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Strategies and outcomes of CDSS implementation for antimicrobial stewardship in hospital settings: a systematic review

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Abstract

Objectives Optimal implementation strategies and clinical outcomes of Clinical Decision Support Systems (CDSS) for antimicrobial prescribing in hospital settings have not been systemically evaluated. This review explores how CDSS for antimicrobial stewardship (AMS) have been implemented in secondary and tertiary care, focusing on strategies used, clinical and implementation outcomes.

Methods A systematic search was conducted including studies published up to December 2022. Primary studies describing CDSS implementation strategies in secondary and tertiary care were included. Strategies were analysed using the Expert Recommendations for Implementing Change (ERIC) framework. Implementation outcomes reported in the studies were extracted and categorized according to Proctor's framework. Quality assessment was performed using the Integrated quality Criteria for the Review Of Multiple Study designs (ICROMS).

Results Screening of 2,189 papers identified 12 studies meeting inclusion criteria, all focusing on antimicrobial prescribing in high-income countries. Most CDSS were expert systems ($n = 11$), primarily designed for infectious disease physicians ($n = 7$). Pre-implementation assessments, such as workflow analysis, user surveys and multidisciplinary meetings, were conducted in only five of the 12 studies. Studies used a median of 11 out of 73 ERIC implementation strategies. The most frequently reported strategies belonged to the following ERIC categories: developing stakeholder interrelationships ($n = 11$), training and educating users ($n = 11$), evaluative strategies ($n = 10$), provision of interactive assistance ($n = 5$), adaptation and tailoring to context ($n = 5$). In contrast, strategies aimed at supporting clinicians ($n = 3$) and changing infrastructure ($n = 2$) were less commonly used. No study reported strategies related to patient and service user engagement or financial strategies. Clinical outcomes were considered effective in two studies and partially effective in four, while the remaining studies did not evaluate them. A median of three implementation outcomes was reported per study, with appropriateness ($n = 10$), adoption ($n = 9$) and acceptability ($n = 9$) being the most examined. Overall, initial adoption was slow but improved over time, enhancing compliance with policy indicators.

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Conclusions The implementation strategies of CDSS for AMS in hospital settings are variably reported, with many studies providing limited detail on strategy selection, application, or outcomes, highlighting the need for more systematic and comprehensive evaluation in future research.

Keywords Clinical decision support systems, Antimicrobial stewardship, Implementation strategies, Implementation outcomes, Antimicrobial prescribing, Hospital setting

Background

The inappropriate prescription of antimicrobials, which is estimated to lie between 25 and 63% of antibiotic prescriptions, is considered to be among the top drivers of antimicrobial resistance (AMR) [1–3]. The overuse of antibiotics is a driving force for the development of antibiotic-resistant bacteria [4], which are already a challenge in many clinical instances. AMR leads to drastic increases in healthcare costs, resulting from increased and prolonged hospital stays, long term disability, an increase in socio-economic problems and an increase in mortality [5, 6]. Additionally, the inappropriate prescription of antimicrobials also leads to an increased risk of adverse drug reactions, as approximately 24% of all adverse drug reactions are related to antibiotic therapy [7].

AMR is a multisectoral problem that requires a multi-disciplinary national approach through the development of antimicrobial stewardship programmes (ASP) [8]. Antimicrobial stewardship (AMS) is currently defined as *'a coherent set of actions which promote using antibiotics in ways that ensure sustainable access to effective therapy for all who need them'* [9], aiming to tackle AMR by preserving the efficacy of current antibiotics for future generations and optimizing their use by limiting the spread of (multi)-drug-resistant infections [8]. As a result, the implementation of ASP is highly recommended for all healthcare settings with guidance provided by international organizations such as the World Health Organization [9, 10]. ASP includes a number of interventions including persuasive interventions, restrictive interventions and structural interventions [11].

Several studies have suggested that ASP could be promoted and enhanced with the implementation of Clinical Decision Support Systems (CDSS) [12, 13], software that support clinicians in making diagnostic and therapeutic decisions to improve patient care, treatment and outcomes [13, 14]. CDSS provide users with up-to-date medical knowledge, evidence-based guidance and support in reviewing patient data to select the most appropriate antimicrobial prescriptions and diagnostic tests, thereby enhancing antimicrobial stewardship [12, 15]. Most CDSS are expert systems, relying on predefined rules and clinical knowledge, whereas machine learning CDSS use algorithms to learn patterns from large datasets, enabling predictions and personalized recommendations for antimicrobial prescribing [16].

CDSS have so far been employed in several medical fields and studies evaluating their effectiveness have reported improvements in appropriateness of care, preventive services, clinical outcomes and healthcare costs [15, 17]. Nevertheless, the success of a CDSS is highly reliant on its appropriate integration within a complex organizational environment [18], and the suboptimal implementation of a CDSS within a workflow can lead to several drawbacks, significantly reducing the quality, efficacy and safety of the delivery of care. Moreover, inadequate user training can result in frustration and inappropriate display of information can trigger alert fatigue, which together may reduce clinician engagement and limit the successful adoption of CDSS within clinical workflows [14].

The primary challenges in assessing CDSS implementation stem from a lack of conceptual clarity and precise descriptions of the adopted strategies. This often results in the use of inconsistent terms and definitions, as well as vague or incomplete descriptions of implementation strategies. Moreover, the evaluation of the implementation context is frequently lacking, either not being conducted at all or inadequately detailed, further complicating the interpretation of the data. As a result, this has long hampered the efforts to identify, test and develop implementation strategies. Implementation outcomes aim to assess the effectiveness of implementation strategies and processes. Assessment of CDSS implementation strategies and outcomes could therefore optimize implementation of AMS thus contributing to a better transferability to diverse settings [19]. In an attempt to tackle this problem, Powell et al. aimed at gathering input from a multi-disciplinary range of stakeholders by developing a compilation of 73 implementation strategies definitions and terms, summarized in the Expert recommendations for Implementing Change (ERIC) study [20, 21].

