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Review Article

Electronic clinical decision support tools in antibiotic prescribing: A systematic review

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Abstract

The inappropriate use of antibiotics has led to an increase in bacterial resistance and a rise in adverse reactions, putting patients' lives at risk and generating high costs for the healthcare system. The objective of this systematic review is to evaluate electronic decision support tools in antibiotic management. A search for related articles was conducted in the PubMed, Scopus, and DOAJ databases, following the PRISMA methodology, and studies written in English were selected. Five observational studies and four implementation studies were evaluated using the ROBINS-I tool to determine the risk of bias. Out of a total of 143 identified publications, 15 met the inclusion criteria. The selected studies showed significant improvements in the appropriateness of antibiotic prescriptions after implementing CDSS tools. These 15 tools proved effective in reducing prescription errors, improving adherence to clinical guidelines, and decreasing medication-related adverse events. However, their effectiveness critically depends on proper implementation, ongoing training, and adaptation to specific clinical contexts. Future studies should address current barriers and explore the long-term sustainability of CDSS, in addition to conducting detailed economic analyses to justify investment in these technologies.

INTRODUCTION

Antibiotics have played a fundamental role in human history, saving millions of lives and facilitating the execution of complex surgical procedures since their discovery in the 1930s[1,2]. Unfortunately, the inappropriate use of these drugs in humans and animals triggered an alarming global problem: the development of resistant[3,4] and multi-resistant bacteria, which worsen the course of infections, prolong hospital stays, and increase healthcare costs[5,6]. In addition, more resistant bacteria have emerged in recent decades than new antibacterial molecules, worsening the situation in critical environments such as hospitals. Some alternatives that have emerged as part of therapy to combat them include pathogen-focused treatments, the use of phages, modulation of gut microbiota, repurposing existing drugs using predictive mathematical models to optimize their selection and efficacy[7,9].

Although the use of technology in healthcare is not new, its application is hopeful, especially highlighting the role of artificial intelligence in proposing new antibiotic molecules from natural products, combining existing drugs, and even predicting resistance to different antibiotics based on genetic content and genome composition. However, machine learning is limited when new variants or genetic mutations appear[10,11], revealing that improvements are still needed. Technological programs are designed to improve treatments with high-risk or essential drugs, aiming to monitor and control their use. Some of these focused on antibiotic therapy can even generate antibiograms to optimize professionals' time, improve diagnosis, and medical care[12]. These programs or systems are known as Clinical Decision Support Systems (CDSS), which provide physicians with patient-related information and intelligently filter relevant data, presenting it at the required time to optimize treatment quality[13].

The tools can be classified based on their characteristics, as detailed below: a) by system function, b) the approach to providing advice, c) communication style, d) human-computer interaction, and e) the decision-making process[14]. In the first case, they try to answer what is true and what to do, thus managing available information for use in differential diagnosis, such as WebMD® or Diagnosaurus®[15,16]; others can suggest which test to order for a differential diagnosis or which drug to prescribe for the patient's current condition, like ClinicalKey® or UpToDate®[17,18], Currently, several programs address both questions sequentially. In the second case, depending on the approach to providing advice, they required prior action by the user, such as clicking a button or opening a tab to issue medical information, being one of the least effective tools. However, it highlighted the challenge of avoiding excessive alert generation[19,20].

Thirdly, the models are classified according to communication style, which can be consultative or critical. In the case of consultative systems, the system acts as an advisor, posing questions and suggesting actions; for example, when a prescription is entered, the system asks for the diagnosis and advises on dosage or an alternative treatment. In contrast, the critical system allows the user to decide on the dosage

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and, if necessary, alerts if the dose is too low to achieve the therapeutic effect (21). Fourthly, there are systems based on human-computer interaction, where this interaction has become extremely fast, user-friendly, and easily accessible. At this point, integrating electronic health records is essential to subsequently provide advice via pop-up windows, sound alarms, or chatbots, practices implemented during the SARS-CoV2 pandemic due to the hospital crisis and shortage of healthcare personnel for in-person care[22,23].

