resistance rate to imipenem at 0.3 and 1.3% [69].

(5) Did interventions used to improve antimicrobial prescribing differ in different clinical conditions? How effective were they likely to be?

Antimicrobial agents were prescribed for skin infections including prophylaxis for the prevention of surgical site infections (n=12) [22, 32, 37, 42, 43, 49, 50, 52, 53, 58, 64, 67], upper or lower respiratory tract infection (n=9) [25, 30, 33, 53, 54, 57, 60, 65, 68], bacteraemia (n=7) [39, 46, 47, 51, 62, 66, 71], *Clostridium difficile* associated diarrhoea (n=2) [44, 72], and

non-specified/more than three indications (n=23) [23, 24, 26-29, 31, 34-36, 38, 40, 41, 45, 48, 56, 59, 61, 63, 69, 70, 73, 75].

Different pharmacist interventions appeared to be used with some specific clinical conditions. Nine studies assessed the effectiveness of interventions in improving antimicrobial prophylaxis for the prevention of surgical site infections [22, 37, 42, 43, 50, 52, 58, 64, 67]. The majority (n=8) (all NRS) used combined interventions of audit and feedback with education [22, 37, 42, 43, 50, 52, 58, 64]. The use of these combined interventions in improving antimicrobial prophylaxis accounted for the majority of the studies that evaluated audit and feedback (n=11). Nine studies demonstrated significant improvements in target AMS practice after intervention delivery, including receiving proper antimicrobial agent and timing of the first dose before surgery, receiving proper duration of antimicrobial use after surgery, or both. Four studies assessed the effectiveness of interventions on the duration of antimicrobial agent used after the completion of surgical procedure and all showed statistically significant reductions [37, 42, 43, 58].

When pharmacist interventions were used to promote an intravenous to an oral antimicrobial switch therapy (n=10), four studies evaluated combined interventions, and physical reminders (n=4) were only used in a combination with education [25, 29, 31, 63]. Three of these studies (1 RCT and 2 NRS) reported compliance with antimicrobial switch therapy criteria and demonstrated significant increases in compliance [25, 29, 31]. The duration of intravenous antimicrobial use was significantly shorter a day after the interventions had been delivered [29, 31].

Of seven studies (all NRS) that evaluated interventions in improving antimicrobial use in patients with bacteraemia, educational outreach based upon the review of individual cases with the provision of recommendations through prompt and verbal communication was only used in this clinical setting to help adjust antimicrobial dosage regimen in a timely manner. Evidence-based protocol or algorithm developed by Pharmacy and Therapeutics Committees was mainly used to help pharmacists tailor their recommendations. Of four studies that reported compliance with target practice, all evaluated the intervention on *Staphylococcus aureus* bacteraemia and showed significant increases in compliance with AMS practice after intervention delivery, particularly proper selection and early prescribing of anti-staphylococcal agent [39, 46, 62, 71]. Of five studies that evaluated mortality [39, 51, 62, 66, 71], only one [62] reported a significant reduction. Six studies evaluated length of hospital stay [39, 46, 47, 51, 62, 66] but only one [51] reported a significant shorter of length of stay compared with control.

Discussion

To our knowledge, this is the first systematic review to evaluate and report the effectiveness and components of pharmacist-led AMS interventions in improving antimicrobial use for hospital inpatients. The majority of studies demonstrated improved antimicrobial use. Although we were unable to conduct meta-analysis to calculate an absolute effect of pharmacist interventions, we found consistency of evidence from RCTs and NRS that education-based interventions increased compliance with target AMS practice and reduced the duration of antimicrobial therapy. The evidence consistently demonstrated a significant reduction of intravenous antimicrobial therapy as a result of switch interventions and this reflects a previous Cochrane review [3].

Education was the major intervention used by pharmacists to improve antimicrobial prescribing for hospital inpatients and this reflects their expertise, which plays an essential and unique role in optimising prescribing through the provision of education and training for prescribers [14, 76]. Educational interventions influence antimicrobial prescribing behaviour and improve antimicrobial prescribing competency through several mechanisms, including enhancing a better understanding of antimicrobial use and raising awareness of antimicrobial resistance [8, 77]. Our findings concur with a systematic review that investigated interventions involving pharmacists in improving antimicrobial prescribing in general practice settings [17]. Education was the main intervention component and was effective in increasing guideline compliance and decreasing antimicrobial prescribing by general practitioners [17].

The mode of communication of antimicrobial recommendations or data-related to AMS has previously been identified as one of the essential components to improve antimicrobial prescribing and to promote AMS success [7]. Direct or verbal communication between intervention deliverer and prescribers is more effective than non-direct contact in AMS and is necessary for some clinical conditions [8]. We found consistency of evidence that the provision of educational intervention through face-to-face contact with prescribers was mainly used and effective in improving guideline compliance for the treatment of a life-threatening condition of bacteraemia. This finding reflects a previous study that direct consultation with infectious disease specialists was associated with improved compliance with evidence-based practice as well as clinical outcomes in treating patients with bacteraemia [78]. Direct consultation was compared with usual care whereby microbiologic results were only reported and communicated through electronic-based system [78]. In addition, direct communication has been found to help build relationship with non-AMS staff which may then facilitate the acceptance of and compliance with AMS activities [7, 79].

Combined interventions compared with single intervention, were more likely to achieve greater compliance with target AMS practice, particularly with audit and feedback. These have been

mentioned elsewhere as a strategy to optimise antimicrobial use [3] including reported from other clinical areas [80] that multiple interventions were effective than a single intervention in improving guidance compliance. Interventions which included audit and feedback were more successful and effective than those did not [81]. Audit and feedback has been proposed as an effective performance measurement which helps promote and encourage practice change [81]. It has been cited as the most effective behaviour change technique to improve antimicrobial prescribing [3]. Whilst audit and feedback can be effective in improving antimicrobial prescribing particularly when feedback is provided as case-based education [8, 11], only 11 studies in this review reported the use of audit and feedback (combined with education). As such, there is scope for pharmacists to engage with audit and feedback to improve antimicrobial use in hospital settings. Our review also indicated that audit and feedback was mainly used to influence antimicrobial prophylaxis for surgery, which represents a major indication of antimicrobial consumption in hospitals worldwide [82]. Historically, AMS has been universally challenging within surgical specialities [83] and as such, our findings are encouraging in terms of this aspect of AMS.

Although a previous systematic review reported that AMS interventions were associated with a reduction of infections due to *Clostridium difficile* [84], our review did not find consistency of evidence of this effect. The most likely explanation for this difference is because the earlier review mostly included studies that used restriction and when intervention type was stratified, a significant effect was found for restriction [84]. Restriction was seldom used in our review. One study included in our review demonstrated a significant reduction of *Clostridium difficile* with the use of restriction [54]. The positive effect of restriction on microbial outcomes is likely because it has an immediate and greater effect in reducing antimicrobial use compared with education, and thus it has been recommended for use when urgent reduction in antimicrobial consumption is needed [85]. The few studies that evaluated restriction in our review may be due to the recommendations from the 2017 Cochrane review [3] and previous literature [86, 87] which suggest that interventions that apply rules to influence physicians' prescribing behaviour, including preauthorisation using expert approval, were found to be highly associated with negative professional culture and relationships in the long term due to breakdown in communication between infection specialists and clinical teams [3, 86, 87]. Professional relationships and communication are perceived by infection specialists, including pharmacists, to be key to successful and sustainable AMS programmes [7, 79, 88].

No consistency of evidence was achieved in relation to pharmacist interventions and reduced length of hospital stay. This outcome is influenced by hospital and patient factors. A study reported a significant inter-hospital variations in length of stay due to infections, and a shorter stay was found in hospitals with good hygiene [89]. Good hospital hygiene management reduces microbial colonisation and thus reduces the risk of hospital-acquired infections caused

by multi-drug resistant organisms, which are the most common complication during inpatient hospital care [90]. For patient factors, hospitalised patients are more likely to be elderly, severely ill, and have more comorbidities and these were also found to be constituents with prolonged length of stay [91].

There are concerns whether AMS interventions could limit or delay antimicrobial therapy and thus may affect mortality [92]. We found that pharmacist-led interventions were not associated with any increase in mortality. This probably indicates that pharmacist interventions can safely reduce unnecessary antimicrobial use without increasing mortality. This finding is consistent with previous studies which demonstrated that AMS reduced antimicrobial consumption in hospitals and did not affect patient mortality [75, 92].

Although our review highlighted the effectiveness of pharmacist-led interventions, a review of pharmacist involvement in improving antimicrobial use in general practice settings has shown that interventions were more likely to be successful in improving antimicrobial prescribing when they were facilitated by a pharmacist-general practitioner collaborative team [17]. This could be relevant to AMS in hospitals. Interventions could be more accepted if they were delivered by a group of healthcare professionals that shares expertise and responsibilities, particularly including physicians. Physicians have been perceived as clinical leaders and their engagement has enabled many hospital initiatives to succeed and accelerate acceptance across hospitals [93]. Future research efforts should be dedicated in exploring the effectiveness of AMS interventions led by pharmacists in combination with infectious disease health professionals, or ward physicians or nurses whose practices are embedded in daily patient care. It might also be worth exploring factors that affect this difference. These are required not only to bridge the evidence gap of our review, but also to inform and prioritise a collaboration between pharmacists and other healthcare professionals to better implement hospital-based AMS programmes. Intervention duration in our review lasted 1 to 6 months, an evaluation of sustainability or acceptability of pharmacist-led interventions by physicians is also required.

Limitations of this review

While we sought to conduct a systematic review, only three databases were searched and there is the possibility that relevant studies may have been missed. The effectiveness of the interventions reported in this review may not represent impact solely due to pharmacists. Hospital-based AMS programmes could be supported by other healthcare professionals. The interventions evaluated may also have been affected by existing AMS activities or other infection control programmes. Most included studies were NRS. It is likely that the effectiveness of interventions conducted and reported by NRS may be influenced by different factors when compared with those reported by RCTs [94]. Selection bias of settings and participants were commonly reported in the NRS included in this review. Medical wards where

most AMS interventions had been established were often included. Medical staff may have been familiar with AMS activities and this may have facilitated acceptance of and compliance with pharmacist interventions. The analysis of data from the inclusion of additional clinical trials may help confirm and strengthen our findings. The data derived from 52 studies, however, could be considered as an exploratory which will help indicate the effective elements and trends of pharmacist-led interventions, and inform further research in this area.

Strengths of this review

Our review has several strengths. To our knowledge, this is the first systematic review to evaluate the effectiveness and components of pharmacist-led AMS interventions in improving antimicrobial use for hospital inpatients. We followed standard practice of systematic review by following PRISMA guidelines and registered our review with PROSPERO. We applied the comprehensive search strategies used in the earlier Cochrane review to help identify all relevant studies regarding *"interventions in improving antimicrobial use (search terms also included antibiotic, antibacterial, and anti-infective)" and "hospital inpatient settings"*. We report a wide variety of outcomes to demonstrate the effectiveness of AMS interventions for hospital inpatients. We included studies undertaken in all acute care settings (secondary care, tertiary care, teaching, and non-teaching hospitals) and we found data from all economic income level countries. The proportion of studies from LMICs in our review is almost double compared with the earlier Cochrane review [3] and this may depict the growing response to the WHO call launched in 2015 on tackling antimicrobial resistance at a global scale [1]. Although most studies were undertaken in teaching hospitals, the findings derived from this review demonstrate the benefits of a simple and basic intervention of education which could be rolled out by pharmacists in most hospitals, regardless of size or resource.

Implications and recommendations for practice

We highlight the effectiveness of pharmacist-led interventions in hospital-based AMS programmes. We recommend that hospitals include pharmacists within their AMS programmes and the use of multiple interventions, such as education-based interventions plus audit and feedback, for a greater improvement in antimicrobial prescribing. In many LMICs or small hospitals where the low levels of the implementation of AMS programmes are due to a lack of infectious disease expertise [10], hospitals could consider and incorporate pharmacists to help operate and deliver AMS interventions, as well as develop and promote these programmes. When AMS programmes are planned, pharmacists could introduce a simple intervention of education which is less resource consuming and suitable for hospitals with limited resources [8]. Interventions should be particularly focused and targeted in inpatient settings where board-spectrum antimicrobial agents are often prescribed which creates a high risk of the emergence of multidrug-resistant organisms [95].

Conclusions

Pharmacist education-based interventions were effective in increasing compliance with target AMS practice in hospital settings. Greater compliance was more likely achieved with multiple interventions. Pharmacist-led AMS interventions reduced the duration of antimicrobial therapy without adversely affecting mortality. Hospitals should consider incorporating pharmacists to help deliver AMS interventions and promote these programmes.

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TABLES

This manuscript comprises five tables.

Table I Summary characteristics of included studies (n=52)

Table II Characteristics of randomised controlled studies (n=6)

Table III Characteristics of controlled before-and-after studies (n=8)

Table IV Characteristics of interrupted-time-series studies (n=5)

Table V Characteristics of before-and-after (pre-and-post) studies (n=33)

Table I Summary characteristics of included studies (n=52)

Characteristics	Categories	Number of studies
Study design	Randomised controlled trial	6
	Controlled before-and-after study	8
	Interrupted-time-series study	5
	Before-and-after study	33
Place of study	North America	27
	Asia	17
	Europe	4
	Africa	2
	Australia	2
Study year	≤2000	5
	2001-2010	4
	2011-2020	43
Setting	Teaching hospital	45
	Non-teaching hospital	5
	Both	2
Number of hospitals	Single centre	39
	Multicentre	13
Antimicrobial target for pharmacist intervention	Definitive therapy	15
	Empiric therapy	4
	Definitive and empiric therapy	12
	Intravenous to oral antimicrobial switch therapy	10
	Prophylaxis for prevention of surgical site infections	9
	Not specified	2
Classification of intervention components*	Educational outreach involving individual patient review and recommendations for change	45
	Dissemination of educational materials using group meetings	19
	Academic detailing	12
	Audit and Feedback	11

	Reminders	8
	Restriction (pre-authorisation or formulary restriction)	3
Classification of clusters of intervention components**	Education	33
	Education + audit and feedback	8
	Education + reminders	5
	Education + restriction	3
	Education + audit and feedback + reminders	3
Duration of intervention (months)	1 - 6	27
	7 - 12	16
	> 12	9
Primary prescribing outcomes	Compliance with target practice	41
	Duration of antimicrobial treatment	34
Secondary outcomes		
Clinical outcome	Length of hospital stay	34
	Mortality	19
Microbiological outcome	Infections due to antimicrobial-resistant organisms or *Clostridium difficile*	10

**According to the EPOC taxonomy; **According to their intervention function outlined by Davey et al* [3].

Table II Characteristics of randomised controlled studies (n=6)

Study and year	Setting(s)	Country	Patients (clinical problems) and number of patients reviewed or reported	Antimicrobial target for pharmacist intervention	Intervention components	Intervention duration (months)	Effect size of pharmacist interventions				
							Compliance with target ASP practice	Duration of antimicrobial therapy (DOT) (days)	Mortality (%)	Length of hospital stay (LOS) (days)	Microbial outcomes
Education only intervention											
Bailey 1997 [24]	Two tertiary care teaching hospitals	United States	Patients who required IV antimicrobials for at least three or four days (51 intervention group *vs* 51 control group)	IVOST	*EO* (recommendations provided through verbal communication)	7	Intervention 28/51 (54.9%) *vs* control 23/51 (45.1%) **	Mean DOT of IV antimicrobials: intervention (0.8) *vs* control (2.2) *	-	Mean LOS: Intervention (4.9) *vs* control (4.6) **	-
Dranitsaris 2001 [27]	Two tertiary care teaching hospitals	Canada	Adult patients who had presumptive infection and required IV cefotaxime (162 intervention group *vs* 147 control group)	Empirical and definitive therapy	*EO* (recommendations provided through verbal communication)	6	Intervention (122/162) (75.3%) *vs* control (102/147) (69.4%) **	Mean DOT: intervention (4.3±3.1) *vs* control (4.8±4.6) **	-	-	-
Shen 2011 [33]	One tertiary care teaching hospital	China	Patients who had respiratory tract infection admitted in respiratory wards and required antimicrobials (176 intervention group *vs* 178 control group)	Empirical and definitive therapy	*EO* (recommendations provided through verbal communication)	10	Intervention (153/176) (86.9%) *vs* control (112/178) (62.9%) **	-	-	Mean LOS: intervention (14.2±6.2) *vs* control (15.8±6.0) *	-

Van Schoonev eld 2020 [73]	One teaching hospital	United States	Adult patients who had infection and required IV antimicrobials (135 intervention group *vs* 156 control group)	IVOST	*EO* (recommendations provided through verbal communication during ward round activities)	2	Intervention as ATO-A (75/135) (55.6%) *vs* control as UC-A (70/156) (44.9%) **	Median DOT: intervention (7.0 (IQR 2.0-69.0)) *vs* control (7.0 (IQR 2.0-78.0)) **	Intervention (3/135) (2.2%) *vs* control (5/156) (3.2%) **	-	CDI rate: intervention (4/135) (3.0%) *vs* control (2/156) (1.3%) **
Education-based plus other interventions											
Walker 1998 [25]	One non-teaching community hospital	United States	Patients who had community-acquired pneumonia and required IV ceftriaxone (25 intervention group *vs* 25 control group)	IVOST	*DM*, *EO* (recommendations only made and noted in medical chart), and *RMD*	12	Intervention (22/25) (88.0%) *vs* control (9/25) (36.0%) *	-	-	-	-
Strom 2010 [30]	Two teaching hospitals	United States	Patients who required trimethoprim-sulfamethoxazole with an already-active warfarin use (194 intervention group *vs* 148 control group)	Non-specified	*EO* (recommendations provided through verbal communication via discussion with pharmacists), and *RT* (expert approval)	7	Intervention (111/194) (57.2%) *vs* control (20/148) (13.5%) *	-	-	-	-

*AD: academic detailing; AF: audit and feedback; DM: dissemination of educational materials with group meetings; EO: educational outreach; RMD: reminders; RT: restriction; IVOST: intravenous to oral antimicrobial switch therapy; * The difference of effect between intervention and control groups that shows p-value < 0.05; ** The difference of effect between intervention and control groups that shows p-value ≥ 0.05*

Table III Characteristics of controlled before-and-after studies (n=8)