The aim of this systematic review was to analyze how, and in which contexts, CDSS for antimicrobial prescribing have been implemented in hospital settings and to evaluate their effectiveness on both clinical and implementation outcomes.

Methods

Search strategy

This systematic review was performed following PRISMA guidelines [22]. This study has been recorded on the international database of prospectively registered

systematic reviews, PROSPERO (Registration number: 165636). The databases Pubmed/MEDLINE, EMBASE, Cochrane Database and Web of Science were searched for relevant articles published from 2001 until December 2022 by using the search criteria tailored for each database, described in the Supplementary material (Table S1). Search terms were tailored for each database, using MeSH terms where applicable. The specific search strategies were created with the assistance of a medical reference librarian with expertise in systematic review searching, and were then reviewed by the authors. We used a combination of CDSS keywords plus antimicrobial use keywords plus implementation keywords. The search criteria were broad and intended to capture all the currently published studies that have been performed within the field of CDSS implementation for AMS in both secondary and tertiary care.

Study selection

Prospective and retrospective studies, as well as randomized, observational, diagnostic, mixed-methods and qualitative studies were all included whenever they reported original research on the strategies adopted for the implementation of CDSS for AMS in both secondary and tertiary care settings. All types of CDSS were included, such as knowledge-based systems (expert systems), machine learning-based systems, hybrid systems, and alert/reminder systems designed to support antimicrobial prescribing decisions. Computerized physician order entry (CPOE) systems and order sets (checklists) were excluded unless they were described as distinct CDSS interventions with explicitly reported implementation strategies. Systematic reviews or any kind of study that did not report original data were excluded. Studies reporting original data on CDSS implementation in primary care settings were excluded because these systems are typically implemented within smaller, less complex organizational structures. As a result, the implementation strategies and contextual factors influencing CDSS adoption in primary care may not be directly transferable to secondary and tertiary care settings, which involve larger multidisciplinary teams, more complex workflows, and greater organizational and infrastructural requirements. Two authors (LG and NPS) independently screened the study titles and their respective abstracts against inclusion and exclusion criteria via the use of the Covidence platform and when necessary, disparities between authors opinions were discussed to reach consensus.

Data extraction and implementation strategies for CDSS

Included studies were independently reviewed and data extracted. The information recorded included general information about the study (location and duration of

the study), the study design(s) used for the evaluation of CDSS implementation, primary and secondary outcomes whenever described within the study and detailed information about the CDSS under analysis. CDSS data included: type of CDSS (solicited or unsolicited information; with solicited CDSS providing guidance or alerts in response to a clinician actively requesting support, and unsolicited CDSS proactively delivering recommendations or alerts based on patient data or prescribing behavior, without a direct request from the user); CDSS infrastructure (expert system or machine learning); CDSS delivery platform (integrated within the hospital electronic health record (EHR) or standalone software); CDSS developers and its users, the CDSS country of origin, the infections targeted by the CDSS and the outcomes of the CDSS in relation to ASP.

Clinical outcome results were extracted by evaluating each study independently, primarily focusing on key metrics such as reduction in antimicrobial use, lengths of stay, mortality, healthcare-associated infection rates and costs following CDSS implementation. When studies reported other relevant clinical outcomes, such as adherence to prescribing guidelines, improvements in medical knowledge, or patient–clinician interactions, these were also extracted and summarized to provide a more comprehensive overview of the impact of CDSS interventions.

The CDSS were also evaluated against the Expert Recommendations for Implementing Change (ERIC) list, a refined compilation of 73 implementation strategies terms and definitions, published by Powell et al. in 2015 together with the collaboration of a wide range of stakeholders with an expertise in clinical practice and implementation science [20, 21]. The ERIC checklist gathers 73 strategies grouped into 9 different categories: Use of evaluative and iterative strategies, provide interactive assistance, adapt and tailor to context, develop stakeholder interrelationship, train and educate stakeholders, support clinicians, engage with patients and with service users, utilize financial strategies and change infrastructure. For each included study, the individual strategies adopted and described within the methods, results and supplementary materials (when available) were mapped to ERIC strategies. Two authors independently performed the mapping of the implementation activities and discrepancies were resolved through discussion and consensus, with involvement of a third author if necessary. When a reported strategy corresponded to more than one ERIC definition, the strategy that best reflected its primary goal was selected. Each strategy was counted once per study, regardless of frequency or duration of use; and when studies provided insufficient details to allow for classification, that specific ERIC strategy was labelled as “not reported”.

Implementation outcomes were categorized using the using Proctor's list framework, which proposes eight conceptually distinct implementation outcomes that can be measured [23]. Outcomes were included when studies explicitly reported implementation-related measures or when such measures could be clearly inferred from the description. The domains of the framework used to evaluate the selected studies were: (a) acceptability, (b) adoption, (c) appropriateness, (d) feasibility, (e) fidelity, (f) implementation costs, (g) penetration and (h) sustainability. Adoption was defined as initial or sustained use of the CDSS by intended users and was assessed using indicators such as system downloads, frequency of use or compliance with CDSS recommendations. Appropriateness referred to the perceived fit or relevance of the CDSS for the clinical context and was identified through outcomes demonstrating alignment with clinical needs or improvements in antibiotic prescribing practices. Acceptability was assessed through user satisfaction surveys, interviews or qualitative feedback. Feasibility was identified through reported ease of use, workflow integration or technical performance, while fidelity was assessed based on adherence to CDSS recommendations. Penetration was defined as the reach or spread of the intervention within the target setting. Outcomes were not required to be explicitly labelled using Proctor's terminology by the original authors; however, they had to align conceptually with the framework definitions to be included. All the extracted data were checked by the authors and any disagreement was amended through discussion.