However, most attention in recent decades has focused on tools that provide recommendations for specific decision-making using decision trees, Bayesian models[24,25], neural networks[26], support vector machines[27] and artificial intelligence[28], improving outcome prediction and prioritizing treatments, among others.

The application of these tools in healthcare has proven helpful, particularly in processes such as checking drug-disease interactions, individualized dosing in patients with renal or hepatic insufficiency, providing recommendations on laboratory tests during drug use, the duration of antibiotic therapy, and suggestions for switching pharmaceutical forms, among others. As a result, there has been a significant reduction in prescription and administration errors, particularly with antibiotics[29,30].

Despite various studies indicating the importance of implementing these systems to reduce prescription errors and optimize economic resources, it has been observed that they have only been developed in high-income countries[31], posing the challenge of developing programs tailored to the population characteristics of less advantaged countries.

For this reason, a literature review focused on electronic tools for antibiotic prescribing support is proposed.

METHODOLOGY

Search Strategy

The systematic search was conducted in PubMed, Scopus, and DOAJ using the PRISMA methodology. The search syntax was defined after a pilot review of the literature ("Clinical Decision Support System" AND "Antibiotic Stewardship" AND "implementation", "Antibiotic Stewardship Program" AND "CDSS" AND "hospital", "Clinical Decision Support" AND "Implementation" AND "Hospital Setting"), with the incorporation of Boolean operators to make the search more efficient. Articles discussing software that supports antibiotic prescription and written in English were included.

Selection of Articles for Review

The titles and abstracts of the identified articles were independently analyzed, excluding duplicate studies and those that met the inclusion criteria (software contributing to the prescription of an antibiotic treatment). Studies that did not mention software for antibiotic prescription in the title or abstract were excluded, as well as systematic reviews and meta-analyses, which were not included in this work.

Quality Assessment of the Included Studies

As a result of the search, five observational studies and four implementation studies were found, and the decision was made to use the ROBINS-I tool (Risk of Bias in Non-randomized Studies of Interventions) (32) to assess the risk of bias in the articles.

Data Extraction

Data extraction was performed using an Excel spreadsheet, selecting characteristics such as the database, authors, year, type of study, study objective, software name, main feature, input parameters, output parameters, and validation methodology.

RESULTS

Search Results

The search for scientific articles was conducted through PubMed (n=342), DOAJ (n=13), and Scopus (n=88) during April 2024. As a result, 143 publications were found. Ten duplicate references were excluded. The titles and abstracts of 133 publications were reviewed, and those that did not meet the inclusion criteria were excluded (n=108). Finally, 25 full articles were read, of which 15 were selected to be included in this review (Figure 1).

Quality Assessment of the Included Studies

According to the ROBINS-I tool (Risk Of Bias In Non-randomized Studies of Interventions), one article was found to have a low risk of bias[33] , seven showed a moderate risk of bias[34,35,36,37,38,39,40,41,42,43,44,45] and one study was identified as high risk[46,47] (Table 1).

Study Characteristics

The studies collected for this systematic review encompass various approaches to the implementation and validation of clinical decision support tools. Most focus on improving antibiotic prescribing in diverse healthcare settings, particularly in primary care and hospital environments.

Each study provides a detailed analysis of how these tools were integrated into daily clinical practice, their recommendation mechanisms based on patient data, and their interaction with healthcare professionals. Both prospective and retrospective studies are included, allowing for a comprehensive evaluation of the impact and utility of these tools. The studies assess parameters such as adherence to clinical guidelines, accuracy of recommendations, and physician acceptance.

The validation of the tools was conducted by comparing the recommendations generated by the software with actual prescription decisions, demonstrating their potential to optimize antibiotic use and improve clinical outcomes. Overall, the studies highlight a multidisciplinary and collaborative approach, reflecting the need to combine technology with clinical expertise to achieve more rational and effective prescribing. All studies are detailed in Table 2.