Study and year	Setting(s)	Country	Patients (clinical problems) and number of patients reviewed or reported	Antimicrobial target for pharmacist intervention	Intervention components	Intervention duration (months)	Effect size of pharmacist interventions				
							Compliance with target ASP practice	Duration of antimicrobial therapy (DOT) (days)	Mortality	Length of hospital stay (LOS) (days)	Microbial outcomes
Education only intervention											
Pastel 1992 [23]	One community teaching hospital	United States	Adult patients who required restricted antimicrobial agent(s) for empirical treatment (63 intervention group *vs* 38 control group)	Empirical Therapy	*EO* (recommendations provided through verbal communication)	2.25	Intervention (56/63) (88.9%) *vs* control (28/38) (73.7%) **	-	-	-	-
Heyerly 2016 [46]	One tertiary-care community non-teaching hospital	United States	Adult patients who had positive blood cultures of gram-positive pathogens (107 intervention group *vs* 190 control group)	Definitive therapy	*EO* (recommendations provided through verbal communication)	9	Intervention (30/107) (28.0%) *vs* control (20/190) (10.5%) *	-	-	Mean LOS: intervention 11.0 *vs* control 11.0 **	-
Okada 2016 [47]	One tertiary care teaching hospital	Japan	Patients who were admitted at the haematological medical ward and required anti-MRSA agents (74 intervention group *vs* 71 control group)	Empirical and definitive therapy	*EO* (non-specified mode of communication)	23	-	Median DOT of anti-MRSA agents: intervention (10.0 (IQR 4.0-14.0)) *vs* control (11.0 (IQR 4.0-18.0)) **	-	Median LOS: intervention (48.0 (26.0-429.0)) *vs* control (70.0 (10.0-691.0)) **	-

Shannon 2016 [48]	One community non-teaching hospital	United States	Adult patients who had a reported beta-lactam allergy and required at least one alternative (non-beta lactam) antibiotic during admission (63 intervention group *vs* 63 control group)	Empirical and definitive therapy	*AD* and *EO* (non-specified mode of communication)	7	Intervention (36/63) (57.1%) *vs* control (14/63) (22.2%) *	Mean DOT: intervention (13.0±11.8) *vs* control (14.6±11.9) **	Intervention (1/63) (1.6%) *vs* control (4/63) (6.3%) **	Mean LOS: intervention (9.4±7.7) *vs* control (8.2±7.1) **	CDI rate: intervention (1/63) (1.6%) *vs* control (1/63) (1.6%) **
Li 2017 [55]	Six tertiary care teaching hospitals (8 ICU units of 4 in control and 4 in intervention group)	China	Adult patients who had critically ill admitted in intensive care unit and required antimicrobial within 24 hours after hospitalisation (353 intervention group *vs* 224 control group)	Empirical therapy	*EO* (recommendations provided through verbal communication during ward rounds)	2	Intervention (260/353) (73.7%) *vs* control (152/224) (67.9%) **	Median DOT of empirical use: intervention (2.7 (IQR 1.9-6.2)) *vs* control (3.0 (IQR 1.4-4.6)) *	Intervention (68/353) (19.3%) *vs* control (65/224) (29.0%) *	Median LOS: intervention (17.0 (IQR 12.0-29.0)) *vs* control (18.0 (IQR 11.0-31.0)) **	Multi-drug resistant infection rate: intervention (84/353) (23.8%) *vs* control (71/224) (31.7%) *
Education-based plus other interventions											
Landgren 1988 [22]	Twelve hospitals (4 teaching and 8 non-teaching hospitals)	Australia	Patients who underwent surgery (445 intervention group *vs* 397 control group)	Antimicrobial prophylaxis	*AF*, *DM*, *AD*, and *RMD*	6	Intervention (250/445) (56.2%) *vs* control (143/397) (36.0%) *	-	-	-	-
Dunn 2011 [31]	One teaching hospital	Ireland	Adult patients who had infection and required IV antimicrobial during the first four days of admission (72 intervention group *vs* 44 control group) (Data from phase II)	IVOST	*DM*, *EO* (recommendations provided through verbal communication), and *RMD* (stickers)	7	Intervention (52/72) (71.7%) *vs* control (24/44) (55.5%) *	Median IV DOT: intervention (3.0) *vs* control (4.0) *	-	-	-

Apisarnthanarak 2015 [38]	One tertiary care teaching hospital	Thailand	Adult patients who had presumptive infection and required one antimicrobial prescription admitted in medical wards (104 intervention group *vs* 150 control group)	Empirical and definitive therapy	*AD, EO* (recommendations provided through verbal communication during ward rounds), and *RMD*	9	Intervention 96/104 (92.3%) *vs* control 105/150 (70.0%) *	Mean DOT: intervention (8.4±3.0) *vs* control (17.5±20.0) *	Intervention (10/104) (9.6%) *vs* control (10/150) (6.7%) **	Mean LOS: intervention (18.7±17.0) *vs* control (28.8±7.0) *	-

*AD: academic detailing; AF: audit and feedback; DM: dissemination of educational materials with group meetings; EO: educational outreach; RMD: reminders; RT: restriction; IVOST: intravenous to oral antimicrobial switch therapy; * The difference of effect between intervention and control groups that shows p-value < 0.05; ** The difference of effect between intervention and control groups that shows p-value ≥ 0.05*

Table IV Characteristics of interrupted-time-series studies (n=5)

Study and year	Setting(s)	Country	Patients (clinical problems) and number of patients reviewed or reported	Antimicrobial target for pharmacist intervention	Intervention components	Intervention duration (months)	Effect size of pharmacist interventions[¥]				
							Compliance with target ASP practice	Duration of antimicrobial therapy (DOT)	Mortality	Length of hospital stay (LOS)	Microbial outcomes
Education only intervention											
Newland 2012 [34]	One tertiary teaching children's hospital	United States	Paediatric patients who required selected board spectrum antimicrobial agents in the lists monitored by AMS team	Empirical and definitive therapy	*EO* (non-specified mode of communication)	30	-	DOT decreased 12.0% per month per 1,000 patient-day during intervention period *	-	LOS decreased 13.0% per month per 1,000 patient-day during intervention period *	-
Campbell 2017 [53]	One community teaching hospital	Canada	Patients who required IV antimicrobial agent admitted in surgery, respiratory, and medical wards	Empirical and definitive therapy	*EO* (recommendations provided through verbal communication)	Surgical (51), respirator (48), and medical (30) wards	-	Linear trend of DOT before and after intervention: decreased 12.0% in surgical ward, 10.0% in respiratory ward, and 20.0% in medical ward (per 1,000 patient-day) during intervention period *	Linear trend of mortality before and after intervention: changed 0.99 to 0.97 in surgical ward, 11.5 to 12.2 in respiratory ward, and 7.4 to 5.0 in medical ward (cases per 1,000 patient-day) **	Linear trend of LOS before and after intervention: changed 4.7 to 4.3 in surgical ward, 9.6 to 8.5 in respiratory ward, and 10.2 to 10.3 in medical ward (days per 1,000 patient-day) **	Linear trend of CDI rate before and after intervention: decreased 0.8 to 0.4 in surgical ward, 2.4 to 0.8 in respiratory ward, and 0.8 to 0.4 in medical ward (cases per 1,000 patient-day) **
Nault 2017 [56]	One tertiary care teaching hospital	Canada	Patients who required IV or oral antimicrobial agent(s)	Empirical and definitive therapy	*EO* (recommendations only made and noted in clinical decision-support system)	36	Trend change of proportion of prescriptions that did not adhere with guideline decreased 0.1% per month over time of intervention period **	Trend change of DOT decreased 1.4 days per 1,000 patient-day over time of intervention period *	-	Trend change of LOS decreased 0.1 day over time of intervention period *	-

Hwang 2018 [61]	One secondary care teaching hospital	Korea	Adult patients who required anaerobe antibiotic	Empirical therapy	*EO* (non-specified mode of communication)	5	-	Trend change of DOT of metronidazole decreased 13.9 days per 1,000 patient-day/month *	-	-	-
Education-based plus other interventions											
Wang H 2019 [69]	One tertiary care teaching hospital	China	All patients who were admitted in inpatient settings and required IV or oral antimicrobials	Non-specified	*AF* (feedback to all medical staff every month in meetings), *AD*, and *EO* (recommendations provided through verbal communication)	25	Trend change in compliance with target practice increased 1.2% per month during intervention period *	-	-	-	(1) Trend change of levofloxacin-resistant *E. coli* decreased 1.6% per year* while imipenem-resistant *E. coli* increased 0.3% per year* during intervention period (2) Trend change of levofloxacin-resistant *K. pneumoniae* decreased 3.0% per year** while imipenem-resistant *K. pneumoniae* increased 1.3% per year* during intervention period

*AD: academic detailing; AF: audit and feedback; DM: dissemination of educational materials with group meetings; EO: educational outreach; RMD: reminders; RT: restriction; IVOST: intravenous to oral antimicrobial switch therapy; ¥ The intervention effect is measured against the pre-intervention trend; * Trend of change of post-intervention measured against pre-intervention that shows p-value < 0.05: ** Trend of change of post-intervention measured against pre-intervention that shows p-value ≥ 0.05*

Table V Characteristics of before-and-after (pre-and-post) studies (n=33)

Study and year	Setting(s)	Country	Patients (clinical problems) and number of patients reviewed or reported	Antimicrobial target for pharmacist intervention	Intervention components	Intervention duration (months)	Effect sizes of pharmacist interventions				
							Compliance with target ASP practice	Duration of antimicrobial therapy (DOT) (days)	Mortality	Length of hospital stay (LOS) (days)	Microbial outcomes
Education only intervention											
Martínez 2000 [26]	Two tertiary care teaching hospitals	Spain	Patients who had infection and required IV clindamycin at least 72 hours (204 post-INT group *vs* 269 pre-INT group)	IVOST	*DM*	6	Post-INT (107/204) (52.5%) *vs* pre-INT (57/269) (21.1%) *	Mean DOT of IV clindamycin decreased 1.3 days in post-INT compared with pre-INT (no raw data shown) *	-	Median LOS: post-INT (14.5 (IQR 5.0-59.0)) *vs* pre-INT (13.0 (IQR 4.0-50.0)) **	CDI rate: post-INT (1/204) (0.5%) *vs* pre-INT (10/269) (3.7%) **
Ho 2005 [28]	One tertiary care teaching hospital	Canada	Adult patients who required IV ciprofloxacin at least 48 hrs and were candidates for IV to oral antimicrobial conversion (201 post-INT group *vs* 244 pre-INT group)	IVOST	*DM* and *EO* (recommendations noted in medical chart or discussed with physicians if antimicrobials needed to be converted to oral form prior 48 hours of IV ciprofloxacin initiation)	4	Post-INT (136/201) (67.7%) *vs* pre-INT (130/244) (53.3%) *	-	-	Mean LOS: post-INT (17.0 (range 1.0-165.0)) *vs* pre-INT (12.0 (range1.0-84.0)) **	-
Grill 2011 [32]	One teaching hospital	Germany	Adult patients who were admitted in surgical wards and required antimicrobial for a proven or suspected infection (321 post-INT group *vs* 317 pre-INT group)	IVOST	*EO* (recommendations provided through verbal communication during ward rounds)	6	Post-INT (85/480 of administrations) (17.7%) *vs* pre-INT (49/452 administrations) (10.8%) *	Mean IV DOT: post-INT (8.0) *vs* pre-INT (10.0) *	-	Median LOS: post-INT (19.0 (IQR 3.0-130.0)) *vs* pre-INT (18.0 (IQR 3.0-220.0)) **	-

Yen 2012 [35]	One tertiary teaching hospital	Taiwan	Patients who required IV levofloxacin for more than 48 hours (37 post-INT group *vs* 42 pre-INT group)	IVOST	*EO* (recommendations only made and noted in medical records)	2	-	Mean IV levofloxacin: post-INT (6.6±4.4) *vs* pre-INT (8.3±3.8) **	-	Mean LOS: post-INT (16.1±9.3) *vs* pre-INT (27.2±18.5) *	-
Cappelletty 2013 [36]	One tertiary care teaching hospital	United States	Adult patients who required one of the selected antimicrobial agents for at least 72 hours (45 post-INT group *vs* 51 pre-INT group)	Empirical and definitive therapy	*EO* (recommendations provided through verbal communication via discussion)	3	Post-INT (33/45) (73.3%) *vs* pre-INT (34/51) (66.7%) **	Mean DOT: post-INT (4.8±1.4) *vs* pre-INT (5.6±2.2) **	-	-	-
Phillips 2015 [40]	One tertiary care teaching hospital	Australia	Adult patients who had infection and required vancomycin for documented therapy (45 post-INT group *vs* 53 pre-INT group)	Definitive therapy	*DM* and *AD*	8	(1) Appropriate maintenance dose of vancomycin: post-INT (29/45) (64.4%) *vs* pre-INT (28/53) (52.8%) ** (2) Dosage adjustment when vancomycin levels were outside of target: post-INT (24/34) (70.6%) vs pre-INT (21/39) (53.9%) **	Median vancomycin DOT: post-INT (6.0 (IQR 4.0-16.5)) *vs* pre-INT (10.0 (IQR 4.3-13.8)) **	-	Median LOS: post-INT (16.0 (IQR 9.0-29.5)) *vs* pre-INT (20.0 (IQR 10.5-32.5)) **	-
Tavakoli-Ardakani 2015 [41]	One teaching hospital	Iran	Adult patients who required IV vancomycin admitted in intensive care unit and haematology-oncology wards (82 post-INT group *vs* 77 pre-INT group)	Empirical and definitive therapy	*EO* (recommendations provided through verbal communication via discussion)	6	Post-INT (54/82) (65.9%) *vs* pre-INT (42/77) (54.6%) **	-	-	-	-

Brumley 2016 [44]	One community teaching hospital	United States	Adult patients who had positive *Clostridium difficile* infection (83 post-INT group *vs* 89 pre-INT group)	Definitive therapy	*DM* and *EO* (recommendations provided through verbal communication during ward rounds)	3	Post-INT (67/83) (80.7%) *vs* pre-INT (40/89) (44.9%) *	-	Post-INT (3/83) (3.6%) *vs* pre-INT (1/89) (1.1%) **	Mean LOS: post-INT (6.8) *vs* pre-INT (7.1) **	-
Ellis 2016 [45]	One tertiary care teaching hospital	United States	Adult patients who were admitted in geriatric psychiatric unit and had presumptive infection (95 prescriptions for 70 patients in post-INT group *vs* 71 prescriptions for 63 patients in pre-INT group)	Empiric and definitive therapy	*EO* (non-verbal communication)	6	Post-INT (63/95) (66.3%) *vs* pre-INT (36/71) (50.7%) *	Mean DOT: post-INT (174/1,000 patient-day) *vs* pre-INT (174/1,000 patient-day) **	-	-	-
Yu 2016 [49]	One tertiary care teaching Children's hospital	United States	Paediatric patients who had purulent MSSA or MRSA skin infection (103 post-INT group *vs* 121 pre-INT group)	Definitive therapy	*AD* and *EO* (non-specified mode of communication)	12	Post-INT (91/103) (88.3%) *vs* pre-INT (90/121) (74.4%) *	-	-	Median LOS: post-INT (2.0 (0.7-5.1)) *vs* pre-INT (2.5 (IQR 0.6-9.5)) *	-
Beganovic 2017 [51]	One tertiary care teaching hospital	United States	Adult and paediatric patients who had positive blood culture (123 patients (126 blood cultures) in post-INT group *vs* 116 patients (126 blood cultures) in pre-INT group)	Definitive therapy	*EO* (recommendations provided through verbal communication)	3	-	Mean DOT: post-INT (15.9±11.1) *vs* pre-INT (18.6±12.0) **	Post-INT (15/123) (12.2%) *vs* pre-INT (12/116) (10.3%) **	Mean LOS: post-INT (9.0±7.3) *vs* pre-INT (15.0±22.7) *	-

Willis 2017 [57]	One tertiary community teaching hospital	United States	Adult patients who had respiratory tract infections (all types of pneumonia or Chronic Obstructive Pulmonary Diseases) and required IV vancomycin for MRSA coverage (150 post-INT group *vs* 150 pre-INT group)	Definitive therapy	*EO* (prompt recommendations provided through verbal communication)	6	-	Median vancomycin DOT: post-INT (2.1 (IQR 1.4±3.9)) *vs* pre-INT (4.2± (IQR2.8-5.8)) *	Post-INT (3/150) (2.0%) *vs* pre-INT (3/150) (2.0%) **	Median LOS: post-INT (7.0 (IQR 5.0±9.0)) *vs* pre-INT (8.0± (IQR 4.2-10.0)) **	-
Ohashi 2018 [62]	One tertiary care teaching hospital	Japan	Adult patient who had MRSA bacteraemia (51 post-INT group *vs* 43 pre-INT group)	Definitive therapy	*DM* and *EO* (prompt recommendations provided through verbal communication)	31	Post-INT (42/51) (82.4%) *vs* pre-INT (27/43) (62.3%) *	-	Post-INT (11/51) (21.6%) *vs* pre-INT (18/43) (41.8%) *	Median LOS: post-INT (35.0 IQR (22.0-59.0)) *vs* pre-INT (52.5 IQR (23.8-70.0)) **	-
Bianchini 2019 [65]	One tertiary care teaching hospital	United States	Patients who were admitted in intensive care unit and had pneumonia (91 post-INT group *vs* 91 pre-INT group)	Definitive therapy	*EO* (recommendations only made and noted in electronic medical record)	5	Post-INT 53/91 (58.2%) *vs* pre-INT 24/91 (26.4%) *	Median DOT: post-INT (7.0 (IQR 6.0-8.0)) *vs* pre-INT (7.0 (IQR 6.0-10.0)) **	Post-INT (7/91) (7.7%) *vs* pre-INT (13/91) (14.3%) **	Median LOS: post-INT (9.0 (IQR 7.0-16.0)) *vs* pre-INT (9.0 (IQR 6.0-15.0)) **	Multi-drug resistant infection rate: post-INT (2/91) (2.2%) *vs* pre-INT (6/91) (6.6%) ** CDI rate: post-INT (0/91) (0%) *vs* pre-INT (1/91) (1.1%) **