Quality assessment

Quality assessment was performed using the Integrated quality Criteria for the Review Of Multiple Study designs (ICROMS) [24] which supports and facilitates the review of multiple and heterogeneous studies by ensuring that only studies with a relevant and robust methodology meet the inclusion criteria of a study review. In this systematic review we only assessed the criteria falling within the "qualitative studies" category. Studies were given 2 points if a specific criterion was met, 1 point if this was not described in detail and was thus unclear, and 0 points if the criteria was not met or not described. The final score resulting from the sum of all criteria was then calculated to give a final quality score to each study. According to ICROMS, studies with a score lower than 60% of the total achievable score from that category should be labelled as poorly reliable and characterized by a high risk of bias. Studies scoring between 60% and 80% should instead be classified as medium reliability with a medium risk of bias; whereas studies with a score higher than 80% could be considered reliable and with a low risk of bias. Nevertheless, since the aim of this study was to evaluate and analyse the currently available relevant literature on CDSS implementation strategies adopted in secondary and tertiary care, studies scoring lower than 60% in this quality assessment were not excluded from analysis.

Results

Study selection and characteristics

The screening and eligibility processes are reported in Fig. 1. Although a large number of records were initially

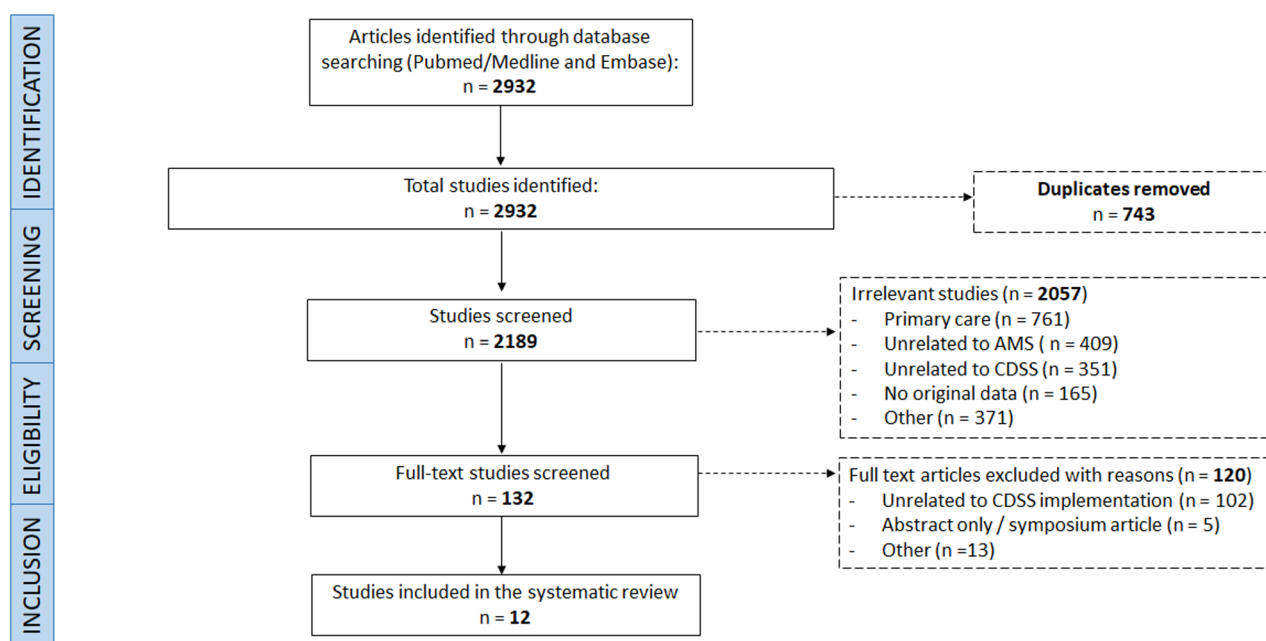


Fig. 1 PRISMA flow diagram: Schematic representation of the articles encountered in the literature, followed by the exclusion and inclusion numbers according to our chosen criteria

identified, only a small proportion met the inclusion criteria at full-text review. The initial search identified 2932 titles and abstracts, of which 743 (25%) duplicates were removed. The remaining 2189 were screened and 132 (6%) underwent full-text eligibility review. The most common reasons for exclusion were the absence of original data on implementation strategies, focus on CDSS effectiveness without describing implementation processes, inclusion of primary care settings or description of generic CPOE tools or order sets without clearly defined CDSS functionality, all reflecting a broader limitation in the literature, where CDSS for antimicrobial stewardship are widely used in practice but implementation strategies are infrequently and inconsistently reported. Ultimately, 12 (9%) were included, describing original research on CDSS implementation in secondary and tertiary care settings between 2013 and 2022. Additional information on the search strategy and included studies can be found in supplementary tables S1 and S2.