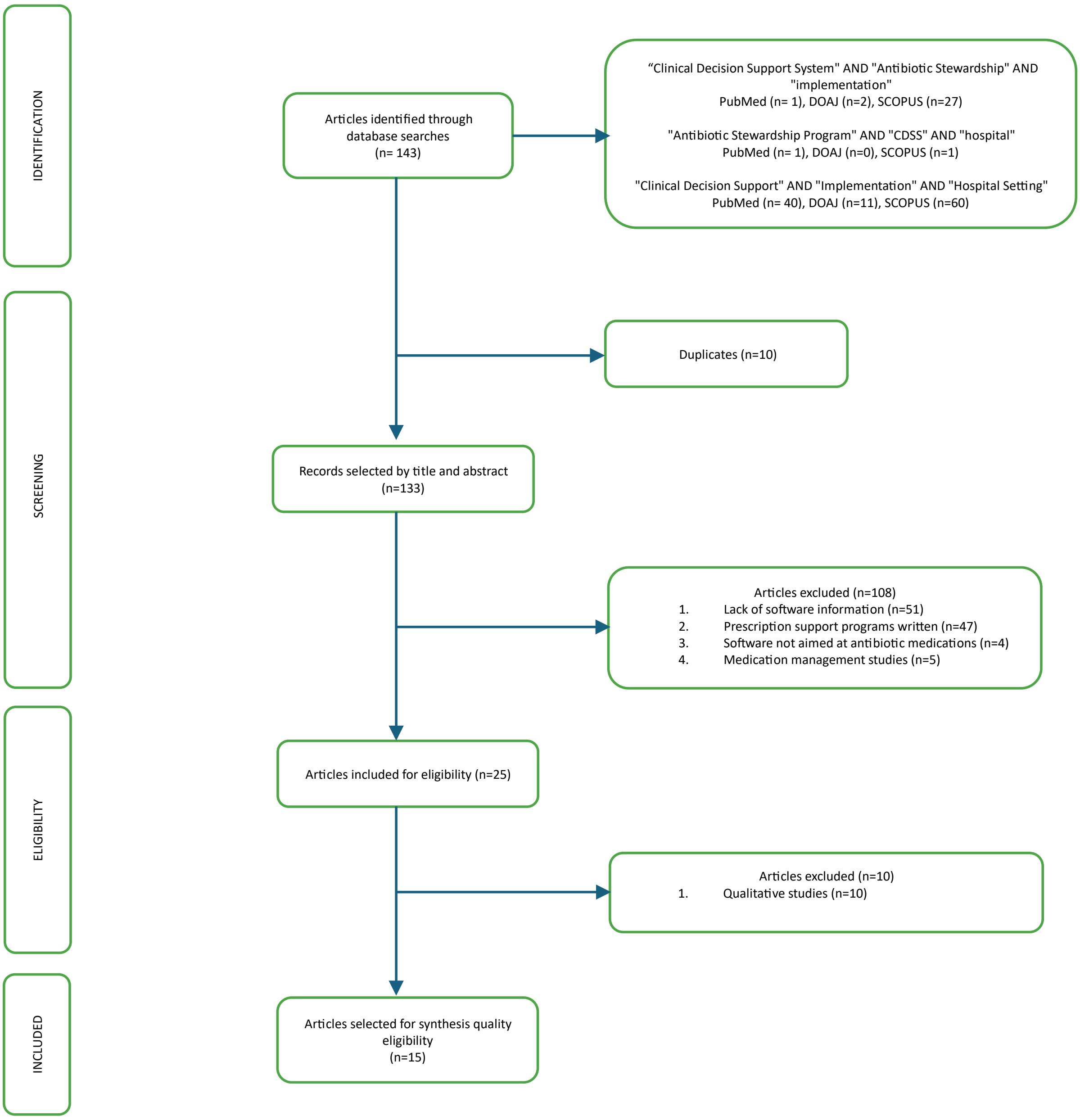

Figure 1. PRISMA Flow Diagram

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Table 1: Bias Evaluation Parameters