Box 2019 [66]	Five tertiary care teaching hospitals (5 acute cares that compose in Scripps Health)	United States	Adult patients who had bacteraemia caused by non-resistant gram-negative bacteria (539 post-INT group *vs* 512 pre-INT group)	Definitive therapy	*DM* and *EO* (recommendations provided through verbal communication)	12	-	Median DOT of anti-pseudomonal (per patient-day): post-INT (0.2 (IQR 0-0.4)) *vs* pre-INT (0.4 (IQR 0-0.7)) *	Post-INT (28/539) (5.2%) *vs* pre-INT (36/512) (7.0%) **	Median LOS: post-INT (5.0 (IQR 4.0-7.0)) *vs* pre-INT (5.0 (IQR 4.0-7.0)) **	-
Butt 2019 [67]	One tertiary care teaching hospital	Pakistan	Patients who underwent surgical procedures (225 post-INT group *vs* 225 pre-INT group)	Antimicrobial prophylaxis	*DM* and *AD*	4	Post-INT (28/225) (12.4%) *vs* pre-INT (3/225) (1.3%) *	Mean DOT: post-INT (2.3 ± 1.5) *vs* pre-INT (2.8 ± 1.7) *	-	Mean LOS: post-INT (4.5 ± 3.4) *vs* pre-INT (5.4 ± 4.8) *	-
Pham 2019 [68]	One community teaching hospital	United States	Adult patients who had pneumonia (all types of pneumonia) and required IV vancomycin for MRSA coverage (72 post-INT group *vs* 138 pre-INT group)	Definitive therapy	*DM* and *EO* (non-specified mode of communication)	6	-	Mean DOT of IV vancomycin: post-INT (1.4±1.2) *vs* pre-INT (2.5±1.3) *	Post-INT (5/72) (6.9%) *vs* pre-INT (18/138) (13.0%) **	Mean LOS: post-INT (8.9±8.0) *vs* pre-INT (8.9±5.8) **	-
Xin 2019 [70]	One tertiary care teaching hospital	China	Patients who had infection and required carbapenem (518 post-INT group *vs* 515 pre-INT group)	Definitive therapy	*AD* and *EO* (recommendations provided through verbal communication via discussion)	12	Post-INT (307/518) (59.3%) *vs* pre-INT (112/515) (21.7%) *	Mean DOT: post-INT (7.4±0.9) *vs* pre-INT (13.3±1.8) *	Post-INT (49/518) (9.5%) *vs* pre-INT (92/515) (17.9%) *	Mean LOS: post-INT (9.3±1.5) *vs* pre-INT (15.9±2.2) *	-

Arensman 2020 [71]	Seven tertiary care teaching hospitals (Advocate Aurora Health Hospitals)	United States	Adult patients who had positive *Staphylococcus aureus* bacteraemia (121 post-INT group *vs* 87 pre-INT group)	Definitive therapy	*EO* (recommendations provided through verbal communication	8	Post-INT (from period III) (92/121) (76.0%) *vs* pre-INT (from period II) (47/87) (54.0%) *	-	Post-INT (6/121) (4.9%) *vs* pre-INT (2/87) (2.3%) **	Mean LOS: post-INT (12.0±10.7) *vs* pre-INT (8.9±6.2) *	-
Bishop 2020 [72]	One tertiary care teaching hospital	United States	Adult patients who had positive *Clostridium difficile* infection (113 post-INT group *vs* 120 pre-INT group)	Definitive therapy	*EO* (recommendations provided through verbal communication via telephone with documenting in electronic heath medical record in pharmacy progress note section)	17	Post-INT 65/113 (57.5%) *vs* pre-INT 50/120 (41.7%) *	-	Post-INT (3/113) (2.7%) *vs* pre-INT (10/120) (8.3%) **	Median LOS: post-INT (11.0) *vs* pre-INT (12.0) **	-
Education-based plus other interventions											
McLaughlin 2005 [29]	One tertiary care teaching hospital	United Kingdom	Patients who were admitted in medical wards and required IV antimicrobial (IV-treated infection episodes: 107 post-INT group *vs* 118 in pre-INT group)	IVOST	*AF* (feedback to medical staff through presentation and inserted data in medical chart, no frequency documented), *DM*, and *RMD* (stickers labelled in medical chart and posters)	1	Post-INT (71/79) (89.9%) *vs* pre-INT (15/90) (16.7%) *	Median IV DOT of group II: post-INT (2.0 (IQR 1.0-16.0)) *vs* pre-INT (3.0 (IQR 1.0-22.0)) * (Data of DOT based on all patients recruited)	-	Median LOS: post-INT (10.0 (IQR 1.0-108.0)) *vs* pre-INT (13.0 (IQR 1.0-72.0)) *	-

Zhang 2014 [37]	One tertiary care teaching hospital	China	Patients who required antimicrobial for the prevention of preoperative surgery admitted in urological ward (193 post-INT group *vs* 171 pre-INT group)	Antimicrobial prophylaxis	*AF* (feedback to all clinical departments including hospital administration; no frequency documented) and *EO* (verbal communication with real time monitoring)	6	Post-INT (60/80) (75.0%) *vs* pre-INT (36/88) (40.9%) *	Mean DOT: post-INT (2.9) *vs* pre-INT (7.6) * (Data of DOT based on all patients recruited)	-	-	-
Nguyen 2015 [39]	One tertiary care teaching hospital	United States	Adult patients who had positive MSSA or MRSA bacteraemia (88 post-INT group *vs* 82 pre-INT group)	Definitive therapy	*DM*, *EO* (verbal communication), and *RMD* (pocket size guidelines)	9	Post-INT (74/88) (84.1%) *vs* pre-INT (46/82) (56.1%) *	-	Post-INT (10/88) (11.4%) *vs* pre-INT (16/82) (19.5%) **	Median LOS: post-INT (9.0 IQR 5.0-20.0)) *vs* pre-INT (9.0 IQR 5.0-17.0)) **	-
Wang J 2015 [42]	One tertiary care teaching hospital	China	Patients who underwent elective caesarean section admitted in maternity ward (197 post-INT group *vs* 197 pre-INT group)	Antimicrobial prophylaxis	*AF* (feedback to all health professionals including hospital administration every two weeks), *AD*, and *EO* (verbal communication)	3	Correct for both choice and dose: post-INT (185/197) (93.9%) *vs* pre-INT (7/197) (3.6%) *	Mean DOT of antimicrobial prophylaxis use: post-INT (1.9) *vs* pre-INT (4.1) *	-	Mean LOS: post-INT (6.2) *vs* pre-INT (6.2) **	-
Zhou Y 2015 [43]	One tertiary care teaching hospital	China	Adult patients who underwent clean and clean-contaminated operations admitted in urological ward (11 post-INT group *vs* 36 pre-INT group)	Antimicrobial prophylaxis	*AF* (feedback to all clinical departments every month through meetings), *DM*, *AD*, and *EO* (recommendations provided through verbal communication during ward rounds)	6	Correct timing of antimicrobial use (0.5-2 hrs prior to surgery): post-INT (8/11) (72.7%) *vs* pre-INT (7/36) (19.4%) *	(1) Year 2010 vs 2012: post-INT (1.3±0.5) *vs* pre-INT (3.9±1.6) * (2) Year 2010 vs 2013: post-INT (2.0±1.4) *vs* pre-INT (3.9±1.6) *	-	-	-

Zhou L 2016 [50]	One tertiary care teaching hospital	China	Patients who underwent cardiothoracic surgery (508 post-INT group *vs* 342 pre-INT group)	Antimicrobial prophylaxis	*AF* (feedback to leadership in cardiothoracic surgery departments every week through meeting), *DM*, and *EO* (recommendations provided through verbal communication during ward rounds)	17	Post-INT (496/508) (97.6%) *vs* pre-INT (157/342) (45.9%) *	-	-	Mean LOS: post-INT (20.9±8.9) *vs* pre-INT (23.3±8.9) *	Resistance rate of *S. aureus* to clindamycin: post-INT 25.9% *vs* pre-INT 60.0% ** Resistance rate of *E. cloacae* to imipenem: post-INT 1.7% *vs* pre-INT 9.4% ** Resistance rate of *K. pneumoniae* to ceftazidime: post-INT 7.7% *vs* pre-INT 12.5% **
Brink 2017 [52]	Thirty-four private (urban and rural) non-teaching hospitals	South Africa	Patients who underwent surgical procedures	Antimicrobial prophylaxis	*AF* (feedback to surgeons every month in theatre rooms with additional emails and presented during journal clubs) and *EO* (recommendations noted in medical chart or sent through mobile phone messages)	16	Post-INT (83.3%) *vs* pre-INT (66.8%) * (no raw data of number of prescriptions shown)	-	-	-	-

Shea 2017 [54]	Four tertiary care (teaching and non-teaching) hospitals	United States	Patients who required one of quinolones for pneumonia or Chronic Obstructive Pulmonary Diseases exacerbation (130 post-INT group *vs* 232 pre-INT group)	Empirical and definitive therapy	*DM*, *EO* (recommendations provided through verbal communication), and *RT* (using antibiotic formulary restriction)	15 (phase I: 3 and phase II: 12)	Phase I and II: post-INT (74/130) (56.9%) *vs* pre-INT (74/232) (31.9%) *	Mean DOT phase I: post-INT (21.5±6.4) *vs* pre-INT (41.0±4.4) * Phase II: post-INT (4.8±3.6) *vs* pre-INT (41.0±4.4) *	-	-	Mean CDI rate (per month per 10,000 patient-day) of phase I and II: post-INT (2.2±1.4) *vs* pre-INT (4.0±2.1) *
Yang 2017 [58]	One tertiary teaching hospital	China	Patients who underwent vascular and interventional radiology procedures (177 post-INT group *vs* 162 pre-INT group)	Antimicrobial prophylaxis	*AF* (feedback to all medical departments via meetings and published on hospital website for other professionals), *AD*, and *EO* (recommendations sent through intranet system and provided through verbal communication via telephone)	6	Post-INT (174/177) (98.3%) *vs* pre-INT (134/162) (82.7%) *	Mean DOT of antimicrobial prophylaxis use: post-INT (0.5±1.0) *vs* pre-INT (0.9±2.0) *	-	-	-
Eljaaly 2018 [59]	One community teaching hospital	United States	Adult patients who had infection and required one of restricted antibiotics for ≥ 3 days (83 post-INT group *vs* 83 pre-INT group)	Definitive therapy	*EO* (verbal communication) and *RT* (using expert approval)	3	-	Median DOT for restricted antimicrobials: post-INT (4.0 (IQR 3.0-5.0)) *vs* pre-INT (5.0 (IQR 4.0-8.8)) *	Post-INT (2/83) (2.4%) *vs* pre-INT (8/83) (9.6%) **	Median LOS: post-INT (6.0 (IQR 5.0-9.0)) *vs* pre-INT (8.0 (IQR 5.0-17.0)) *	-

Fooland 2018 [60]	Three teaching hospitals	United States	Adult patients who had pneumonia (293 post-INT group *vs* 307 pre-INT group)	Empirical therapy	*AF* (feedback to physicians in primary teams via direct and verbal communication, no frequency documented), *DM*, and *EO* (verbal communications)	6	Post-INT (120/287) (41.8%) *vs* pre-INT (17/304) (5.6%) *	Median DOT: post-INT (6.0 (IQR 5.0-7.0)) *vs* pre-INT (9.0 (IQR 7.0-10.0)) *	Post-INT (3/293) (1.0%) *vs* pre-INT (7/298) (2.3%) **	-	CDI rate: post-INT (0/293) (0%) *vs* pre-INT (0/294) (0%) **
Sze 2018 [63]	Eight district non-teaching hospitals	Malaysia	Adult patients who had infection and required IV antimicrobial at least 48 hours (76 patients (77 courses) in post-INT group *vs* 72 patients (79 courses) in pre-INT group)	IVOST	*DM* and *RMD* (using stickers labelled in medical chart)	2	-	Mean DOT of IV antimicrobial: post-INT (2.8±1.2) *vs* pre-INT (4.1±1.6) *	-	Mean LOS: post-INT (4.1±1.7) *vs* pre-INT (5.5±3.2) *	-
Abubakar 2019 [64]	Two tertiary care teaching hospitals	Nigeria	Adult women who underwent elective and emergency obstetric and gynaecologic surgeries for clean, clean-contaminated and contaminated wounds (238 post-INT group *vs* 226 pre-INT group)	Antimicrobial prophylaxis	*AF* (feedback to obstetricians and gynaecologists through group meetings), *DM*, *AD*, and *RMD* (using posters)	3	Post-INT 103/238 (43.3%) *vs* pre-INT 32/226 (14.2%) *	-	-	Mean LOS: post-INT (6.1±2.6) *vs* pre-INT (6.4±2.8) **	-

*AD: academic detailing; AF: audit and feedback; DM: dissemination of educational materials with group meetings; EO: educational outreach; RMD: reminders; RT: restriction; IVOST: intravenous to oral antimicrobial switch therapy; Pre-INT: pre-intervention (baseline); Post-INT: post-intervention (follow up); * The difference of effect between pre- and post-intervention that shows p-value < 0.05; ** The difference of effect between pre- and post-intervention that shows p-value ≥ 0.05*

FIGURES

This manuscript comprises three figures.

Figure 1: PRISMA flow diagram search strategy for the review

Figure 2: Risk of bias graph for each risk of bias criterion according to a Cochrane risk of bias tool presented as percentages for RCTs (n=6)

Figure 3: Risk of bias graph for each risk of bias criterion according to the ROBINS-I risk of bias assessment tool presented as percentages for NRS (n=46)

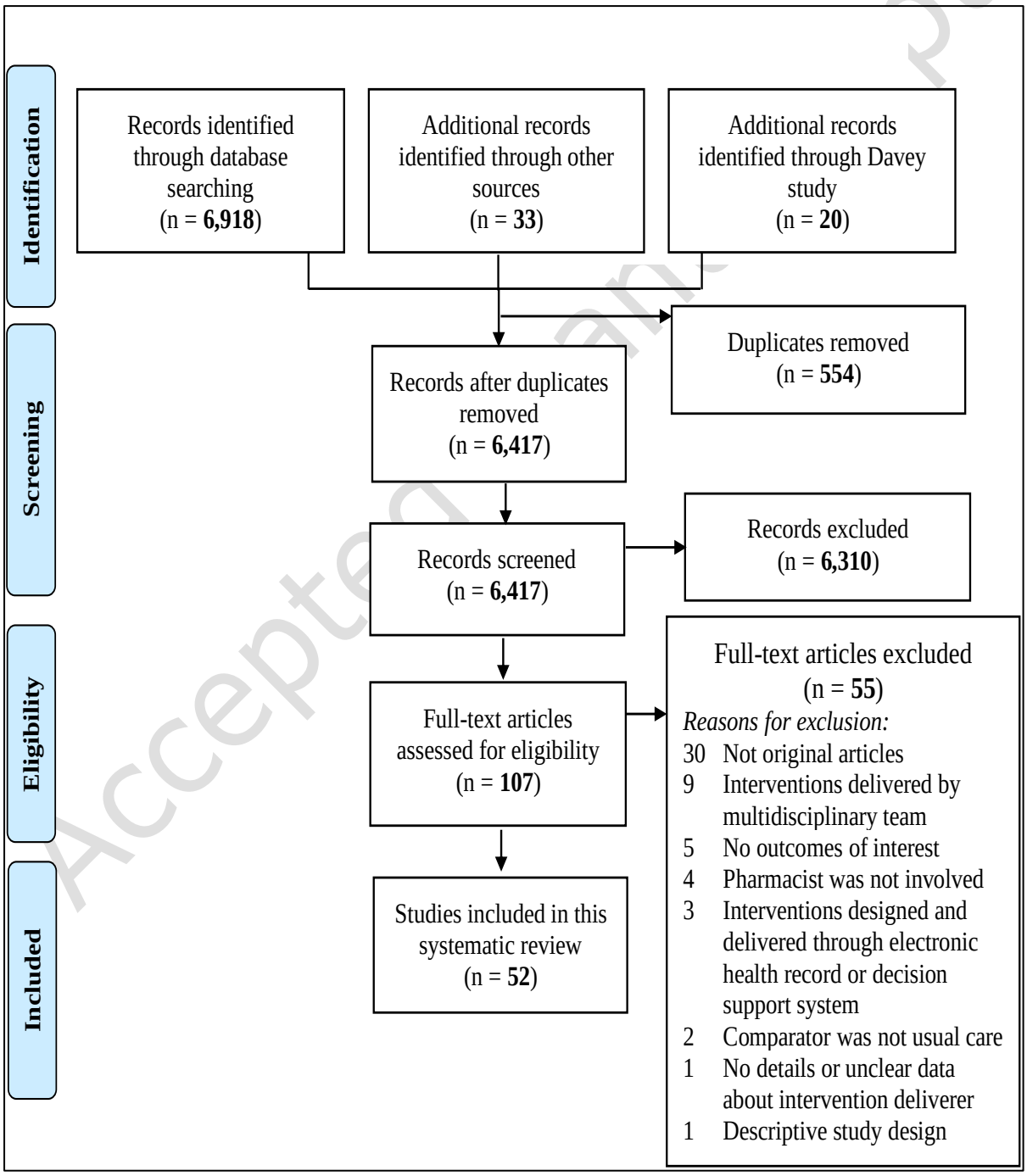

Figure 1: PRISMA flow diagram search strategy for the review

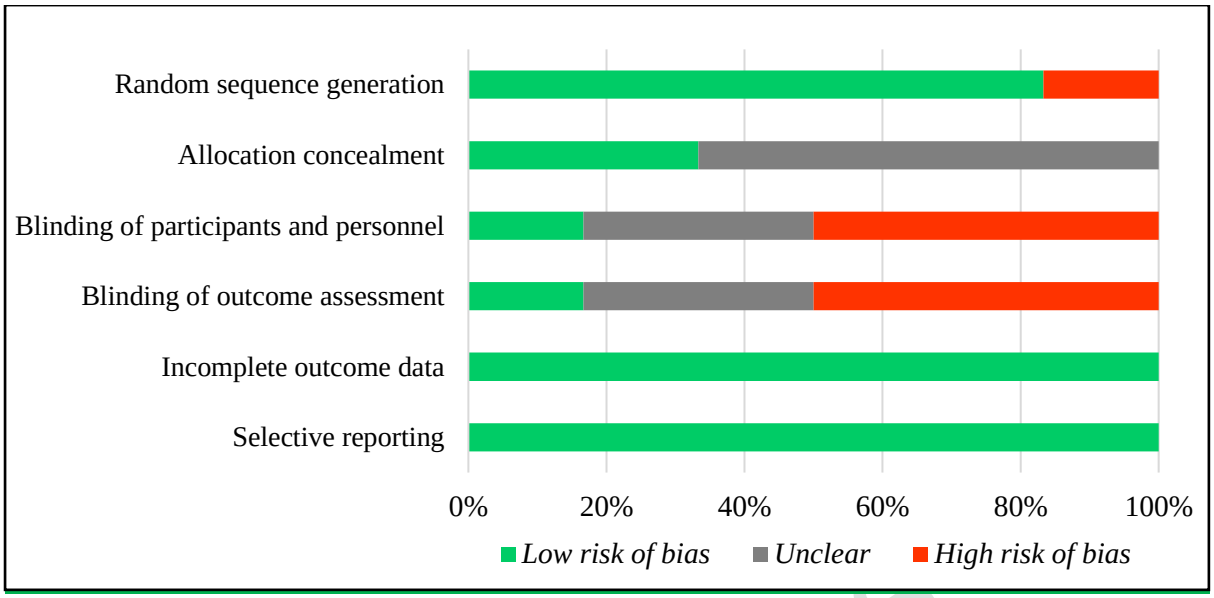

Figure 2: Risk of bias graph for each risk of bias criterion according to a Cochrane risk of bias tool presented as percentages for RCTs (n=6)