CDSS characteristics and study settings

Study setting

Among the 12 selected studies, two reported CDSS implementation for AMS in secondary care and seven were reported in tertiary care, while three spanned both secondary and tertiary care. Half were multi-center ($n=6$) involving three to five centers. All studies were conducted in high-income countries (HIC) (USA, $n=5$; UK, $n=2$; Australia, $n=1$; Singapore, $n=1$; Germany, $n=1$; Spain, $n=1$; and Portugal, $n=1$). Study duration ranged from six months to six years, with only two studies conducting pre- and post-implementation analyses. Most CDSS tools were developed and implemented locally at the hospital where they were designed, indicating site-specific approaches.

Characteristics of CDSS for AMS

The majority of CDSS offered “solicited information” ($n=9$) and were expert systems ($n=11$), developed with multidisciplinary input from infectious disease (ID) physicians, clinicians, microbiologists, pharmacists, nurses, information technology staff and programmers. Targeted users included ID physicians ($n=7$), surgeons ($n=1$), microbiologists ($n=2$), hospital pharmacists ($n=4$) and nurses ($n=1$). CDSS integration within the electronic health records (EHR) was reported in half of the studies ($n=6$). Three tools were developed as standalone software, while web-based platforms ($n=5$) were more frequently used than smartphone-based platforms ($n=3$). Half of the CDSS ($n=6$) were designed for a broad range of infections, whereas the other half targeted specific clinical syndromes, most commonly respiratory infections ($n=3$), sepsis ($n=2$) or urinary tract infections ($n=1$) (Table 1).

Strategies for CDSS implementation in secondary and tertiary care

Overall, 66% ($n=48/73$) of ERIC strategies were adopted in at least one study (Fig. 2). Conversely, 34% ($n=25/73$) of ERIC strategies were not adopted in any study. The most commonly used strategies belonged to the categories of “Develop stakeholder interrelationships” (with 92% of the studies adopting at least 1 strategy from this category); “Train and educate stakeholders” (92%); “Use evaluative and iterative strategies” (83%); “Provide interactive assistance” (42%); “Adapt and tailor to context” (42%); “Support clinicians” (25%) and “Change infrastructure” (17%). In contrast, the categories “Engage patients and service users” and “Utilize financial strategies” were fully neglected. The 10 most adopted strategies were: audit and provide feedback ($n=10$), Promote network weaving ($n=8$); identify early adopters ($n=7$); conduct educational meetings ($n=7$); create a learning collaborative ($n=6$); obtain and use consumers and family feedback ($n=6$); use advisory boards and workgroups ($n=5$); assess for readiness and identify barriers and facilitators ($n=5$); promote adaptability ($n=5$). Two studies adopted all the strategies described in two different categories: Nachtigall et al. adopted all four strategies described in the category “Provide interactive assistance”, whereas Simoes et al. adopted all four strategies described in “Adapt and tailor to context” as well as 80% of “Use of evaluative and iterative strategies”. The median number of strategies described per study was 11 (IQR=8), corresponding to 15% of the 73 ERIC strategies.

Pre-implementation assessments, such as workflow analysis, user surveys and multidisciplinary meetings, were conducted in only five of the 12 studies, indicating that most implementations lacked structured evaluation of context and needs before rollout. Bond et al. integrated education initiative guidelines development to align users with objectives. Charani et al. (2013, 2017) used surveys and focus groups to gather baseline information and assess smartphone usage to ensure that the application was designed to be both practical and effective. Hum et al. evaluated prescribing practices to design an effective tool, while Simoes et al. used multidisciplinary meetings to address prescription challenges.

Outcome of CDSS use in antimicrobial stewardship

Outcomes were broadly categorized into process outcomes, reflecting prescribing behavior or guideline adherence, and clinical outcomes, reflecting patient-level effects. Reported process outcomes included improvements in antimicrobial prescribing quality ($n=5$), adherence to guidelines and policies ($n=3$), and medical knowledge ($n=2$). Reported clinical outcomes included reductions in antimicrobial use, healthcare-associated infection rates, length of hospital stay, and mortality. For

Table 1 Summary of the included studies reporting study settings and CDSS characteristics

CDSS characteristics	N = 12 (%)
Location of the study	
Income country classification:	
High income country	12 (100%)
Low and middle income country	0
Number of countries involved:	
One country	12 (100%)
Multiple countries	0
System setting	
Care level:	
Tertiary care	7 (58%)
Secondary care	2 (17%)
Both	3 (25%)
Number of centers:	
Monocentric	6 (50%)
Multicentric	6 (50%)
Type of center:	
General hospital	6 (50%)
University hospital	6 (50%)
Other	0
Primary outcome	
Clear and explicit definition of the primary outcome:	
Yes	12 (100%)
No	0
Clinical decision support systems	
Type/s of CDSS:	
Solicited information	9 (75%)
Unsolicited information (alert / prompts)	3 (25%)
Dose optimisation	1 (8%)
De-escalation	1 (8%)
Surveillance	1 (8%)
Infrastructure providing CDSS:	
Expert system	11 (92%)
Machine learning	1 (8%)
Platforms for CDSS delivery	
Systems integrated in hospital electronic medical records:	
Yes	6 (50%)
No	2 (17%)
Not specified	4 (33%)
Stand-alone software:	
Yes	3 (25%)
Not specified	9 (75%)
Delivery platform	
Web based	5 (42%)
Smartphone	3 (25%)
Not specified	4 (33%)
Users of the CDSS*	
Infectious disease physicians	7 (58%)
Hospital pharmacists	4 (33%)
Microbiologists	2 (17%)
Surgeons	1 (8%)
Emergency medicine doctors	1 (8%)
Nurses	1 (8%)
Infections	

Table 1 (continued)

CDSS characteristics	N= 12 (%)
Infections targeted:	
Bacterial infections	12 (100%)#
Viral infections	1 (1%)#
Fungal infections	1 (1%)#
Parasitic infections	0
Type of infection/s:	
Respiratory tract	3 (25%)
Sepsis	2 (17%)
Urinary tract	1 (8%)
Multiple sites of infection	6 (50%)

*Each study could have multiple outcomes, users or diseases

#One study included antibiotics, antivirals and antifungals



Fig. 2 Mapping of ERIC implementation strategies used in studies assessing CDSS for AMS. 1–10 (light blue) “Use of evaluative and iterative strategies”; 11–14 (orange) “Provide iterative assistance”; 15–18 (green) “Adapt and tailor to context”; 19–35 (beige) “Develop stakeholders’ interrelationships”; 36–46 (purple) “Train and educate stakeholders”; (pink) 47–51 “Support clinicians”; 52–56 (yellow) “Engage patients and service users”; 57–65 (bright green) “Utilize financial strategies”; 66–73 (bright blue) “Change infrastructure”

example, Bond et al. reported decreased antimicrobial use and costs, reduced healthcare-associated infection rates, shorter hospital length of stay (LOS), and improved mortality. Keller et al. observed fewer urinalysis and urine culture orders, leading to reduced antibiotics use, whereas Nachtigall et al. reported both a reduction in antibiotic use and decreased mortality. Dean et al. reported decreased mortality among patients with community-acquired pneumonia. Other studies focused primarily on process outcomes, such as guideline adherence and improvements in prescriber knowledge (e.g., Charani et al., 2013, 2017; Simoes). Overall, two studies (Bond and Nachtigall) were deemed clinically effective, while three studies achieved partial effectiveness (improved guideline adherence or reduced antibiotic use) [25, 26],

and the remaining studies had limited or no observed clinical impact (Table 2) [27].

Table 2 provides a comprehensive summary of the study characteristics included in this review, along with the findings related to implementation outcomes, clinical effectiveness, and quality appraisal. Our analysis deemed four studies to have achieved an effective implementation of CDSS, two studies achieved partial effective implementation while the remaining six had an overall ineffective implementation. Clinical effectiveness was only achieved by two studies, partial effectiveness was reported in four studies and the remaining seven studies were clinically ineffective. The risk of bias was deemed low only in four studies, medium in two and high in four. Supplementary Table 3 presents the detailed clinical

Table 2 Summary of the study characteristics included in this review, along with the findings related to implementation outcomes, clinical effectiveness, and quality appraisal

Study characteristics				Intervention		Implementation		Clinical effectiveness		Quality appraisal
Reference	Country	Design	Setting	Description	ERIC domains of Implementation	Outcome categories	Effective	Outcomes	Effective	Risk of bias
Bond, 2017 [1]	Australia	Interrupted time series study	Secondary and tertiary care	To examine the outcomes of multisite ASP implementation supported by a centrally deployed CDSS.	- Use of evaluative and iterative strategies; - Provide iterative assistance; - Develop stakeholders' interrelationships; - Train and educate stakeholders	Adoption, Penetration	E	Adequacy to guidelines, Antimicrobial expenses	E	L
Charani, 2013 [2]	UK	Mixed methods in-depth case-study design	Secondary and tertiary care	To develop, adopt, and implement a CDSS across multiple hospitals, focussing on assessing its uptake and acceptability among clinicians and pharmacists; with the aim to explore how effectively it could serve for antimicrobial prescribing.	- Use of evaluative and iterative strategies; - Adapt and tailor to context - Develop stakeholders' interrelationships; - Train and educate stakeholders; - Support clinicians; - Change infrastructure	Acceptability, Adoption, Appropriateness, Feasibility, Implementation Costs, Penetration	E	Adequacy to guidelines	PE	L
Charani, 2017 [3]	UK	Quasi-experimental design and interrupted time series	Secondary care	To assess the impact of integrating a CDSS into an existing ASP on antibiotic prescribing practices, focusing on compliance with the prescribing policy	- Use of evaluative and iterative strategies; - Provide iterative assistance; - Develop stakeholders' interrelationships; - Train and educate stakeholders	Acceptability, Adoption, Appropriateness, Fidelity	E	Adequacy to guidelines	PE	M
Chow, 2016 [4]	Singapore	Quasi-experimental design	Tertiary care	To assess the implementation process and effectiveness of the ARUSC system in guiding antibiotic prescribing practices and controlling AMR by comparing launches initiated by auto-trigger versus the physicians themselves, and to evaluate user acceptance of the recommendations.	- Use of evaluative and iterative strategies; - Provide iterative assistance; - Adapt and tailor to context; - Develop stakeholders' interrelationships	Acceptability, Adoption, Appropriateness, Fidelity, Penetration, Sustainability	E	Adequacy to guidelines	I	M
Dean, 2020 [5]	USA	Quasi-experimental design	Tertiary care	To evaluate the implementation of the CDSS in ED settings to improve delivery of care and to understand how to increase CDSS adoption among clinicians by identifying factors that influence its successful implementation.	- Use of evaluative and iterative strategies; - Develop stakeholders' interrelationships; - Train and educate stakeholders; - Support clinicians	Acceptability, Adoption, Appropriateness, Fidelity	I	Improved quality of care	I	H
Hoff, 2018 [6]	USA	Descriptive implementation design	Tertiary care	To implement a mobile CDSS application to support AMS, with the goal to expand its influence through clinical diagnosis and treatment recommendations integrated into the mobile application.	- Use of evaluative and iterative strategies; - Adapt and tailor to context; - Develop stakeholders' interrelationships; - Train and educate stakeholders; - Change infrastructure	Acceptability, Adoption	I	Adequacy to guidelines, Decrease healthcare expenses	I	H
Hum, 2014 [7]	USA	Prospective observational design	Tertiary care	To develop and implement a CDSS tool designed to improve antibiotic prescribing practices and to evaluate user acceptance of the CDSS tool among healthcare providers	- Use of evaluative and iterative strategies; - Develop stakeholders' interrelationships; - Train and educate stakeholders	Acceptability, Adoption, Appropriateness, Penetration	PE	—	I	L
Jones, 2019 [8]	USA	Multicenter observational study	Secondary care	To examine physician interactions with a CDSS and to gain insights into how contextual factors and clinical reasoning impact the acceptance or rejection of CDSS recommendations in a real-world setting.	- Use of evaluative and iterative strategies; - Develop stakeholders' interrelationships; - Train and educate stakeholders	Acceptability, Adoption, Appropriateness, Feasibility	I	Improved quality of care	I	N/A
Keller, 2018 [9]	USA	Quasi-experimental study	Tertiary care	To design and evaluate an intervention to reduce unnecessary urinalysis tests by minimizing the overuse of urine testing and inappropriate antibiotic treatment	Train and educate stakeholders	Appropriateness	I	Decreased use of antibiotics	PE	N/A
Nachtigall, 2014 [10]	Germany	Prospective 'before/after' cohort study	Tertiary care	To evaluate the long-term effects of implementing a CDSS on the adherence to guidelines for antibiotic therapy	- Use of evaluative and iterative strategies; - Provide iterative assistance; - Adapt and tailor to context; - Develop stakeholders' interrelationships; - Train and educate stakeholders	Appropriateness	I	Adequacy to guidelines, Decreased duration of antibiotic therapy	E	L
Rodriguez-Maresca, 2014 [11]	Spain	Prospective quasi-experimental design	Tertiary care	To evaluate the effectiveness of GERB-based applications in improving the appropriateness of empiric antibiotic prescriptions	Train and educate stakeholders	—	I	Adequacy to guidelines	I	H
Simões, 2018 [12]	Portugal	Participatory design study	Secondary and tertiary care	To support ASPs through the co-design and implementation, in collaboration with healthcare workers, of a surveillance and clinical decision-support system to monitor antibiotic resistance and improve antibiotic prescription.	- Use of evaluative and iterative strategies; - Provide iterative assistance; - Adapt and tailor to context - Develop stakeholders' interrelationships; - Train and educate stakeholders; - Support clinicians	Acceptability, Adoption, Appropriateness	PE	Adequacy to guidelines	I	H