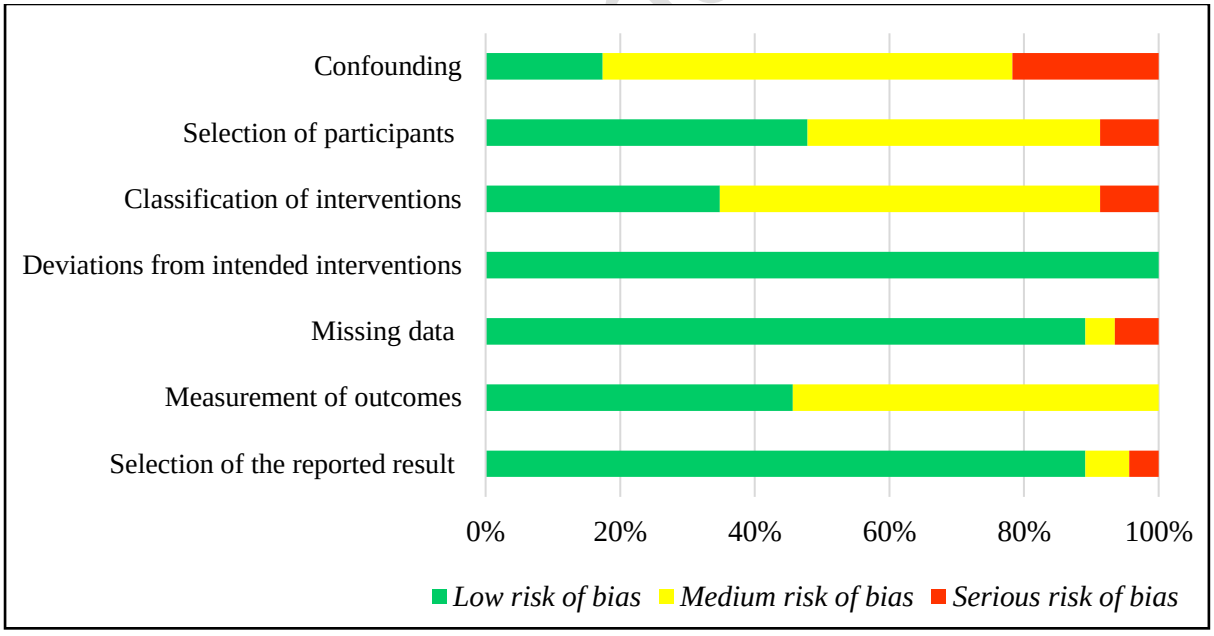

Figure 3: Risk of bias graph for each risk of bias criterion according to the ROBINS-I risk of bias assessment tool presented as percentages for NRS (n=46)

SUPPLEMENTARY DATA

Title

"A systematic review and narrative synthesis of pharmacist-led education-based antimicrobial stewardship interventions and their effect on antimicrobial use in hospital inpatients"

Table of contents

PRISMA CHECKLIST

Table S1: PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Table S2 in supplementary data
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3-4
Data items	11	List and define all variables for which data were sought (e.g. PICOS, funding sources) and any assumptions and simplifications made.	3-4

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	3-4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	4
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5 (Figure 1)
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5-6 (Table I-V) and Table S3 in supplementary data
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table S4 and S5 in supplementary data
Risk of bias across studies	20	Present results of any assessment of risk of bias across studies (see Item 15).	6 (Figure 2-3)
Results of individual studies	21	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	6-11, Table S3 in supplementary data
Synthesis of results	22	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14-15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15-16
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other supports, role of funders for the systematic review.	16

Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol*, 62 (2009). 1006-12.

SEARCH STRATEGIES AND RESULTS FROM THE SEARCHES

Table S2.1 Search strategies and results from MEDLINE (OvidSP®) (search up to 31st July 2020)

	Search strategies	Results
1	(hospital$ and antibiotic?).ti.	2721
2	((antibiotic? or alamethicin? or amdinocillin? or amdinocillin pivoxil? or amikacin? or amoxicillin? or amoxicillin-potassium clavulanate combination? or amphotericin? or ampicillin? or anisomycin? or antimycin? or aurodox? or azithromycin? or azlocillin? or aztreonam? or bacitracin? or bacteriocin? or bambermycin? or bongkrekic acid? or brefeldin? or butirosin sulfate? or calcimycin? or candicidin? or capreomycin? or carbenicillin? or carfecillin? or cefaclor? or cefadroxil? or cefamandole? or cefatrizine? or cefazolin? or cefixime? or cefmenoxime? or cefmetazole? or cefonicid? or cefoperazone? or cefotaxime? or cefotetan? or cefotiam? or cefoxitin? or cefsulodin? or ceftazidime? or ceftizoxime? or ceftriaxone? or cefuroxime? or cephacetrile? or cephalexin? or cephaloglycin? or cephaloridine? or cephalosporin? or cephalothin? or cephamycin? or cephapirin? or cephradine? or chloramphenicol? or chlortetracycline? or citrinin? or clarithromycin? or clavulanic acid? or clavulanic acid? or clindamycin? or cloxacillin? or colistin? or cyclacillin? or dactinomycin? or daptomycin? or demeclocycline? or dibekacin? or dicloxacillin? or dihydrostreptomycin sulfate? or diketopiperazine? or distamycin? or doxycycline? or echinomycin? or edeine? or enviomycin? or erythromycin? or erythromycin estolate? or erythromycin ethylsuccinate? or filipin? or floxacillin? or fluoroquinolone? or fosfomycin? or framycetin? or fusidic acid? or gentamicin? or gramicidin? or hygromycin? or imipenem? or josamycin? or kanamycin? or kitasamycin? or lactam? or lasalocid? or leucomycin? or lincomycin? or lincosamide? or lucensomycin? or lymecycline? or mepartricin? or methacycline? or methicillin? or mezlocillin? or mikamycin? or minocycline? or miocamycin? or moxalactam? or mupirocin? or mycobacillin? or nafcillin? or natamycin? or nebramycin? or neomycin? or netilmicin? or netropsin? or nigericin? or nisin? or norfloxacin? or novobiocin? or nystatin? or ofloxacin? or oleandomycin? or oligomycin? or oxacillin? or oxytetracycline? or paromomycin? or penicillanic acid? or penicillic acid? or penicillin?? or piperacillin? or pivampicillin? or polymyxin b? or polymyxin? or pristinamycin? or prodigiosin? or ribostamycin? or rifabutin? or rifamycin? or ristocetin? or rolitetracycline? or roxarsone? or roxithromycin? or rutamycin? or sirolimu? or sisomicin? or spectinomycin? or spiramycin? or streptogramin?? or streptomycin? or streptovaricin? or sulbactam? or sulbenicillin? or sulfamerazine? or sulfamethoxypyridazine? or talampicillin? or teicoplanin? or tetracycline? or thiamphenicol? or thienamycin? or thiostrepton? or ticarcillin? or tobramycin? or troleandomycin? or tunicamycin? or tylosin? or tyrocidine? or tyrothricin? or valinomycin? or vancomycin? or vernamycin? or viomycin? or virginiamycin? or beta-lactams) adj2 (resistant or resistance) adj10 (best practice? or (chang$ adj (practice or clinical practice)) or evidence-base? or policy or policies or pathway? or ((treatment or care) adj (algorithm? or pathway? or protocol)) or collaborat$ or computeri?ed or computer-supported or decision-mak$ or (support adj decision?) or formulary or guidance or (guideline? adj (adher$ or implement$ or concord$ or comply or complian$)) or interdisciplin$ or interprofession$ or multidisciplin$ or multi-disciplin$ or notification? or order entry or (pharmacist? adj2 (led or initiat$ or intervention? or participat$)) or policy or policies or (prescrib$ adj (practice? or method? or algorithm? or protocol? or habit?)) or (quality adj (manag$ or improv$ or circle?)) or ((patient? or medical or electronic) adj2 record?) or reminder? or rotating or rotation or team$)).ti,ab.	793
3	(antibiotic? and (education$ or continuing-education$ or cme or decision-making or evidence-based or ebm or guidance or guideline? or habit? or impact or improper$ or inappropriat$ or influenc$ or intervention? or management or overprescrib$ or overuse or overusing or pattern? or policy or policies or prescribing or prudent$ or stewardship? or rational or unnecessary or "use" or "usage")).ti.	12785
4	(antibiotic? adj4 (education$ or continuing-education$ or cme or decision-making or evidence-based or ebm or guidance or guideline? or habit? or impact or improper$ or inappropriat$ or influenc$ or intervention? or management or overprescrib$ or overuse or overusing or pattern? or policy or policies or prescribing or prudent$ or rational or stewardship or unnecessary or "use" or "usage")).ab.	35698
5	antibiotic?.ti. and evidence-based.hw.	389
6	((antimicrobial? or anti-microbial? or penicillin?) and (stewardship or guidance or guideline? or policy or policies)).ti.	1569
7	((antimicrobial? or anti-microbial? or penicillin?) adj3 (stewardship or guidance or guideline? or policy or policies)).ab.	2390
8	(antibiotic? adj5 (hour? or immediat$ or emergency)).ab. or (antibiotic? and (hour? or immediat$ or emergency)).ti. or (antibiotic? adj3 (rotat$ or timing or time or decision$ or notification or appropriat$)).ab. or (antibiotic? and (rotat$ or timing or time or decision$ or notification or appropriat$)).ti.	12743
9	or/3-8	56060
10	exp Anti-Bacterial Agents/	725230
11	antibiotic?.ti,ab.	289962

12	(alamethicin or amdinocillin or amdinocillin pivoxil or amikacin or amoxicillin or amoxicillin-potassium clavulanate combination or amphotericin or ampicillin or anisomycin or antimycin or aurodox or azithromycin or azlocillin or aztreonam or bacitracin or bacteriocins or bambermycins or bongkrekic acid or brefeldin or butirosin sulfate or calcimycin or candicidin or capreomycin or carbenicillin or carfecillin or cefaclor or cefadroxil or cefamandole or cefatrizine or cefazolin or cefixime or cefmenoxime or cefmetazole or cefonicid or cefoperazone or cefotaxime or cefotetan or cefotiam or cefoxitin or cefsulodin or ceftazidime or ceftizoxime or ceftriaxone or cefuroxime or cephacetrile or cephalexin or cephaloglycin or cephaloridine or cephalosporins or cephalothin or cephamycins or cephapirin or cephradine or chloramphenicol or chlortetracycline or citrinin or clarithromycin or clavulanic acid or clavulanic acids or clindamycin or cloxacillin or colistin or cyclacillin or dactinomycin or daptomycin or demeclocycline or dibekacin or dicloxacillin or dihydrostreptomycin sulfate or diketopiperazines or distamycins or doxycycline or echinomycin or edeine or enviomycin or erythromycin or erythromycin estolate or erythromycin ethylsuccinate or filipin or floxacillin or fluoroquinolones or fosfomycin or framycetin or fusidic acid or gentamicins or gramicidin or hygromycin or imipenem or josamycin or kanamycin or kitasamycin or lactams or lasalocid or leucomycins or lincomycin or lincosamides or lucensomycin or lymecycline or mepartricin or methacycline or methicillin or mezlocillin or mikamycin or minocycline or miocamycin or moxalactam or mupirocin or mycobacillin or nafcillin or natamycin or nebramycin or neomycin or netilmicin or netropsin or nigericin or nisin or norfloxacin or novobiocin or nystatin or ofloxacin or oleandomycin or oligomycins or oxacillin or oxytetracycline or paromomycin or penicillanic acid or penicillic acid or penicillin? or piperacillin or pivampicillin or polymyxin b or polymyxins or pristinamycin or prodigiosin or ribostamycin or rifabutin or rifamycins or ristocetin or rolitetracycline or roxarsone or roxithromycin or rutamycin or sirolimus or sisomicin or spectinomycin or spiramycin or streptogramin? or streptomycin or streptovaricin or sulbactam or sulbenicillin or sulfamerazine or sulfamethoxypyridazine or talampicillin or teicoplanin or tetracycline or thiamphenicol or thienamycins or thiostrepton or ticarcillin or tobramycin or troleandomycin or tunicamycin or tylosin or tyrocidine or tyrothricin or valinomycin or vancomycin or vernamycin or viomycin or virginiamycin or beta-lactams).ti,ab.	355177
13	(infection control$ or nosocomial$ or cross infection? or hospital acquired infection? or mrsa).ti,ab.	61931
14	methicillin resistan$.ti,ab.	25953
15	aminoglycosides/ or metronidazole/ or anti-infective agents/ or anti-infective agents, urinary/	76653
16	or/10-15	961724
17	(programs or programmes).ti.	39412
18	empiric.ti.	1383
19	(quality adj3 improvement?).ti.	10011
20	(adherence or alert? or benchmark$ or (change adj3 treatment) or computer assist$ or computer support or computeri?ed or clinical decision$ or dosing or education$ or formulary or guidance or guideline? or impact or intervention or justification or methicillan-resistant or overuse or over-prescrib$ or overprescrib$ or pathway? or pharmacist? or policy or policies or program or programme or (quality adj3 improv$) or reminder? or resistance or restriction? or rotation? or timing or turnaround or unnecessary).ti.	1090888
21	or/17-20	1124225
22	16 and 21	69701
23	22 not 9	59268
24	(randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti.	1164976
25	exp animals/ not humans.sh.	4711295
	Remark: command no.26 in Davey is equal to no.51 in this search***	
26	intervention?.ti. or (intervention? adj6 (clinician? or collaborat$ or community or complex or design$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or gp or general practice? or hospital? or impact? or improv$ or individuali? e? or individuali?ing or interdisciplin$ or multicomponent or multi-component or multidisciplin$ or multi-disciplin$ or multifacet$ or multi-facet$ or multimodal$ or multi-modal$ or personali?e? or personali?ing or pharmacies or pharmacist? or pharmacy or physician? or practitioner? or prescrib$ or prescription? or primary care or professional$ or provider? or regulatory or regulatory or tailor$ or target $ or team$ or usual care)).ab.	225054
27	(pre-intervention? or preintervention? or "pre intervention?" or post-intervention? or postintervention? or "post intervention?").ti,ab.	20016
28	(hospital$ or patient?).hw. and (study or studies or care or health$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw.	964101
29	demonstration project?.ti,ab.	2386
30	(pre-post or "pre test$" or pretest$ or posttest$ or "post test$" or (pre adj5 post)).ti,ab.	100574
31	(pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab.	971
32	trial.ti. or ((study adj3 aim?) or "our study").ab.	999044

33	(before adj10 (after or during)).ti,ab	447642
34	("quasi-experiment$" or quasiexperiment$ or "quasi random$" or quasirandom$ or "quasi control$" or quasicontrol$ or ((quasi$ or experimental) adj3 (method$ or study or trial or design$))).ti,ab,hw.	127067
35	("time series" adj2 interrupt$).ti,ab,hw.	2684
36	(time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month$ or hour? or day? or "more than")).ab.	15612
37	pilot.ti.	58801
38	pilot projects/ [ml]	122080
39	(clinical trial or controlled clinical trial or multicenter study).pt. [ml]	763548
40	(multicentre or multicenter or multi-centre or multi-center).ti.	45981
41	random$.ti,ab. or controlled.ti.	1012428
42	(control adj3 (area or cohort? or compare? or condition or design or group? or intervention? or participant? or study)).ab. not (controlled clinical trial or randomized controlled trial).pt. [ml]	550672
43	"comment on".cm. or review.ti,pt. or randomized controlled trial.pt. [ml]	3865099
44	review.ti.	382901
45	(rat or rats or cow or cows or chicken? or horse or horses or mice or mouse or bovine or animal?).ti.	1520127
46	exp animals/ not humans.sh.	4711295
47	(animal$ not human$).sh,hw.	4668848
48	*experimental design/ or *pilot study/ or quasi experimental study/ [em]	38008
49	("quasi-experiment$" or quasiexperiment$ or "quasi random$" or quasirandom$ or "quasi control$" or quasicontrol$ or ((quasi$ or experimental) adj3 (method$ or study or trial or design$))).ti,ab.	127067
50	("time series" adj2 interrupt$).ti,ab.	2456
51	42 not 44	541649
52	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 51	4125387
53	or/43-47	8551838
54	52 not 53	2822204
55	9 or 23	
56	54 and 55	20811
57	**limit 56 to (yr="2015 -Current")**	**1742**
	Last search 31 July 2020	

Table S2.2: Search strategies and results from Embase (OvidSP®) (search up to 31st July 2020)

	Search strategies	Results
1	exp *antibiotic agent/	618122
2	(bundle or bundles or education$ or continuing-education$ or cme or decision-making or guidance or (guideline? adj2 (adherence or implement$ or complian$ or comply$)) or improper$ or inappropriat$ or incorrect$ or nurse led or overprescrib$ or overuse or overusing or pharmacist initiated or physician? practice? or policy or policies or practice pattern? or (prescribing adj2 (ebm or evidence-based or habit? or pattern? or practice or practices)) or prudent$ or rational or stewardship or unnecessary or underprescrib$).ti.	358130
3	("antibiotic use" or "antibiotic usage").ti.	3613
4	(hospital$ and antibiotic?).ti.	5060