Table 2 (continued)

Effectiveness ratings: *E* Effective (green), *PE* Partially effective (orange), *NE* Not effective (red), *I* Inconclusive

Risk of bias ratings *H* High (red), *M* Moderate (orange), *L* Low (green)

Other abbreviations *ARUSC* Antibiotic Resistance Utilization and Surveillance-Control, *ASP* Antimicrobial stewardship programme, *AMR* Antimicrobial resistance, *CDSS* clinical decision support systems, *ED* Emergency department, *GERB* Guía Electrónica de Resistencias Bacterianas, *UTI* Urinary tract infection

Table 3 Implementation outcomes described in the studies according to the proctor framework

Proctor's implementation outcomes	Bond, 2017	Charani, 2013	Charani, 2017	Chow, 2016	Dean, 2020	Hoff, 2018	Hum, 2014	Jones, 2019	Keller, 2018	Nachtigall, 2014	Rodriguez-Maresca, 2014	Simoes, 2018
Acceptability		✓	✓	✓	✓	✓	✓	✓				✓
Adoption	✓	✓	✓	✓	✓	✓	✓	✓				✓
Appropriateness	✓	✓	✓	✓	✓		✓	✓	✓	✓		✓
Feasibility		✓						✓				
Fidelity			✓	✓	✓							
Implementation costs		✓										
Penetration	✓	✓		✓			✓					
Sustainability				✓								

Table 4 Criteria from integrated quality criteria for systematic review of multiple study designs used to assess quality of the studies included in the review

Quality criteria		Study design: QUAL											
Dimension	Specific criteria	Bond, 2017	Charani, 2013	Charani, 2017	Chow, 2016	Dean, 2020	Hoff, 2018	Hum, 2014	Jones, 2019	Keller, 2018	Nachtigall, 2014	Rodriguez-Maresca, 2014	Simoes, 2018
1. Clear aim and justification	A. Clear statement of the aim of the research?	2	2	2	2	2	1	2	N/A	N/A	2	2	2
	D. Appropriateness of qualitative methodology were data collected appropriately to address research aims?	2	2	2	1	1	0	2	N/A	N/A	2	1	1
2. Managing bias in sampling between groups	E. Appropriate study design	2	2	2	1	1	0	2	N/A	N/A	2	1	1
	F. Sampling and recruitment	2	2	1	2	1	0	2	N/A	N/A	2	1	2
3. Managing bias in outcome measurement and blinding	F. Reliable primary outcome measures	2	2	1	2	1	1	2	N/A	N/A	2	0	1
4. Managing bias in follow-up	C. Incomplete outcome data address	0	0	1	0	0	0	0	N/A	N/A	0	0	0
5. Managing bias in other study aspects	C. Data collection appropriate to address research aims	2	2	1	1	1	0	2	N/A	N/A	2	0	1
6. Analytical rigour	C. Analysis sufficiently rigorous/free from bias	2	2	1	1	0	1	2	N/A	N/A	1	0	0
7. Managing bias in reporting/ethical consideration	A. Free of selective outcome reporting	0	0	0	0	0	0	0	N/A	N/A	2	0	0
	B. Limitations addressed	2	1	1	2	0	0	2	N/A	N/A	2	2	2
	C. Conclusions clear and justified	2	2	2	2	1	0	2	N/A	N/A	2	1	1
	D. Free of other bias	0	0	0	0	0	0	0	N/A	N/A	2	0	0
	E. Ethics issues addressed	2	2	1	1	0	0	0	N/A	N/A	1	0	0
Final score		77%	73%	58%	58%	31%	12%	69%	N/A	N/A	85%	31%	42%

✓✓ 2 points (criteria was met); ✓ 1 point (criteria was not described in detail); 0: criteria was not met/described; *N/A: not applicable

outcomes of the CDSS use in antimicrobial stewardship in the 12 studies.

Proctor's implementation outcomes

Implementation outcomes reported in 11 studies were mapped to Proctor's framework, with a median of 3–4 outcomes per study (Table 3). The most commonly adopted outcome were “appropriateness” ($n=10$) and “adoption” ($n=9$), followed by “acceptability” ($n=8$). Metrics such as downloads, usage rates and compliance were used to measure adoption, while appropriateness was evaluated through outcomes confirming that the implementation improved antibiotic prescribing and aligned with clinical needs. Surveys and feedback measured acceptability while feasibility was evaluated through feedback and usage patterns. Fidelity was assessed via adherence to CDSS recommendations. Penetration was measured by assessing the reach and spread of the intervention within the setting. No study evaluated long-term sustainability.

Assessment of study methods

Quality assessment showed that six studies scored lower than 60%, highlighting a high risk of bias (Table 4). Four studies scored between 60 and 80%, suggesting moderate reliability, while only one exceeded 80%, indicating minimal bias.

Discussion

The currently available studies exclusively describe the strategies adopted for CDSS implementation in HICs, primarily within tertiary care ($n=7$, 58%). The small number of included studies should not be interpreted as limited use of CDSS in clinical practice, but rather as a consequence of the focused aims of this review. While many CDSS for antimicrobial prescribing are described in the literature, few studies report original data on implementation strategies using sufficient methodological detail to allow comparative analysis. Most CDSS were solicited information systems ($n=9$, 75%) and expert systems ($n=11$, 92%), often integrated within hospital

EHRs ($n=6$, 50%). Web-based platforms ($n=5$, 42%) were the preferred delivery methods over smartphones ($n=3$, 25%). CDSS were mainly developed for infectious disease physicians ($n=7$, 58%) and primarily targeted bacterial infections ($n=12$, 100%), with one study also including decision support for antiviral and antifungal therapies.

When comparing implementation strategies to the ERIC list, only 23 (31.5%) of the 73 strategies were used, with a median of 11 per study (IQR=8). The most commonly adopted strategies focused on “training and education of stakeholders”, with the organization of educational meetings ($n=7$) and creating learning collaboratives ($n=6$), developing ($n=5$) and distributing ($n=4$) educational material, as well as the provision of ongoing consultation ($n=5$). The development of stakeholders’ interrelations strategies was also widely used, with studies reporting strategies on the promotion of networking weaving ($n=8$), identification of the early adopters ($n=7$), the use of advisory boards and workgroups ($n=6$), training for leadership ($n=5$), organization of implementation team meetings ($n=4$) and conducting local consensus discussion ($n=3$).

The primary evaluated outcomes from CDSS implementation included improved adherence to guidelines, enhancing the quality of antibiotic prescription ($n=8$). Despite these improvements, risk of bias was a concern in 9 out of 12 studies. Implementation outcomes often neglected sustainability and implementation costs, followed by a relatively poor attention to feasibility, fidelity and penetration. Adoption, appropriateness and acceptability were the most commonly assessed. Adoption metrics such as downloads, compliance and usage tracking validated clinical outcomes, often reporting reduced antibiotic prescriptions and mortality. Initial acceptability and adoption rates were slow and influenced by subjective factors, including physician age and perceived usefulness, with junior physicians being more inclined to use CDSS than their senior counterparts. Guideline adherence varied: some CDSS achieved rapid adoption, while others experienced initial resistance followed by gradual acceptance. Overall adoption of CDSS tended to lead to significant improvements in compliance with policy indicators and increased prescribers’ awareness.

It is important to note that local hospital workflows, organizational culture, and existing clinical processes strongly influence implementation success, emphasizing the need for implementation strategies that are tailored to the specific institutional context rather than applied uniformly across settings. Misalignment between CDSS design and established workflows can lead to resistance, reduced usability, and limited adoption, even when the underlying technology is robust.

Comparison with prior works

Evaluative and iterative strategies were the most commonly reported and included audit, and feedback from users [28]. However, “support of clinicians” and “provision of interactive assistance” were generally neglected, despite being critical for effective adoption [29]. Studies found that lack of engagement and tool understanding, especially among experienced clinicians, often leads to resistance, negatively influencing younger clinicians and delaying adoption [29]. Strategies for “adaptation and tailoring to context” were fully adopted only by Simoes et al.; whereas Hoff et al. adopted five out of the eight strategies of “change infrastructure” aiming at ensuring readiness towards potential infrastructure adjustments. CDSS implementation is both a technical and organizational process, highlighting the crucial role of social context. Rejection often stems from unforeseen disruptions to clinical workflows, requiring implementation strategies to align with organizational structures and users’ roles [29, 30]. Our analysis also observed that “engagement with patients and service users” and “financial strategies” were not reported. Patient education and shared financial strategies are crucial for fostering adoption and guiding other settings towards implementation. Detailed implementation strategies are essential for identifying what drives successful adoption and to adapt them to new settings. Yusof et al. highlighted that CDSS implementation is challenging due to organizational and human factors interplay [31], with improvements in one area potentially causing unanticipated disruptions in others [29]. Utilizing a standardised framework like ERIC can facilitate comparisons across different settings and time periods, including during technological advancements or public health crises. Ensuring long-term sustainability is crucial for the enduring success of CDSS implementation.