5	((antibiotic? or alamethicin? or amdinocillin? or amdinocillin pivoxil? or amikacin? or amoxicillin? or amoxicillin-potassium clavulanate combination? or amphotericin? or ampicillin? or anisomycin? or antimycin? or aurodox? or azithromycin? or azlocillin? or aztreonam? or bacitracin? or bacteriocin? or bambermycin? or bongkrekic acid? or brefeldin? or butirosin sulfate? or calcimycin? or candicidin? or capreomycin? or carbenicillin? or carfecillin? or cefaclor? or cefadroxil? or cefamandole? or cefatrizine? or cefazolin? or cefixime? or cefmenoxime? or cefmetazole? or cefonicid? or cefoperazone? or cefotaxime? or cefotetan? or cefotiam? or cefoxitin? or cefsulodin? or ceftazidime? or ceftizoxime? or ceftriaxone? or cefuroxime? or cephacetrile? or cephalexin? or cephaloglycin? or cephaloridine? or cephalosporin? or cephalothin? or cephamycin? or cephapirin? or cephradine? or chloramphenicol? or chlortetracycline? or citrinin? or clarithromycin? or clavulanic acid? or clavulanic acid? or clindamycin? or cloxacillin? or colistin? or cyclacillin? or dactinomycin? or daptomycin? or demeclocycline? or dibekacin? or dicloxacillin? or dihydrostreptomycin sulfate? or diketopiperazine? or distamycin? or doxycycline? or echinomycin? or edeine? or enviomycin? or erythromycin? or erythromycin estolate? or erythromycin ethylsuccinate? or filipin? or floxacillin? or fluoroquinolone? or fosfomycin? or framycetin? or fusidic acid? or gentamicin? or gramicidin? or hygromycin? or imipenem? or josamycin? or kanamycin? or kitasamycin? or lactam? or lasalocid? or leucomycin? or lincomycin? or lincosamide? or lucensomycin? or lymecycline? or mepartricin? or methacycline? or methicillin? or mezlocillin? or mikamycin? or minocycline? or miocamycin? or moxalactam? or mupirocin? or mycobacillin? or nafcillin? or natamycin? or nebramycin? or neomycin? or netilmicin? or netropsin? or nigericin? or nisin? or norfloxacin? or novobiocin? or nystatin? or ofloxacin? or oleandomycin? or oligomycin? or oxacillin? or oxytetracycline? or paromomycin? or penicillanic acid? or penicillic acid? or penicillin?? or piperacillin? or pivampicillin? or polymyxin b? or polymyxin? or pristinamycin? or prodigiosin? or ribostamycin? or rifabutin? or rifamycin? or ristocetin? or rolitetracycline? or roxarsone? or roxithromycin? or rutamycin? or sirolimu? or sisomicin? or spectinomycin? or spiramycin? or streptogramin?? or streptomycin? or streptovaricin? or sulbactam? or sulbenicillin? or sulfamerazine? or sulfamethoxypyridazine? or talampicillin? or teicoplanin? or tetracycline? or thiamphenicol? or thienamycin? or thiostrepton? or ticarcillin? or tobramycin? or troleandomycin? or tunicamycin? or tylosin? or tyrocidine? or tyrothricin? or valinomycin? or vancomycin? or vernamycin? or viomycin? or virginiamycin? or beta-lactams) adj2 (resistant or resistance) adj10 (best practice? or (chang$ adj (practice or clinical practice)) or evidence-base? or policy or policies or pathway? or ((treatment or care) adj (algorithm? or pathway? or protocol)) or collaborat$ or computeri?ed or computer-supported or decision-mak$ or (support adj decision?) or formulary or guidance or (guideline? adj (adher$ or implement$ or concord$ or comply or complian$)) or interdisciplin$ or interprofession$ or multidisciplin$ or multi-disciplin$ or notification? or order entry or (pharmacist? adj2 (led or initiat$ or intervention? or participat$)) or policy or policies or (prescrib$ adj (practice? or method? or algorithm? or protocol? or habit?)) or (quality adj (manag$ or improv$ or circle?)) or ((patient? or medical or electronic) adj2 record?) or reminder? or rotating or rotation or team$)).ti,ab.	1206
6	(antibiotic? and (bundle or bundles or education$ or continuing-education$ or cme or decision-making or guidance or (guideline? adj2 (adherence or implement$ or complian$ or comply$)) or improper$ or inappropriat$ or incorrect$ or nurse led or overprescrib$ or overuse or overusing or pharmacist initiated or physician? practice? or policy or policies or practice pattern? or (prescribing adj2 (ebm or evidence based or habit? or pattern? or practice or practices)) or prudent$ or rational or stewardship or unnecessary or underprescrib$)).ti.	3495
7	(antibiotic? adj3 (bundle or bundles or education$ or continuing-education$ or cme or decision-making or guidance or (guideline? adj2 (adherence or implement$ or complian$ or comply$)) or improper$ or inappropriat$ or incorrect$ or nurse led or overprescrib$ or overuse or overusing or pharmacist initiated or physician? practice? or policy or policies or practice pattern? or (prescribing adj2 (ebm or evidencebased or habit? or pattern? or practice or practices)) or prudent$ or rational or stewardship or unnecessary or underprescrib$)).ab.	13026
8	((antimicrobial? or anti-microbial? or penicillin?) and (bundle or bundles or education$ or continuing-education$ or cme or decisionmaking or guidance or (guideline? adj2 (adherence or implement$ or complian$ or comply$)) or improper$ or inappropriat$ or incorrect $ or nurse led or overprescrib$ or overuse or overusing or pharmacist initiated or physician? practice? or policy or policies or practice pattern? or (prescribing adj2 (ebm or evidence-based or habit? or pattern? or practice or practices)) or prudent$ or rational or stewardship or unnecessary or underprescrib$)).ab. or ((antimicrobial? or anti-microbial? or penicillin?) and (bundle or bundles or education$ or continuing-education$ or cme or decision-making or guidance or (guideline? adj2 (adherence or implement$ or complian$ or comply$)) or improper$ or inappropriat$ or incorrect$ or nurse led or overprescrib$ or overuse or overusing or pharmacist initiated or physician? practice? or policy or policies or practice pattern? or (prescribing adj2 (ebm or evidence-based or habit? or pattern? or practice or practices)) or prudent$ or rational or stewardship or unnecessary or underprescrib$)).ti.	19525
9	1 and 2	4160
10	or/3-8	36165
11	9 or 10	37259
12	intervention?.ti. or (intervention? adj6 (clinician? or collaborat$ or community or complex or design$ or doctor? or educational or family doctor? or family physician? or family practitioner? or financial or gp or general practice? or hospital? or impact? or improv$ or individuali? e? or individuali?ing or interdisciplin$ or multicomponent or multi-component	

	or multidisciplin$ or multi-disciplin$ or multifacet$ or multi-facet$ or multimodal$ or multi-modal$ or personali?e? or personali?ing or pharmacies or pharmacist? or pharmacy or physician? or practitioner? or prescrib$ or prescription? or primary care or professional$ or provider? or regulatory or regulatory or tailor$ or target $ or team$ or usual care)).ab	
13	(pre-intervention? or preintervention? or "pre intervention?" or post-intervention? or postintervention? or "post intervention?").ti,ab.	38199
14	(hospital$ or patient?).hw. and (study or studies or care or health$ or practitioner? or provider? or physician? or nurse? or nursing or doctor?).ti,hw.	3090631
15	demonstration project?.ti,ab.	3388
16	(pre-post or "pre test$" or pretest$ or posttest$ or "post test$" or (pre adj5 post)).ti,ab.	215007
17	(pre-workshop or post-workshop or (before adj3 workshop) or (after adj3 workshop)).ti,ab.	2146
18	trial.ti. or ((study adj3 aim?) or "our study").ab.	1826081
19	(before adj10 (after or during)).ti,ab.	735733
20	(time points adj3 (over or multiple or three or four or five or six or seven or eight or nine or ten or eleven or twelve or month$ or hour? or day? or "more than")).ab.	28591
21	pilot.ti.	98011
22	(multicentre or multicenter or multi-centre or multi-center).ti.	85503
23	random$.ti,ab. or controlled.ti.	1637170
24	review.ti.	574045
25	or/12-23	6500456
26	25 not 24	6345392
27	11 and 26	17772
28	**limit 27 to (yr="2015 -Current")**	**2584**
	Last search 31 July 2020	

Table S2.3: Search strategies and results from Cochrane Central Register of Controlled Trial (search up to 31st July 2020)

	Search strategies	Results
1	(antibiotic?):ti,ab,kw	30315
2	((antibacterial or anti-bacterial or antiinfective or anti-infective or antimicrobial) and (agent? or drug?)):ti,ab,kw	17363
3	((alamethicin? or amdinocillin? or amdinocillin pivoxil? or amikacin? or amoxicillin? or amoxicillin-potassium clavulanate combination? or amphotericin? or ampicillin? or anisomycin? or antimycin? or aurodox? or azithromycin? or azlocillin? or aztreonam? or bacitracin? or bacteriocin? or bambermycin? or bongkrekic acid? or brefeldin? or butirosin sulfate? or calcimycin? or candicidin? or capreomycin? or carbenicillin? or carfecillin? or cefaclor? or cefadroxil? or cefamandole? or cefatrizine? or cefazolin? or cefixime? or cefmenoxime? or cefmetazole? or cefonicid? or cefoperazone? or cefotaxime? or cefotetan? or cefotiam? or cefoxitin? or cefsulodin? or ceftazidime? or ceftizoxime? or ceftriaxone? or cefuroxime? or cephacetrile? or cephalexin? or cephaloglycin? or cephaloridine? or cephalosporin? or cephalothin? or cephamycin? or cephapirin? or cephradine? or chloramphenicol? or chlortetracycline? or citrinin? or clarithromycin? or clavulanic acid? or clavulanic acid? or clindamycin? or cloxacillin? or colistin? or cyclacillin? or dactinomycin? or daptomycin? or demeclocycline? or dibekacin? or dicloxacillin? or dihydrostreptomycin sulfate? or diketopiperazine? or distamycin? or doxycycline? or echinomycin? or edeine? or enviomycin? or erythromycin? or erythromycin estolate? or erythromycin ethylsuccinate? or filipin? or floxacillin? or fluoroquinolone? or fosfomycin? or framycetin? or fusidic acid? or gentamicin? or gramicidin? or hygromycin? or imipenem? or josamycin? or kanamycin? or kitasamycin? or lactam? or lasalocid? or leucomycin? or lincomycin? or lincosamide? or lucensomycin? or lymecycline? or mepartricin? or methacycline? or methicillin? or mezlocillin? or mikamycin? or minocycline? or miocamycin? or moxalactam? or mupirocin? or mycobacillin? or nafcillin? or natamycin? or nebramycin? or neomycin? or netilmicin? or netropsin? or nigericin? or nisin? or norfloxacin? or novobiocin? or nystatin? or ofloxacin? or oleandomycin? or oligomycin? or oxacillin? or oxytetracycline? or paromomycin? or penicillanic acid? or penicillic acid? or penicillin?? or piperacillin? or pivampicillin? or polymyxin b? or polymyxin? or pristinamycin? or prodigiosin? or ribostamycin? or rifabutin? or rifamycin? or ristocetin? or rolitetracycline? or roxarsone? or roxithromycin? or rutamycin? or sirolimu? or sisomicin? or spectinomycin? or spiramycin? or streptogramin?? or streptomycin? or streptovaricin? or sulbactam? or sulbenicillin? or sulfamerazine? or sulfamethoxypyridazine? or talampicillin? or teicoplanin? or tetracycline? or thiamphenicol? or thienamycin?	26978

	or thiostrepton? or ticarcillin? or tobramycin? or troleandomycin? or tunicamycin? or tylosin? or tyrocidine? or tyrothricin? or valinomycin? or vancomycin? or vernamycin? or viomycin? or virginiamycin? or beta-lactams) and (prescrib$ or resistance or "use" or "usage" or utlii?ation)):ti,ab,kw	
4	((antibacterial agent? or anti-bacterial agent?) and (prescrib$ or resistance or "use" or "usage" or utili?ation)):ti,ab,kw	9807
5	("stewardship"):ti,ab,kw	366
6	((antibiotic* or antimicrobial*) and (prescrib* or prescrip*)):ti,ab,kw	2698
7	#1 or #2 or #3 or #4 or #5 or #6	14256
8	**Limit 7 to with Cochrane Library publication date from Jan 2015 to July 2020, in Trials non CT.gov, non ICTRP**	**2,592**

CHARACTERISTICS AND OUTCOMES OF INCLUDED STUDIES (N=52)

Abbreviation	Full term	Abbreviation	Full term
AD	Academic detailing	ID	Infectious disease
AF	Audit and Feedback	IQR	Interquartile range
CDI	*Clostridium difficile* infection	IV	Intravenous
COPD	Chronic obstructive pulmonary diseases	IVOST	Intravenous to oral antibiotic switch therapy
DM	Dissemination of educational materials with group meetings	LOS	Length of hospital stay
DOT	Day of antimicrobial therapy	RMD	Reminder
EO	Educational outreach	RT	Restriction
ICU	Intensive care unit		

Table S3: Characteristics of included studies in PICO elements

Landgren 1988		***Pastel 1992***	
Methods	***Study design:*** CBA	Methods	***Study design:*** CBA
Participants	***Patients:*** Patients who underwent surgery (number of patients receiving antimicrobial: 445 intervention vs 397 control) ***Intervention recipients:*** All surgeons and anaesthetists at 12 hospitals ***Antimicrobial target for intervention:*** antimicrobial prophylaxis ***Setting:*** Twelve hospitals (4 teaching and 8 non-teaching hospitals), Australia	Participants	***Patients:*** Adult patients requiring restricted antimicrobial for empirical treatment (63 intervention vs 38 control) ***Intervention recipients:*** All physicians (private, house staff (medical and surgical residents), and ID consultants) ***Antimicrobial target for intervention****:* empirical therapy ***Setting:*** A community teaching hospital, USA
Interventions	***Intervention component:*** AF (audit every three weeks and feedback provided to surgeons, anaesthetists, and nurses), DM, AD, & RMD ***Intervention duration (month):*** 6 ***Intervention deliverer:*** A clinical pharmacist	Interventions	***Intervention component:*** EO (modify empirical antimicrobial regimens based on receipt of microbiologic data when data become available) (verbal) ***Intervention duration (month):*** 2.25 ***Intervention deliverer:*** clinical pharmacists
Comparator	Usual care (6 hospitals were used as control in year 1, then intervention and control hospitals were crossed over in year 2)	Comparator	Usual care
Outcomes	***Compliance with target practice****:* intervention (250/445) (56.2%) vs control (143/397) (36.0%) (p=0.04) ***DOT (day):*** - ***Mortality:*** - ***LOS (day)****:* - ***Microbial outcome****:* -	Outcomes	***Compliance with target practice****:* intervention (56/63) (88.9%) vs control (28/38) (73.7%) (p=0.35) ***DOT (day)****:* - ***Mortality:*** - ***LOS (day):*** - ***Microbial outcome:*** -
Note		Note	

Bailey 1997		***Walker 1998***	
Methods	***Study design****:* RCT	Methods	***Study design****:* RCT
Participants	***Patients****:* Patients receiving IV antimicrobials for at least three or four days (51 intervention vs 51 control) ***Intervention recipients****:* All physicians at 2 hospitals (excluding ICU settings) ***Antimicrobial target for intervention****:* IVOST ***Setting****:* Two tertiary care teaching hospitals, USA	Participants	***Patients****:* patients with community-acquired pneumonia requiring IV ceftriaxone (25 intervention vs 25 control) ***Intervention recipients:*** all ward physicians ***Antimicrobial target for intervention:*** IVOST ***Setting:*** one non-teaching community hospital, USA
Interventions	***Intervention component****:* EO (verbal) ***Intervention duration (month)****:* 7 ***Intervention deliverer****:* clinical pharmacists	Interventions	***Intervention component:*** DM, EO (non-verbal: documented in chart), & RMD ***Intervention duration (month):*** 12 ***Intervention deliverer:*** clinical pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice:*** (1) Patients who were switched from IV to oral antimicrobials: intervention 23/51 (45.10%) vs control 28/51 (54.90%) (p=0.43) (2) Patients who were discontinued antimicrobials: intervention 28/51 (54.90%) vs control 23/51 (45.10%) (p=0.43) ***Mean DOT (day):*** IV: intervention (0.8) vs control (2.2) (p=0.01) ***Mortality****:* - ***Mean LOS (day):*** intervention (4.9) vs control (4.6) (p=0.95) ***Microbial outcome:*** -	Outcomes	***Compliance with target practice:*** intervention (22/25) (88.0%) vs control (9/25) (36.0%) (p=0.00031) ***DOT (day):*** - ***Mortality:*** - ***LOS (day):*** - ***Microbial outcome:*** -
Note		Note	

Martínez 2000		***Dranitsaris 2001***	
Methods	***Study design****:* BA	Methods	***Study design****:* RCT
Participants	***Patients****:* Patients with infection requiring IV clindamycin at least 72 hours (204 post-intervention vs 269 pre-intervention) ***Intervention recipients****:* All physicians ***Antimicrobial target for intervention****:* IVOST ***Setting****:* Two tertiary care teaching hospitals, Spain	Participants	***Patients****:* Adult patients with infections requiring IV cefotaxime (162 intervention vs 147 control) ***Intervention recipients****:* Ward physicians assigned to the 7 services ***Antimicrobial target for intervention****:* empirical and definitive therapy ***Setting****:* two tertiary care teaching hospitals, Canada
Interventions	***Intervention component****:* DM ***Intervention duration (month)****:* 6 ***Intervention deliverer****:* A clinical pharmacist	Interventions	***Intervention component****:* EO (direct contact: verbal) ***Intervention duration (month)****:* 6 ***Intervention deliverer****:* A clinical pharmacist
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice:*** post-intervention (107/204) (52.5%) *vs* pre-intervention (57/269) (21.1%) (p<0.05)	Outcomes	***Compliance with target practice****:* intervention (122/162) (75.3%) vs control (102/147) (69.4%) (p=0.24) ***DOT (day):*** intervention (4.3±3.1) vs control (4.8±4.6) (p=0.28)

	DOT (day): IV clindamycin decreased 1.3 days in post-intervention compared with pre-intervention (no raw data shown) (p=0.003) ***Mortality****:* - ***Median LOS (day):*** post-intervention (14.5 (IQR 5.0-59.0)) *vs* pre-intervention (13.0 (IQR 4.0-50.0)) (p=0.18) ***Microbial outcome****:* CDI rate: post-intervention (1/204) (0.5%) *vs* pre-intervention (10/269) (3.7%) (0.49%)		***Mortality****:* - ***LOS (day)****:* - ***Microbial outcome****:* -
Note		Note	

Ho 2005		***McLaughlin 2005***	
Methods	***Study design****:* BA	Methods	***Study design****:* BA
Participants	***Patients****:* Adult patients requiring IV ciprofloxacin at least 48 hrs who were candidates for IV to oral antimicrobial conversion (201 post-intervention vs 244 pre-intervention) ***Intervention recipients****:* All physicians ***Antimicrobial target for intervention****:* IVOST ***Setting****:* A tertiary care teaching hospital, Canada	Participants	***Patients****:* Patients admitted in 12 medical wards requiring IV antimicrobial therapy (IV-treated infection episodes: 107 post-intervention vs 118 in pre-intervention) ***Intervention recipients****:* All staff in 12 medical wards (junior doctors and ward nurses) ***Antimicrobial target for intervention****:* IVOST ***Setting****:* A tertiary care teaching hospital, UK
Interventions	***Intervention component****:* DM & EO (proving recommendations in medical chart or having discussion with physicians if antimicrobial needed to be converted to PO prior 48 hours of IV ciprofloxacin initiation) ***Intervention duration (month)****:* 4 ***Intervention deliverer****:* Clinical and ward pharmacists who were educated with special trainings on antimicrobial conversion	Interventions	***Intervention component****:* AF (feedback provided to medical staff through presentation and inserted in medical chart, no frequency documented), DM, & RMD (stickers in medical chart, posters) ***Intervention duration (month)****:* 1 ***Intervention deliverer****:* A clinical pharmacist
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice****:* post-intervention (136/201) (67.7%) *vs* pre-intervention (130/244) (53.3%) (P=0.0026) ***DOT (day)****:* - ***Mortality****:* - ***Mean LOS (day)****:* post-intervention (17.0 (range 1.0-165.0)) *vs* pre-intervention (12.0 (range1.0-84.0)) (p>0.05) ***Microbial outcome****:* -	Outcomes	***Compliance with target practice****:* post-intervention (71/79) (89.9%) *vs* pre-intervention (15/90) (16.7%) (p<0.001) ***Median DOT (day)****:* IV: post-intervention (2.0 (IQR 1.0-16.0)) *vs* pre-intervention (3.0 (IQR 1.0-22.0)) (p<0.01) ***Mortality****:* - ***Median LOS (day)****:* post- intervention (10.0 (IQR 1.0-108.0)) *vs* pre-intervention (13.0 (IQR 1.0-72.0)) (p=0.047) ***Microbial outcome****:* -
Note		Note	We did not include data from phase III because (1) large and unjustified gap between pre and post intervention data (2) Interventions used in phase III was similar to phase II just repeated them for new prescribers