Several studies highlighted how users age, clinical experience and digital health literacy influenced adoption. Understanding user preferences can reduce variability and foster broader acceptance [29]. CDSS can benefit healthcare long-term by reallocating resources to areas where human expertise is essential [32]. Implementation science plays a pivotal role and poor implementation can undermine even well-designed CDSS. Greater investment in implementation strategies is needed rather than developing new systems. Additionally, future research should explicitly address low- and middle-income countries, where evidence on CDSS implementation for antimicrobial stewardship remains scarce and where contextual, infrastructural, and resource-related constraints may substantially influence implementation strategies and outcomes.

Although most CDSS identified in this review were knowledge-based expert systems, also machine learning and artificial intelligence-enabled tools are increasingly

being developed for ASP. AI-driven CDSS have the potential to support more personalized and context-aware recommendations by integrating large datasets, including microbiological data, prescribing patterns and patient-level clinical variables, enhancing prediction of infection risk and optimizing antimicrobial selection [33]. However, the implementation of AI-enabled CDSS presents additional challenges compared with rule-based systems, including limited transparency and interpretability of model outputs, *difficulties in validating models across settings*, concerns about data quality, interoperability and algorithmic bias, which can all influence clinician trust and uptake [34]. From an implementation perspective, clinician trust, interpretability of recommendations and integration within existing workflows are critical determinants of adoption. Future research should therefore focus not only on the technical performance of AI-enabled CDSS, but also on rigorous evaluation of implementation strategies, usability, and long-term sustainability using standardized implementation science frameworks.

Strengths and limitations

This study potentially faced challenges in identifying CDSS implementation strategies due to search constraints as some studies may have been missed. Grey literature was not included, potentially omitting relevant implementation strategies studies. The use of ICROMS mitigated subjective biases during study analysis. Furthermore, the comparative analysis between studies was complicated by heterogeneity in objectives and methods. The use of ERIC and Proctor's frameworks might limit findings, as utilization of other frameworks could yield different outcomes. Interpretations of ERIC strategies were subjective, particularly where strategy definitions overlapped, nevertheless, we believe that our results would still be similar to those found using other analytical frameworks.

Although CDSS embedded within electronic medical records were included when clearly described, implementation strategies for embedded decision support were often insufficiently detailed and difficult to disentangle from broader electronic medical records or CPOE system implementation processes. As a result, some stewardship-related decision support functionalities may be underrepresented in this review. This limitation reflects reporting gaps in the literature rather than an intentional exclusion and may have influenced the range and frequency of implementation strategies identified. CDSS embedded within electronic medical records and CPOE systems represent a priority area for future research, as these platforms are increasingly used in routine care and may face distinct implementation challenges related to

workflow integration, alert fatigue and organizational readiness.

The quality of the studies included was moderate, indicating a moderate level of confidence in the findings, which were influenced by potential biases or methodological shortcomings within the studies themselves. Consequently, while the studies offer valuable insights and provide foundations for drawing conclusions, their findings should be interpreted with caution.

The classification of implementation and clinical effectiveness was based on reported outcomes and thus involved an element of subjectivity, particularly given the heterogeneity in CDSS designs, outcome measures and study methodologies. As most included studies were of moderate to high risk of bias, the findings should be interpreted as indicative rather than definitive. Finally, study inclusion was restricted to publications up to December 2022; therefore, more recent eligible studies may not have been captured.

Conclusions

The implementation strategies of CDSS for AMS in secondary and tertiary care remain inconsistently reported in the literature, are predominantly described in high-income countries and largely rely on stakeholder education. Future efforts could prioritise context-sensitive, multi-component implementation strategies approaches, informed by systematic pre-implementation assessments and supported by established implementation science frameworks. Adaptation of existing frameworks to the specific requirements of CDSS in antimicrobial stewardship, alongside improved reporting standards and long-term evaluation of sustainability and costs, may facilitate more reliable, transferable, and effective implementation. These conclusions are based on a limited and heterogeneous body of evidence and should therefore be interpreted with caution.

Abbreviations

ASP	Antibiotic stewardship programmes
AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
CDSS	Clinical decision support systems
EHR	Electronic health record
ERIC	Expert recommendations for implementing change
HIC	High-income countries
ICROMS	Integrated quality criteria for the review of multiple study designs
ID	Infectious disease
LOS	Length of stay

Supplementary Information

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Supplementary Material 1.

Author contributions

LG: Conception and design, acquisition and analysis of the data, Interpretation of data, drafting of the manuscript, and approval of final version to be published. CD: Conception and design, approval of final version to be published. RA: Conception and design, approval of final version to be published. LC: Conception and design, approval of final version to be published. MT: Conception and design, approval of final version to be published. YK: Conception and design, approval of final version to be published. FXL: Conception and design, critical revision of manuscript and approval of final version to be published. MH: Conception and design, approval of final version to be published. GB: Conception and design, critical revision of manuscript and approval of final version to be published. NPS: Conception and design, analysis of the data, revision of the manuscript, critical revision of manuscript and approval of final version to be published.

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Data availability

All data generated or analysed during this study are included in this published article (and in its supplementary information).

Declarations

Competing interests

The authors declare no competing interests.

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