Strom 2010		***Dunn 2011***	
Methods	***Study design****:* RCT	Methods	***Study design****:* CBA
Participants	***Patients****:* patients who had clinical problem with an already-active warfarin use (194 intervention vs 148 control) ***Intervention recipients****:* Ward physicians ***Antimicrobial target for intervention****:* non-specified ***Setting****:* Two teaching hospitals, USA	Participants	***Patients****:* adult patients with infections requiring IV antimicrobials during the first four days of admission (72 intervention vs 44 control) ***Intervention recipients****:* Junior doctors ***Antimicrobial target for intervention****:* IVOST ***Setting****:* A teaching hospital, Ireland
Interventions	***Intervention component****:* EO (providing recommendation through discussion with pharmacist) & RT (expert approval) ***Intervention duration (month)****:* 7 ***Intervention deliverer****:* A clinical pharmacist	Interventions	***Intervention component****:* DM, EO (verbal) & RMD (stickers) ***Intervention duration (month)****:* 7 ***Intervention deliverer****:* clinical pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice****:* proportion of physicians' response that adhered with recommendations: intervention (111/194) (57.2%) vs control (20/148) (13.5%) (95% CI: 0.045-0.33) ***DOT (day)****:* - ***Mortality****:* - ***LOS (day)****:* - ***Microbial outcome****:* -	Outcomes	***Compliance with target practice****:* (Data from phase II) intervention (52/72) (71.7%) vs control (24/44) (55.5%) (p=0.017) ***Median DOT (day)****:* (data from phase II) IV: intervention (3.0) vs control (4.0) (p=0.02) ***Mortality****:* - ***LOS (day)****:* - ***Microbial outcome****:* -
Note		Note	Phase I for both control and intervention groups used conventional practice whereas the intervention group in phase II used intervention materials. Data included from phase II

Grill 2011		***Shen 2011***	
Methods	***Study design****:* BA	Methods	***Study design****:* RCT
Participants	***Patients****:* Adult patients admitted in surgical wards and received antimicrobials for a proven or suspected infection (321 post-intervention vs 317 pre-intervention) ***Intervention recipients****:* All surgeons in 4 surgery wards ***Antimicrobial target for intervention****:* IVOST ***Setting****:* One teaching hospital, Germany	Participants	***Patients****:* Patients with respiratory infections admitted in respiratory wards requiring antimicrobial agents (176 intervention vs 178 control) ***Intervention recipients****:* All specialist physicians in respiratory wards ***Antimicrobial target for intervention****:* empirical and definitive therapy ***Setting****:* A tertiary care teaching hospital, China
Interventions	***Intervention component****:* EO (providing recommendations during ward round activities) ***Intervention duration (month)****:* 6 ***Intervention deliverer****:* A clinical pharmacist	Interventions	***Intervention component****:* EO (verbal) ***Intervention duration (month)****:* 10 ***Intervention deliverer****:* A clinical pharmacist
Comparator	Usual care	Comparator	Usual care

Outcomes	***Compliance with target practice**:* post- intervention (85/480 of administrations) (17.7%) vs pre-intervention (49/452 administrations) (10.8%) (p=0.001) ***Mean DOT (day)**:* IV: post-intervention (8.0) *vs* pre-intervention (10.0) (p<0.0001) ***Mortality**:* - ***Median LOS (day)**:* post-intervention (19.0 (IQR 3.0-130.0)) *vs* pre-intervention (18.0 (IQR 3.0-220.0)) (p=0.857) ***Microbial outcome**:* -	Outcomes	***Compliance with target practice**:* intervention (153/176) (86.9%) vs control (112/178) (62.9%) vs (p>0.05) ***DOT (day)**:* - ***Mortality**:* - ***Mean LOS (day)**:* intervention (14.2±6.2) vs control (15.8±6.0) (p=0.03) ***Microbial outcome**:* -
Note		Note	

Newland 2012		***Yen 2012***	
Methods	***Study design**:* ITS	Methods	***Study design**:* BA
Participants	***Patients**:* Paediatric patients requiring selected board spectrum antimicrobial agents in the lists monitored by ASP team ***Intervention recipients**:* All ward physicians caring for paediatric patients ***Antimicrobial target for intervention**:* empirical and definitive therapy ***Setting**:* A tertiary teaching children's hospital, USA	Participants	***Patients**:* Patients requiring IV levofloxacin for more than 48 hours (37 post-intervention vs 42 pre-intervention) ***Intervention recipients**:* All ward physicians ***Antimicrobial target for intervention**:* IVOST ***Setting**:* A tertiary teaching hospital, Taiwan
Interventions	***Intervention component**:* EO (non-specified mode of communication) ***Intervention duration (month)**:* 30 ***Intervention deliverer**:* A clinical pharmacist	Interventions	***Intervention component**:* EO (recommendations noted in medical records) ***Intervention duration (month)**:* 2 ***Intervention deliverer**:* Clinical pharmacists
Comparator	Usual care (control was 25 similar children's hospitals that were members of the Child Health Corporation of America)	Comparator	Usual care
Outcomes	***Compliance with target practice**:* - ***DOT (day)**:* decreased 12% per month per 1,000 PD (p<0.001) ***Mortality**:* - ***LOS (day)**:* decreased 13% per month per 1,000 PD (p<0.001) ***Microbial outcome**:* -	Outcomes	***Compliance with target practice**:* - ***Mean DOT**:* IV levofloxacin: post-intervention (6.6±4.4) *vs* pre-intervention (8.3±3.8) (p=0.075) ***Mortality**:* - ***Mean LOS**:* post-intervention (16.1±9.3) *vs* pre-intervention (27.2±18.5) (p=0.001) ***Microbial outcome**:* -
Note	The authors described their intervention as "audit and feedback", but there is no feedback of data over time about progress to goal.	Note	

Cappelletty 2013		***Zhang 2014***	
Methods	***Study design**:* BA	Methods	***Study design**:* BA

Participants	***Patients**:* adult patients receiving selected antimicrobials for at least 72 hours (45 post-intervention vs 51 pre-intervention) ***Intervention recipients**:* All ward physicians ***Antimicrobial target for intervention**:* empirical and definitive therapy ***Setting**:* A tertiary care teaching hospital, USA	Participants	***Patients**:* Patients requiring antimicrobial for preoperative prophylaxis in urological ward (193 post-intervention vs 171 pre-intervention) ***Intervention recipients**:* All surgeons in urological ward ***Antimicrobial target for intervention**:* antimicrobial prophylaxis ***Setting**:* A tertiary care teaching hospital, China
Interventions	***Intervention component**: EO (verbal through discussion)* ***Intervention duration (month)**: 3* ***Intervention deliverer***: ID-trained clinical pharmacist	Interventions	***Intervention component**:* AF (feedback provided to all clinical departments including hospital administration; no frequency documented) & EO (verbal with real time monitoring) ***Intervention duration (month)**:* 6 ***Intervention deliverer**:* A clinical pharmacist with well-trained in infection
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice**:* imipenem prescribing: post-intervention (33/45) (73.3%) *vs* pre-intervention (34/51) (66.7%) (p>0.05) ***Mean DOT (day)**:* imipenem use: post-intervention (4.8±1.4) *vs* pre-intervention (5.6±2.2) (p>0.05) ***Mortality**: -* ***LOS (day)**: -* ***Microbial outcome**: -*	Outcomes	***Compliance with target practice**:* post-intervention (60/80) (75.0%) *vs* pre-intervention (36/88) (40.9%) (p<0.001) ***Mean DOT (day)**:* for prophylaxis use: post-intervention (2.9) *vs* pre-intervention (7.6) (p<0.001) ***Mortality**: -* ***LOS (day)**: -* ***Microbial outcome**: -*
Note		Note	

Apisarnthanarak 2015		***Nguyen 2015***	
Methods	***Study design**:* CBA	Methods	***Study design**:* BA
Participants	***Patients**:* adult patients with presumptive infection requiring one antimicrobial prescription and admitted in 6 medicine units (104 intervention vs 150 control) ***Intervention recipients**:* All ward physicians who required consultations from pharmacist ***Antimicrobial target for intervention**:* empirical and definitive therapy ***Setting**:* One teaching hospital, Thailand	Participants	***Patients**:* Adult patients with positive MSSA or MRSA bacteraemia (88 post-intervention vs 82 pre-intervention) ***Intervention recipients**:* All primary treating physicians ***Antimicrobial target for intervention**:* definitive therapy ***Setting**:* A tertiary care teaching hospital, USA
Interventions	***Intervention component**:* AD, EO (providing recommendations during daily ward rounds), & RMD ***Intervention duration (month)**:* 9 ***Intervention deliverer**:* three clinical pharmacists who had special trainings for infections and ASPs	Interventions	***Intervention component**:* DM, EO (verbal), & RMD (pocket size guidelines) ***Intervention duration (month)**:* 9 ***Intervention deliverer**:* ID pharmacist
Comparator	Usual care	Comparator	Usual care

Outcomes	***Compliance with target practice**:* intervention 96/104 (92.3%) vs control 105/150 (70.0%) (p<0.05) ***Mean DOT (day)**:* intervention (8.4±3.0) vs control (17.5±20.0) (p<0.05) ***Mortality**:* intervention (10/104) (9.6%) *vs* control (10/150) (6.7%) (p>0.05) ***Mean LOS (day)**:* intervention (18.7±17.0) vs control (28.8±7.0) (p<0.05) ***Microbial outcome**:* -	Outcomes	***Compliance with target practice**:* post-intervention (74/88) (84.1%) *vs* pre-intervention (46/82) (56.1%) (p<0.001) ***DOT (day)**:* - ***Mortality**:* post-intervention (10/88) (11.4%) *vs* pre-intervention (16/82) (19.5%) (p=0.2) ***Median LOS (day)**:* post-intervention (9.0 IQR 5.0-20.0)) *vs* pre-intervention (9.0 IQR 5.0-17.0)) (p=0.47) ***Microbial outcome**:* -
Note		Note	

Phillips 2015		***Tavakoli-Ardakani 2015***	
Methods	***Study design**:* BA	Methods	***Study design**:* BA
Participants	***Patients**:* Adult patients with clinical problem receiving vancomycin for documented therapy (45 pre-intervention vs 53 post-intervention) ***Intervention recipients**:* Junior doctors as major target and registered pharmacists (supportive roles) ***Antimicrobial target for intervention**:* definitive therapy ***Setting**:* A tertiary care teaching hospital, Australia	Participants	***Patients**:* adult patients receiving IV vancomycin in the ICU and haematology-oncology ward (82 post-intervention vs 77 pre-intervention) ***Intervention recipients**:* All ward physicians ***Antimicrobial target for intervention**:* empirical and definitive therapy ***Setting**:* One teaching hospital, Iran
Interventions	***Intervention component**:* DM & AD ***Intervention duration (month)**:* 8 ***Intervention deliverer**:* A clinical pharmacist	Interventions	***Intervention component**:* EO (verbal through discussion) ***Intervention duration (month)**:* 6 ***Intervention deliverer**:* A clinical pharmacist
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice**:* (1) Starting maintenance doses that were in accordance with guideline: post-intervention (29/45) (64.4%) *vs* pre-intervention (28/53) (52.8%) (p=0.32) (2) Dosage adjustment when blood concentrations were outside target: post-intervention (24/34) (70.6%) vs pre-intervention (21/39) (53.9%) (p=0.12) ***Median DOT (day)**:* vancomycin use: post-intervention (6.0 (IQR 4.0-16.5)) *vs* pre-intervention (10.0 (IQR 4.3-13.8)) (p=0.31) ***Mortality**:* - ***Median LOS (day)**:* post-intervention (16.0 (IQR 9.0-29.5)) *vs* pre-intervention (20.0 (IQR 10.5-32.5)) (p=0.13) ***Microbial outcome**:* -	Outcomes	***Compliance with target practice**:* post-intervention (54/82) (65.9%) *vs* pre-intervention (42/77) (54.6%)(p=0.50) ***DOT (day)**:* - ***Mortality**:* - ***LOS (day)**:* - ***Microbial outcome**:* -
Note		Note	

Wang (J) 2015		***Zhou (Y) 2015***	
Methods	***Study design****:* BA	Methods	***Study design****:* BA
Participants	***Patients****:* Patients undergoing elective caesarean section in the maternity ward (197 post-intervention vs 197 pre-intervention) ***Intervention recipients****:* All obstetricians ***Antimicrobial target for intervention****:* antimicrobial prophylaxis ***Setting****:* A tertiary care teaching hospital, China	Participants	***Patients****:* Adult patients undergoing clean and clean-contaminated operations in urological ward (11 post-intervention vs 36 pre-intervention) ***Intervention recipients****:* All surgeons and nurses in urology ward ***Antimicrobial target for intervention****:* antimicrobial prophylaxis ***Setting****:* A tertiary care teaching hospital, China
Interventions	***Intervention component****:* AF (feedback provided to all professionals including hospital administration every two weeks), AD, & EO (verbal) ***Intervention duration (month)****:* 3 ***Intervention deliverer****:* A clinical pharmacist	Interventions	***Intervention component****:* AF (feedback provided to all clinical departments on a monthly basis through meetings), DM, AD, & EO (providing recommendations during ward rounds) ***Intervention duration (month)****:* 6 ***Intervention deliverer****:* Clinical pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice****:* (1) Correct choice: post-intervention (186/197) (93.9%) vs pre-intervention (8/197) (4.1%) (p<0.001) (2) Correct choice and dose: post-intervention (185/197) (93.9%) *vs* pre-intervention (7/197) (3.6%) (p<0.001) ***Mean DOT (day)****:* antimicrobial prophylaxis use: post-intervention (1.9) *vs* pre-intervention (4.1) (p<0.001) ***Mortality****: -* ***Mean LOS (day)****:* post-intervention (6.2) *vs* pre-intervention (6.2) (p=0.536) ***Microbial outcome****: -*	Outcomes	***Compliance with target practice****:* administered antimicrobial for pre-operative 0.5-2 hr prior to surgery: post-intervention (8/11) (72.7%) *vs* pre-intervention (7/36) (19.4%) ***Mean DOT (day)****:* (1) 2010 vs 2012: post-intervention (1.3±0.5) *vs* pre-intervention (3.9±1.6), (2) 2010 vs 2013: post-intervention (2.0±1.4) *vs* pre-intervention (3.9±1.6) ***Mortality****: -* ***LOS (day)****: -* ***Microbial outcome****: -*
Note		Note	- Data in 2011 were not used to compare with 2010 as it is a preparing phase and the outcomes reported in the study are associated with only "antimicrobial prophylaxis in urology". - Data of compliance compared between 2010 and 2012-2013.

Brumley 2016		***Ellis 2016***	
Methods	***Study design****:* BA	Methods	***Study design****:* BA
Participants	***Patients****:* Adult patients with positive *Clostridium difficile* infection (83 post-intervention vs 89 pre-intervention) ***Intervention recipients****:* All ward physicians ***Antimicrobial target for intervention****:* definitive therapy ***Setting****:* A community teaching hospital, USA	Participants	***Patients****:* adult patients admitted at geriatric psychiatric unit 95 prescriptions (70 patients) in post-intervention vs 71 prescriptions (63 patients) pre-intervention ***Intervention recipients****:* All prescribing physicians ***Antimicrobial target for intervention****:* empirical and definitive therapy ***Setting****:* A tertiary care teaching hospital, USA

Interventions	***Intervention component:*** DM&EO (communication during care rounds) ***Intervention duration (month):*** 3 ***Intervention deliverer:*** Clinical pharmacists	Interventions	***Intervention component:*** EO (non-verbal communication) ***Intervention duration (month):*** 6 ***Intervention deliverer:*** A clinical pharmacist
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice:*** post-intervention (67/83) (80.7%) *vs* pre-intervention (40/89) (44.9%) (p<0.001) ***DOT (day):*** - ***Mortality:*** CDI-related mortality: post-intervention (3/83) (3.6%) *vs* pre-intervention (1/89) (1.1%) (p=0.35) ***Mean LOS (day):*** post-intervention (6.8) *vs* pre-intervention (7.1) (p=0.75) ***Microbial outcome:*** -	Outcomes	***Compliance with target practice:*** post-intervention (63/95) (66.3%) *vs* pre-intervention (36/71) (50.7%) (p=0.04) ***Mean DOT (day):*** post-intervention (174/1,000 patient-day) *vs* pre-intervention (174/1,000 patient-day) (p=0.99) ***Mortality:*** - ***LOS (day):*** - ***Microbial outcome:*** -
Note		Note	

Heyerly 2016		***Okada 2016***	
Methods	***Study design:*** CBA	Methods	***Study design:*** CBA
Participants	***Patients:*** Adult patients with positive blood cultures of gram-positive pathogens (107 intervention vs 190 control) ***Intervention recipients:*** All primary treating physicians ***Antimicrobial target for intervention:*** definitive therapy ***Setting:*** A tertiary-care community non-teaching hospital, USA	Participants	***Patients:*** Patients admitted at the haematological medical ward requiring anti-MRSA agent (74 intervention vs 71 control) ***Intervention recipients:*** All physicians ***Antimicrobial target for intervention:*** empirical and definitive therapy ***Setting:*** A tertiary care teaching hospital, Japan
Interventions	***Intervention component:*** EO (verbal) ***Intervention duration (month):*** 9 ***Intervention deliverer:*** Clinical pharmacists who had special trainings together with ID pharmacist	Interventions	***Intervention component:*** *EO (non-specified mode of communication)* ***Intervention duration (month):*** 23 ***Intervention deliverer:*** Clinical pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice:*** intervention (30/107) (28.0%) *vs* control (20/190) (10.5%) (p=0.0002) ***DOT (day):*** - ***Mortality:*** - ***Mean LOS (day):*** intervention (11.0) vs control (11.0) (p=1.0) ***Microbial outcome:*** -	Outcomes	***Compliance with target practice:*** - ***Median DOT (day):*** anti-MRSA: intervention (10.0 (IQR 4.0-14.0)) *vs* control (11.0 (IQR 4.0-18.0)) (p=0.38) ***Mortality:*** - ***Median LOS (day):*** intervention (48.0 (26.0-429.0)) *vs* control (70.0 (10.0-691.0)) (p=0.07) ***Microbial outcome:*** -
Note		Note	

Shannon 2016		***Yu 2016***	
Methods	***Study design:*** CBA	Methods	***Study design:*** BA

Participants	***Patients:*** Adult patients with a reported beta-lactam allergy who required at least one alternative (non-beta lactam) antibiotic during admission (63 intervention vs 63 control) ***Intervention recipients:*** All primary treating physicians ***Antimicrobial target for intervention:*** empirical and definitive therapy ***Setting:*** A community non-teaching hospital, USA	Participants	***Patients:*** Paediatric patients with purulent MSSA or MRSA skin infection (103 post-intervention vs 121 pre-intervention) ***Intervention recipients:*** All attending ward physicians ***Antimicrobial target for intervention:*** definitive therapy ***Setting:*** A tertiary care teaching Children's hospital, USA
Interventions	***Intervention component:*** AD & EO (non-specified mode of communication) ***Intervention duration (month):*** 7 ***Intervention deliverer:*** Clinical pharmacists who were educated on the allergy assessment procedure and appropriate recommendations for physicians	Interventions	***Intervention component:*** AD & EO (non-specified mode of communication) ***Intervention duration (month):*** 12 ***Intervention deliverer:*** ID pharmacist
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice:*** intervention (36/63) (57.1%) *vs* control (14/63) (22.2%) (p=0.0019) ***Mean DOT (day):*** intervention (13.0±11.8) *vs* control (14.6±11.9) (p=0.45) ***Mortality:*** intervention (1/63) (1.6%) *vs* control (4/63) (6.3%) (p=0.168) ***Mean LOS (day):*** intervention (9.4±7.7) *vs* control (8.2±7.1) ***Microbial outcome:*** CDI rate: intervention (1/63) (1.6%) *vs* control (1/63) (1.6%) (p=1.0)	Outcomes	***Compliance with target practice:*** post-intervention (91/103) (88.3%) *vs* pre-intervention (90/121) (74.4%) (p=0.008) ***DOT (day):*** - ***Mortality:*** - ***Median LOS (day):*** post-intervention (2.0 (0.7-5.1)) *vs* pre-intervention (2.5 (IQR 0.6-9.5)) (p=0.018) ***Microbial outcome:*** -
Note		Note	

Zhou (L) 2016		***Beganovic 2017***	
Methods	***Study design:*** BA	Methods	***Study design:*** BA
Participants	***Patients:*** Patients undergoing cardiothoracic surgery (received antimicrobial prophylaxis: 508 post-intervention vs 342 pre-intervention) ***Intervention recipients:*** (1) All surgeons including residents and nurses in cardiothoracic ward (2) PAF results were provided to leadership in cardiothoracic surgery department ***Antimicrobial target for intervention:*** antimicrobial prophylaxis ***Setting:*** A tertiary care teaching hospital, China	Participants	***Patients:*** adult and paediatric patients with a positive blood culture ((123 patients (126 blood cultures) in post-intervention vs 116 patients (126 blood cultures) in pre-intervention) ***Intervention recipients:*** All physicians ***Antimicrobial target for intervention:*** definitive therapy ***Setting:*** A tertiary care teaching hospital, USA
Interventions	***Intervention component:*** AF (feedback provided to leadership in cardiothoracic surgery departments on a weekly basis through meeting), DM, & EO (providing recommendations during ward round) ***Intervention duration (month):*** 17 ***Intervention deliverer:*** A clinical pharmacist	Interventions	***Intervention component:*** EO (verbal) ***Intervention duration (month):*** 3 ***Intervention deliverer:*** A pharmacist
Comparator	Usual care	Comparator	Usual care

Outcomes	***Compliance with target practice:*** post-intervention (496/508) (97.6%) *vs* pre-intervention (157/342) (45.9%) (p<0.001) ***DOT (day)****:* - ***Mortality****:* - ***Mean LOS (day)****:* post-intervention (20.9±8.9) *vs* pre-intervention (23.3±8.9) (p<0.001) ***Microbial outcome****:* (1) Clindamycin-*resistant Staphylococcus aureus*: post-intervention 25.9% *vs* pre-intervention 60.0% (p=0.12) (2) Imipenem-resistant *Enterobacter cloacae*: post-intervention 1.7% *vs* pre-intervention 9.4% (p=0.25) (3) Ceftazidime-resistant *Klebsiella pneumoniae* to ceftazidime: post-intervention 7.7% *vs* pre-intervention 12.5% (p=0.25)	Outcomes	***Compliance with target practice****:* - ***Mean DOT (day)****:* post-intervention (15.9±11.1) *vs* pre-intervention (18.6±12.0) (p=0.117) ***Mortality****:* post-intervention (15/123) (12.2%) *vs* pre-intervention (12/116) (10.3%) (p=0.805) ***Mean LOS (day)****:* post-intervention (9.0±7.3) *vs* pre-intervention (15.0±22.7) (p=0.021) ***Microbial outcome****:* -
Note	Drug susceptibility list chosen according to the recommended treatment guideline	Note	

Brink 2017		***Campbell 2017***	
Methods	***Study design****:* BA	Methods	***Study design****:* ITS
Participants	***Patients****:* Patients undergoing surgical procedures ***Intervention recipients****:* Surgeons, anaesthetists, ward nurses ***Antimicrobial target for intervention****:* antimicrobial prophylaxis ***Setting****:* thirty-four private (urban and rural) non-teaching hospitals, South Africa	Participants	***Patients****:* Patients requiring IV antimicrobial admitted in surgery, respiratory, and medical wards ***Intervention recipients****:* All ward physicians ***Antimicrobial target for intervention****:* empirical and definitive therapy ***Setting****:* A community teaching hospital, Canada
Interventions	***Intervention component****:* AF (feedback provided to surgeons monthly in theatre rooms with additional email and presented during journal clubs) & EO (verbal and non-verbal by written in chard or mobile phone messages) ***Intervention duration (month)****:* 16 ***Intervention deliverer****:* clinical pharmacists	Interventions	***Intervention component****:* EO (verbal) ***Intervention duration (month)****:* surgical (51), respiratory (48), and medical (30) ward ***Intervention deliverer****:* ID pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice****:* post-intervention (83.3%) *vs* pre-intervention (66.8%) (p<0.0001) (no raw data of number of prescriptions shown) ***DOT (day)****:* - ***Mortality****:* - ***LOS (day)****:* - ***Microbial outcome****:* -	Outcomes	***Compliance with target practice****:* - ***DOT (day)****:* linear trend before & after intervention: decreased 12.0% in surgical ward, 10.0% in respiratory ward, and 20.0% in medical ward (per 1,000 patient-day over intervention period) (all P<0.05)

			***Mortality**:* trend before & after intervention: changed 0.99 to 0.97 (surgical ward), 11.5 to 12.2 (respiratory ward), and 7.4 to 5.0 (medical ward) cases/1,000 patient-day (all non-significant) ***Mean LOS (day)**:* trend before & after intervention: changed 4.7 to 4.3 (surgical ward), 9.6 to 8.5 (respiratory ward), and 10.2 to 10.3 (medical ward) days/1,000 patient-day (all non-significant) ***Microbial outcome**:* trend of CDI rate before & after intervention: decreased 0.8 to 0.4 (surgical ward), 2.4 to 0.8 (respiratory ward), and 0.8 to 0.4 (medical ward) cases/1,000 patient-day (all non-significant)
Note		Note	The authors described their intervention as "audit and feedback", but there is no feedback of data over time about progress to goal.

Li 2017		***Nault 2017***	
Methods	***Study design:*** CBA	Methods	***Study design**:* ITS
Participants	***Patients:*** adult patients with critically ill admitted in ICU requiring antimicrobial therapy within 24 hours after hospitalisation (353 intervention vs 224 control) ***Intervention recipients:*** All ward physicians in 4 ICU settings ***Antimicrobial target for intervention:*** empirical therapy ***Setting:*** six tertiary care teaching hospitals (8 ICU units were divided into 4 in control and 4 in intervention group), China	Participants	***Patients***: patients with clinical problem requiring IV or oral antimicrobial ***Intervention recipients***: All physicians ***Antimicrobial target for intervention***: empirical and definitive therapy ***Setting***: A tertiary care teaching hospital, Canada
Interventions	***Intervention component:*** EO (interaction during ward round) ***Intervention duration (month):*** 2 ***Intervention deliverer:*** clinical pharmacists who were trained in appropriate antimicrobial use and ASPs	Interventions	***Intervention component***: EO (recommendations made in clinical decision-support system) ***Intervention duration (month)***: 36 ***Intervention deliverer***: ID pharmacist and clinical pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice:*** intervention (260/353) (73.7%) vs control (152/224) (67.9%) (p=0.13) ***Median DOT (day):*** empirical antimicrobial use: intervention (2.7 (IQR 1.9-6.2)) vs control (3.0 (IQR 1.4-4.6)) (p=0.002) ***Mortality:*** intervention (68/353) (19.3%) vs control (65/224) (29.0%) (p=0.007) ***Median LOS (day):*** intervention (17.0 (IQR 12.0-29.0)) vs control (18.00 (IQR 11.0-31.0)) (p=0.544)	Outcomes	***Compliance with target practice***: Trend change of proportion of prescriptions that did not adhere with guideline decreased 0.1% per month over time of the intervention period (p=0.19) ***DOT (day)***: Trend change of DOT decreased 1.4 DOT/1,000 patient-day over time of the intervention period (p<0.01) ***Mortality***: - ***LOS (day)***: Trend change of LOS decreased 0.1 days over time of the intervention period (p<0.01)

	Microbial outcome: multi-drug resistant infection rate: intervention (84/353) (23.8%) vs control (71/224) (31.7%) (p=0.037)		***Microbial outcome***: -
Note	The author described and named the intervention as "audit" but there is no data feedback over time about progress to goal.	Note	The authors described their intervention as "audit and feedback", but there is no feedback of data over time about progress to goal.

Shea 2017		***Willis 2017***	
Methods	***Study design****:* BA	Methods	***Study design****:* BA
Participants	***Patients***: Patients requiring quinolones for pneumonia and COPD exacerbation (130 post-intervention vs 232 pre-intervention) ***Intervention recipients***: All physicians across four hospitals ***Antimicrobial target for intervention***: empirical and definitive therapy ***Setting***: Four tertiary care (teaching and non-teaching) hospitals, USA	Participants	***Patients***: adult patients with respiratory tract infection (all types of pneumonia or COPD) requiring IV vancomycin for MRSA coverage (150 post-intervention vs 150 pre-intervention) ***Intervention recipients***: All physicians ***Antimicrobial target for intervention***: definitive therapy ***Setting***: A tertiary community teaching hospital, USA
Interventions	***Intervention component***: DM, EO (direct and verbal contact), & RT (antimicrobial formulary restriction) ***Intervention duration (month)***: 15 (phase I: 3 & phase II: 12) ***Intervention deliverer***: ID pharmacists	Interventions	***Intervention component***: EO (verbal for prompt recommendations) ***Intervention duration (month)***: 6 ***Intervention deliverer***: ID pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice***: phase I and II: post-intervention (74/130) (56.9%) *vs* pre-intervention (74/232) (31.9%) (p<0.001) ***Mean DOT (day)***: Mean DOT (per 1,000 patient-day): phase I: post-intervention (21.5±6.4) *vs* pre-intervention (41.0±4.4), phase II: post-intervention (4.8±3.6) *vs* pre-intervention (41.0±4.4) ***Mortality***: - ***LOS (day)***: - ***Microbial outcome***: Mean CDI rate (per month per 10,000 patient-day) of phase I and II: post-intervention (2.2±1.4) *vs* pre-intervention (4.0±2.1) (p=0.044)	Outcomes	***Compliance with target practice***: - ***Median DOT (day)***: vancomycin: post-intervention (2.1 (IQR 1.4±3.9)) *vs* pre-intervention (4.2± (IQR2.8-5.8)) (p<0.0001) ***Mortality***: post-intervention (3/150) (2.0%) *vs* pre-intervention (3/150) (2.0%) (p=1.00) ***Median LOS (day)***: post-intervention (7.0 (IQR 5.0±9.0)) *vs* pre-intervention (8.0± (IQR 4.2-10.0)) (p=0.17) ***Microbial outcome***: -
Note		Note	

Yang 2017		***Eljaaly 2018***	
Methods	***Study design****:* BA	Methods	***Study design****:* BA
Participants	***Patients***: Patients undergoing vascular and interventional radiology procedures (177 post-intervention vs 162 pre-intervention) ***Intervention recipients***: All physicians	Participants	***Patients***: adult patients with clinical problem requiring restricted antimicrobials for≥3 days (83 post-intervention vs 83 pre-intervention) ***Intervention recipients***: All ward and ordering physicians

	Antimicrobial target for intervention: antimicrobial prophylaxis ***Setting***: A tertiary teaching hospital, China		***Antimicrobial target for intervention***: definitive therapy ***Setting***: A community teaching hospital, USA
Interventions	***Intervention component***: AF (feedback provided to all departments of medical affairs in meetings and published on hospital website for other professionals), AD, & EO (non-verbal by email & verbal using telephone) ***Intervention duration (month)***: 6 ***Intervention deliverer***: clinical pharmacists who had 1-year training of residency in ward and training in the use of protocol	Interventions	***Intervention component***: EO (verbal) & RT (expert approval) ***Intervention duration (month)***: 3 ***Intervention deliverer***: ID pharmacists, pharmacy practice resident, and pharmacy students
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice***: post-intervention (174/177) (98.3%) *vs* pre-intervention (134/162) (82.7%) (p<0.0001) ***Mean DOT (day)***: antimicrobial prophylaxis use: post-intervention (0.5±1.0) *vs* pre-intervention (0.9±2.0) (p=0.012) ***Mortality***: - ***LOS (day)***: - ***Microbial outcome***: -	Outcomes	***Compliance with target practice***: - ***Median DOT (day)***: all restricted antimicrobials: post-intervention (4.0 (IQR 3.0-5.0)) *vs* pre-intervention (5.0 (IQR 4.0-8.8)) (P<0.001) ***Mortality***: post-intervention (2/83) (2.4%) *vs* pre-intervention (8/83) (9.6%) (p=0.057) ***Median LOS (day)***: post-intervention (6.0 (IQR 5.0-9.0)) *vs* pre-intervention (8.0 (IQR 5.0-17.0)) (p=0.005) ***Microbial outcome***: -
Note	Outcomes were drawn and compared between phase I and Phase III indicating intervention duration for 6 months (2 quarters of phase II & III)	Note	

Fooland 2018		***Hwang 2018***	
Methods	***Study design****:* BA	Methods	***Study design****:* ITS
Participants	***Patients***: adult patients with pneumonia (293 post-intervention vs 307 pre-intervention) ***Intervention recipients***: All attending physicians ***Antimicrobial target for intervention***: empirical therapy ***Setting***: Three teaching hospitals, USA	Participants	***Patients***: adult patients requiring anaerobe antibiotic ***Intervention recipients***: All attending physicians ***Antimicrobial target for intervention***: empirical therapy ***Setting***: A secondary care teaching hospital, Korea
Interventions	***Intervention component***: AF (feedback provided to physicians in primary teams via direct verbal communication, no frequency documented), DM, & EO (verbal) ***Intervention duration (month)***: 6 ***Intervention deliverer***: ID pharmacists	Interventions	***Intervention component***: EO (non-specified mode of communication) ***Intervention duration (month)***: 5 ***Intervention deliverer***: A clinical pharmacist
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice***: post-intervention (120/287) (41.8%) *vs* pre-intervention (17/304) (5.6%) (p<0.001) ***Median DOT (day)***: post-intervention (6.0 (IQR 5.0-7.0)) *vs* pre-intervention (9.0 (IQR 7.0-10.0)) (p<0.001)	Outcomes	***Compliance with target practice***: - ***DOT (day)***: Trend change of DOT of metronidazole decreased 13.9 DOT/1,000patient-day/month (p<0.001) ***Mortality***: -

	Mortality: post-intervention (3/293) (1.0%) *vs* pre-intervention (7/298) (2.3%) (p=0.233) ***LOS (day)***: - ***Microbial outcome***: CDI rate: post-intervention (0/293) (0%) *vs* pre-intervention (0/294) (0%)		***LOS (day)***: - ***Microbial outcome***: -
Note		Note	Data were drawn for minor intervention made by pharmacist

Ohashi 2018		***Sze 2018***	
Methods	***Study design****:* BA	Methods	***Study design****:* BA
Participants	***Patients***: Adult patient with MRSA bacteraemia infection (51 post-intervention vs 43 pre-intervention) ***Intervention recipients***: All attending physicians ***Antimicrobial target for intervention***: definitive therapy ***Setting***: A tertiary care teaching hospital, Japan	Participants	***Patients***: adult patients with clinical problem requiring IV antimicrobial at least 48 hours ((76 patients (77 courses) of post-intervention vs 72 patients (79 courses) of pre-intervention)) ***Intervention recipients***: All ward physicians ***Antimicrobial target for intervention***: IVOST ***Setting***: eight district non-teaching hospitals, Malaysia
Interventions	***Intervention component***: DM & EO (verbal: direct contact or telephone) ***Intervention duration (month)***: 31 ***Intervention deliverer***: ID pharmacist	Interventions	***Intervention component***: DM & RMD (stickers in chart) ***Intervention duration (month)***: 2 ***Intervention deliverer***: *w*ard pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice***: post-intervention (42/51) (82.4%) *vs* pre-intervention (27/43) (62.3%) (p=0.038) ***DOT (day)***: - ***Mortality***: post-intervention (11/51) (21.6%) *vs* pre-intervention (18/43) (41.8%) (p=0.044) ***Median LOS (day)***: post-intervention (35.0 (IQR 22.0-59.0)) *vs* pre-intervention (52.5 (IQR 23.8-70.0)) (p=0.282) ***Microbial outcome***: -	Outcomes	***Compliance with target practice***: - ***Mean DOT (day)***: IV antimicrobial: post-intervention (2.8±1.2) *vs* pre-intervention (4.1±1.6) (p<0.0001) ***Mortality***: - ***Mean LOS (day)***: post-intervention (4.1±1.7) *vs* pre-intervention (5.5±3.2) (p=0.001) ***Microbial outcome***: -
Note		Note	

Abubakar 2019		***Bianchini 2019***	
Methods	***Study design****:* BA	Methods	***Study design****:* BA
Participants	***Patients***: adult women undergoing elective and emergency obstetric and gynaecologic surgeries for clean, clean-contaminated and contaminated wounds (238 post-intervention vs 226 pre-intervention) ***Intervention recipients***: obstetricians and gynaecologists (main target), and clinicians where practices did not align with the guideline	Participants	***Patients***: Patients with pneumonia admitted in ICU settings (91 post-intervention vs 91 pre-intervention) ***Intervention recipients***: All physicians at ICU wards ***Antimicrobial target for intervention***: definitive therapy ***Setting***: A tertiary care teaching hospital, USA

	Antimicrobial target for intervention: antimicrobial prophylaxis ***Setting***: two tertiary care teaching hospitals, Nigeria		
Interventions	***Intervention component***: AF (feedback provided to obstetricians & gynaecologists through their group meetings), DM, AD, & RMD (posters) ***Intervention duration (month)***: 3 ***Intervention deliverer***: A clinical pharmacist	Interventions	***Intervention component***: EO (non-verbal: documented in electronic medical record) ***Intervention duration (month)***: 5 ***Intervention deliverer***: ID Pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice***: post-intervention 103/238 (43.3%) *vs* pre-intervention 32/226 (14.2%) (p<0.001) ***DOT (day)***: - ***Mortality***: - ***Mean LOS (day)***: post-intervention (6.1±2.6) *vs* pre-intervention (6.4±2.8) (p=0.29) ***Microbial outcome***: -	Outcomes	***Compliance with target practice***: post-intervention 53/91 (58.2%) *vs* pre-intervention 24/91 (26.4%) (p<0.05) ***Median DOT (day)***: post-intervention (7.0 (IQR 6.0-8.0)) *vs* pre-intervention (7.0 (IQR 6.0-10.0)) (p=0.35) ***Mortality***: post-intervention (7/91) (7.7%) *vs* pre-intervention (13/91) (14.3%) (p=0.235) ***Median LOS (day)***: post-intervention (9.0 (IQR 7.0-16.0)) *vs* pre-intervention (9.0 (IQR 6.0-15.0)) (p=0.472) ***Microbial outcome***: multi-drug resistant infection rate: post-intervention (2/91) (2.2%) *vs* pre-intervention (6/91) (6.6%) (p=0.278), CDI rate: post-intervention (0/91) (0%) *vs* pre-intervention (1/91) (1.1%)
Note		Note	

Box 2019		***Butt 2019***	
Methods	***Study design****:* BA	Methods	***Study design****:* BA
Participants	***Patients***: adult patients with bacteraemia caused by non-resistant gram-negative bacteria (539 post-intervention vs 512 pre-intervention) ***Intervention recipients***: All attending physicians ***Antimicrobial target for intervention***: definitive therapy ***Setting***: five tertiary care teaching hospitals (5 acute cares that compose Scripps Health), USA	Participants	***Patients***: patients undergoing surgical procedures (225 post-intervention vs 225 pre-intervention) ***Intervention recipients***: **s**urgeons (staff, residents, and fellows) and nurses ***Antimicrobial target for intervention***: antimicrobial prophylaxis ***Setting***: A tertiary care teaching hospital, Pakistan
Interventions	***Intervention component***: DM & EO (verbal) ***Intervention duration (month)***: 12 ***Intervention deliverer***: clinical pharmacists who were properly trained in ID by ID pharmacist	Interventions	***Intervention component***: DM & AD ***Intervention duration (month)***: 4 ***Intervention deliverer***: A clinical pharmacist
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice***: -	Outcomes	***Compliance with target practice***: post-intervention (28/225) (12.4%) *vs* pre-intervention (3/225) (1.3%) (p=0.0005)

	Median DOT (day): anti-pseudomonal antibiotics (per patient-day): post-intervention (0.2 (IQR 0-0.4)) *vs* pre-intervention (0.4 (IQR 0-0.7)) (p<0.0001) ***Mortality***: post-intervention (28/539) (5.2%) *vs* pre-intervention (36/512) (7.0%) (p=0.21) ***Median LOS (day)***: post-intervention (5.0 (IQR 4.0-7.0)) *vs* pre-intervention (5.0 (IQR 4.0-7.0)) (p=0.85) ***Microbial outcome***: -		***Mean DOT (day)***: post-intervention (2.3 ± 1.5) *vs* pre-intervention (2.8 ± 1.7) (p=0.003) ***Mortality***: - ***Mean LOS (day)***: post-intervention (4.5 ± 3.4) *vs* pre-intervention (5.4 ± 4.8) (p=0.023) ***Microbial outcome***: -
Note		Note	

Pham 2019		***Wang (H) 2019***	
Methods	***Study design****:* BA	Methods	***Study design****:* ITS
Participants	***Patients***: adult patients with pneumonia (all types of pneumonia) requiring empirical IV vancomycin or linezolid for MRSA coverage (72 post-intervention vs 138 pre-intervention) ***Intervention recipients***: all physicians in primary care teams ***Antimicrobial target for intervention***: definitive therapy ***Setting***: A community teaching hospital, USA	Participants	***Patients***: All patients with clinical problem ***Intervention recipients***: All ward physicians ***Antimicrobial target for intervention***: non-specified target ***Setting***: A tertiary care teaching hospital, China
Interventions	***Intervention component***: DM&EO (non-specified mode of communication) ***Intervention duration (month)***: 6 ***Intervention deliverer***: ID pharmacist (leader) and clinical pharmacists	Interventions	***Intervention component***: AF (feedback to all medical staff monthly in meetings), AD, & EO (verbal) ***Intervention duration (month)***: 25 ***Intervention deliverer***: ID pharmacists and clinical pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice***: - ***Mean DOT (day)***: IV vancomycin: post-intervention (1.4±1.2) *vs* pre-intervention (2.5±1.3) (p<0.001) ***Mortality***: post-intervention (5/72) (6.9%) *vs* pre-intervention (18/138) (13.0%) (p=0.179) ***Mean LOS (day)***: post-intervention (8.9±8.0) *vs* pre-intervention (8.9±5.8) (p=0.992) ***Microbial outcome***: -	Outcomes	***Compliance with target practice***: Trend change in compliance increased 1.2% per month during intervention (p<0.05) ***DOT (day)***: - ***Mortality***: - ***LOS (day)***: - ***Microbial outcome***: (1) Trend change of levofloxacin-resistant *E. coli* decreased 1.6% per year (p=0.0013) while imipenem-resistant *E. coli* increased 0.3% per year (p=0.0239) (2) Trend change of levofloxacin-resistant *K. pneumoniae* decreased 3.0% per year (p=0.0973) while imipenem-resistant *K. pneumoniae* increased 1.3% per year (p=0.049)
Note		Note	

Xin 2019		***Arensman 2020***	
Methods	***Study design****:* BA	Methods	***Study design****:* BA
Participants	***Patients***: patients with clinical problem requiring carbapenem (518 post-intervention vs 515 pre-intervention) ***Intervention recipients***: All attending physicians ***Antimicrobial target for intervention***: definitive therapy ***Setting***: A tertiary teaching hospital, China	Participants	***Patients****:* All adult patients with positive *Staphylococcus aureus* bacteraemia (121 post-intervention vs 87 pre-intervention) ***Intervention recipients****:* All primary treating physicians ***Antimicrobial target for intervention****:* definitive therapy ***Setting****:* seven tertiary care teaching hospitals (Advocate Aurora Health Hospitals), USA
Interventions	***Intervention component***: AD & EO (verbal: direct discussion) ***Intervention duration (month)***: 12 ***Intervention deliverer***: well-trained clinical pharmacists	Interventions	***Intervention component****:* EO (verbal) ***Intervention duration (month)****:* 8 ***Intervention deliverer****:* ID pharmacists
Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice***: post-intervention (307/518) (59.3%) *vs* pre-intervention (112/515) (21.7%) (p=0.022) ***Mean DOT (day)***: post-intervention (7.4±0.9) *vs* pre-intervention (13.3±1.8) (p=0.012) ***Mortality***: post-intervention (49/518) (9.5%) *vs* pre-intervention (92/515) (17.9%) (p=0.013) ***Mean LOS (day)***: post-intervention (9.3±1.5) *vs* pre-intervention (15.9±2.2) (p=0.014) ***Microbial outcome***: -	Outcomes	***Compliance with target practice****:* post-intervention (from period III) (92/121) (76.0%) *vs* pre-intervention (from period II) (47/87) (54.0%) (p=0.004) ***DOT (day)****:* - ***Mortality****:* post-intervention (6/121) (4.9%) *vs* pre-intervention (2/87) (2.3%) (p=0.6) ***Mean LOS (day)****:* post-intervention (12.0±10.7) *vs* pre-intervention (8.9±6.2) (p=0.01) ***Microbial outcome****:* -
Note		Note	

Bishop 2020		***Van Schooneveld 2020***	
Methods	***Study design****:* BA	Methods	***Study design****:* RCT
Participants	***Patients:*** adult patients with positive CDI (113 post-intervention vs 120 pre-intervention) ***Intervention recipients***: All primary physician teams ***Antimicrobial target for intervention***: definitive therapy ***Setting***: A tertiary care teaching hospital, USA	Participants	***Patients***: adult patients with clinical problem (135 intervention vs 156 control) ***Intervention recipients***: **s**ix medicine teams (5 internal medicine & 1 family medicine) divided for 3 teams in each arm ***Antimicrobial target for intervention***: IVOST ***Setting***: A teaching hospital, USA
Interventions	***Intervention component***: EO (in person or telephone with documenting in electronic heath record via pharmacy progress notes) ***Intervention duration (month)***: 17 ***Intervention deliverer***: clinical pharmacist	Interventions	***Intervention component***: EO (providing recommendations during the ward round) ***Intervention duration (month)***: 2 ***Intervention deliverer***: clinical pharmacists who were incorporated in each medical team and well-trained for several aspects IVOST

Comparator	Usual care	Comparator	Usual care
Outcomes	***Compliance with target practice***: post-intervention 65/113 (57.5%) *vs* pre-intervention 50/120 (41.7%) (p=0.02) ***DOT (day)***: - ***Mortality***: post-intervention (3/113) (2.7%) *vs* pre-intervention (10/120) (8.3%) (p=0.41) ***Median LOS (day)***: post-intervention (11.0) *vs* pre-intervention (12.0) (p=0.99) ***Microbial outcome***: -	Outcomes	***Compliance with target practice***: intervention as ATO-A (75/135) (55.6%) vs control as UC-A (70/156) (44.9%) (p=0.35) ***Median DOT (day)***: DOT per patient: intervention (7.0 (IQR 2.0-69.0)) vs control (7.0 (IQR 2.0-78.0)) (p=0.75) ***Mortality***: intervention (3/135) (2.2%) vs control (5/156) (3.2%) (p=0.50) ***LOS (day)***: - ***Microbial outcome***: CDI rate: intervention (4/135) (3.0%) vs control (2/156) (1.3%) (p=0.19)
Note	The authors described their intervention as "audit and feedback", but there is no feedback of data over time about progress to goal.	Note	UC-A (used as control) and ATO-A (used as intervention) were compared as it is the same intervention period and it allowed data to be compared by RCTs.

RISK OF BIAS ASSESSMENT

Table S4: Risk of bias assessment for RCTs (*n=6*) using Cochrane risk of bias tools

Study and year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Overall risk of bias
Bailey 1997	High risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	High risk of bias
Walker 1998	Low risk of bias	Unclear risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	High risk of bias
Dranitsaris 2001	Low risk of bias	Low risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Strom 2010	Low risk of bias	Low risk of bias	High risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Shen 2011	Low risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Van Schooneveld 2020	Low risk of bias	Unclear risk of bias	Unclear risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	High risk of bias

Table S5: Risk of bias assessment for non-randomized studies (*n=46*) using ROBINS-I risk of bias assessment tools

Study and year	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall risk of bias
Landgren 1988	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Pastel 1992	Low risk of bias	Low risk of bias	Serious risk of bias	Low risk of bias	Serious risk of bias	Medium risk of bias	Serious risk of bias	Serious risk of bias
Martínez 2000	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Ho 2005	Serious risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Serious risk of bias
McLaughlin 2005	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Dunn 2011	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
Grill 2011	Medium risk of bias	Serious risk of bias	Low risk of bias	Low risk of bias	Serious risk of bias	Low risk of bias	Low risk of bias	Serious risk of bias
Newland 2012	Serious risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Serious risk of bias
Yen 2012	Medium risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Cappelletty 2013	Medium risk of bias	Serious risk of bias	Serious risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Medium risk of bias	Serious risk of bias
Zhang 2014	Medium risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Apisarnthanarak 2015	Low risk of bias	Serious risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Serious risk of bias

Nguyen 2015	Serious risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Serious risk of bias
Phillips 2015	Medium risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Tavakoli-Ardakani 2015	Medium risk of bias	Medium risk of bias	Serious risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Serious risk of bias
Wang J 2015	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Zhou Y 2015	Low risk of bias	Serious risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Medium risk of bias	Serious risk of bias
Brumley 2016	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Ellis 2016	Medium risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Heyerly 2016	Serious risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Medium risk of bias	Serious risk of bias
Okada 2016	Low risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Shannon 2016	Serious risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Serious risk of bias
Yu 2016	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Zhou L 2016	Medium risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Beganovic 2017	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Brink 2017	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Campbell 2017	Serious risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Serious risk of bias
Li 2017	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
Nault 2017	Medium risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Shea 2017	Serious risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Serious risk of bias	Medium risk of bias	Low risk of bias	Serious risk of bias
Willis 2017	Medium risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Yang 2017	Medium risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Eljaaly 2018	Medium risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Fooland 2018	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Hwang 2018	Serious risk of bias	Medium risk of bias	Serious risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Serious risk of bias	Serious risk of bias
Ohashi 2018	Medium risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Sze 2018	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Abubakar 2019	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Bianchini 2019	Medium risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Box 2019	Medium risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias
Butt 2019	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias

Pham 2019	Serious risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Serious risk of bias
Wang H 2019	Medium risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Xin 2019	Medium risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Arensman 2020	Medium risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias
Bishop 2020	Medium risk of bias	Medium risk of bias	Medium risk of bias	Low risk of bias	Low risk of bias	Medium risk of bias	Low risk of bias	Medium risk of bias

INTERVENTION COMPONENTS AND MATERIALS

Table S6: Descriptions of intervention components and intervention materials used by pharmacist summarised from 52 studies

Intervention component	Definition (EPOC 2015)	Intervention materials used by pharmacist(s) to optimise antimicrobial use	Pharmacist activities to promote optimal antimicrobial use
"Educational outreach through review individual patients with provision of recommendation for change"	Personal visits by a trained person to healthcare workers in their own settings to communicate clinical data with the aim of stimulating action and changing practice	Pharmacist uses these intervention materials to help assess appropriateness of antimicrobial prescribing and then make pharmaceutical recommendation(s). These include (i) international or local antimicrobial guideline (most commonly used in this review e.g. pneumonia, bacteraemia, skin and soft tissue infection, surgical prophylaxis, *Clostridium difficile* infection), (ii) drug information reference, (iii) a comprehensive care bundle or a collaborative practice agreement established by interdisciplinary, or (iv) clinical decision support triggered by microbiology result (rapid diagnostic test, or culture and susceptibility) or therapeutic drug monitoring data	Pharmacist reviewed individual patients for necessary information including clinical data and patient status with then provided clinical recommendations or advice based on guideline, protocol, algorithm or clinical data triggered by decision support system to physicians through several mechanisms including verbal (face-to-face during ward round, telephone) and/or non-verbal (documentation in pharmacy notes in medical chart or in electronic medical record) for proper antimicrobial management (mainly for antimicrobial dosage regimen modification).
"Dissemination of educational materials with group meetings"	Distribution educational materials to individuals or groups of healthcare workers through meetings or workshops to support clinical care	Local antimicrobial guideline, new antimicrobial policy, intravenous to oral antimicrobial switch therapy protocol, or antimicrobial prescribing reports (e.g. prescribing performance data from pre-intervention phase)	Pharmacist initiated and organised the interdisciplinary antimicrobial guideline/policy development with then proposed to medical hierarchy such as ASP team, senior staff, or hospital administrator for approval. Pharmacist disseminated guideline/policy to physicians or prescriber groups by organising the meetings/workshops/conferences to provide information, discuss relevant issues, and set common goals for optimal antimicrobial use.
"Academic detailing"	Provision of information to healthcare workers with the aim of increasing knowledge and understanding of specific clinical circumstances	Main recommendations or key messages from international or local antimicrobial guidelines, scientific research evidence, principles of antimicrobial pharmacotherapy (antimicrobial spectrum, pharmacology, and pharmacokinetics/pharmacodynamics), hospital antibiogram (a periodic summary of antimicrobial susceptibilities of local bacterial isolates), or case discussion	Pharmacist provided face-to-face educational visits or trainings to physicians, prescriber groups, or ward staff by delivering lectures or presentations to update treatment recommendations or to emphasise key messages regarding optimal antimicrobial use from guidelines with then facilitated interactive discussion with physicians.
"Audit and Feedback"	Any summary of clinical performance of healthcare provided over a specified period of time. This summary may be given in a written, electronic or verbal format	Any summary of antimicrobial prescribing rate, antimicrobial prescribing performance, clinical or process outcome measures related with antimicrobial use over a specified period of time and feedback reports	Pharmacist monitored outcome measures related to antimicrobial use over a specified period of time with then summarised and prepared feedback data to provide to individual physicians, prescriber groups, or hospital administrators.

	and may include recommendations for clinical action.		
"Reminders"	Manual or computerised interventions that prompt health workers to perform an action during a consultation with a patient in the workplace environment	Pocket-size guideline, posters to emphasise key messages from guidelines, alert messages on computerised system (e.g. penicillin allergy alert message, drug interaction alert messages), sticker or message printed on medical chart (e.g. intravenous to oral antimicrobial switch therapy reminder)	Pharmacist developed and utilised several types of manual or computerised materials to help remind physicians in promoting optimal antimicrobial prescribing.
"Restriction" (pre-authorisation using expert approval OR formulary restriction)	Using rules to reduce the opportunity to engage in therapeutic behaviours	Compulsory physician order form (requiring physician to fill out necessary information before approval and dispense antimicrobial), automatic stop order (requiring physician to fill out information to continue antimicrobial), or antimicrobial formulary restriction (to determine antimicrobial classifications that need approval)	Pharmacist applied rules or set antimicrobial prescribing criteria agreed by interdisciplinary to help physicians prescribe properly. Pharmacist developed strategies requiring physicians to assess appropriateness of prescribed antimicrobial agent when necessary by discussion with infectious disease expert (microbiologist, infectious disease physician or pharmacist) for approval when starting or continuing antimicrobial agents.