AUTHOR	EVALUATION PARAMETERS							TOTAL	RISK OF BIAS
	Bias due to confounding	Bias in participant selection	Bias in intervention classification	Bias due to deviations from intended intervention	Bias due to missing data	Bias in outcome measurement	Bias in selection of reported outcomes		
Simões et al., 2018	1	0	0	1	1	0	1	4	Moderate
Nadeau et al., 2021	1	0	0	0	1	0	1	3	Low
Calvo et al., 2022	1	1	0	0	1	0	1	4	Moderate
Akhloufi et al., 2022	1	1	0	0	1	0	1	4	Moderate
Marulanda et al., 2021	1	1	0	0	1	0	1	4	Moderate
Dutta et al., 2022	2	1	0	1	2	0	1	7	High
Wang et al., 2021	1	1	0	0	2	0	1	5	Moderate
Calloway et al., 2013	1	1	0	0	2	0	1	5	Moderate
May et al., 2021	1	1	0	0	2	0	1	5	Moderate
Müller et al., 2021	1	1	1	0	1	1	0	5	Moderate
Manski et al., 2020	1	1	1	0	0	1	0	4	Moderate
Hum et al., 2014	1	1	1	2	1	1	0	7	High
Eudaley et al., 2019	1	1	1	1	1	1	0	6	Moderate
Mann et al., 2020	1	1	1	1	1	1	0	6	Moderate
Delory et al., 2020	1	1	1	1	1	1	0	6	Moderate

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Table 2. Study Characteristics

COUNTRY	AUTHOR	SOFTWARE NAME	FUNCTION	INPUT PARAMETERS	OUTPUT PARAMETERS	VALIDATION			LIMITATION
						Implementation	Evaluation	Outcome	
Portugal	Simões et al., 2018 (48)	HAITooL	Supports antibiotic stewardship programs (ASP) by integrating real-time surveillance systems and clinical decision support systems	Patient data, microbiology results, pharmacy information, vital signs, and data from the hospital information system	Real-time visualizations, alerts and recommendations, reports and analysis, and aggregated and filtered data for clinical decision-making	Hospital-level	User surveys based on Österle principles were applied	HAITool was evaluated as a highly useful and time-saving tool by healthcare workers	No statistically significant reduction in antibiotic consumption and resistance rates has been demonstrated yet.
Canadá	Nadeau et al., 2021 (49)	Antimicrobial Prescription Surveillance System (APSS)	Assists in identifying and reporting potentially inappropriate antimicrobial prescriptions	Demographic data, admission data, vital signs, lab and microbiology results, and pharmacy data	Clinical alerts and recommendations, surveillance reports, antimicrobial treatment duration, and status of recommendations	Hospital-level	Clinical characteristics and mortality risk were compared between patients whose recommendations were accepted and those whose recommendations were rejected	Acceptance of APSS recommendations significantly reduced antimicrobial treatment duration	Lack of data on disease severity and infection type.
España	Calvo et al., 2022 (50)	OntoPharma	Clinical decision support system (CDSS) based on ontologies to reduce prescription errors	Patient demographic data, prescription information, lab results, allergy history, and hospital information system data	Maximum dosage alerts, drug interactions, renal failure adjustments, allergy alerts, and prescription adequacy reports	Hospital-level	The acceptance rate of alerts generated which were evaluated by clinicians	Around 50% of alerts were accepted by clinicians, validating the tool's effectiveness in reducing over-prescription and improving patient safety	Variability in dosages, need to keep the knowledge base up to date, and a 49% alert acceptance rate indicates a need for improved precision and relevance.
Países Lows	Akhloufi et al., 2022 (51)	AB-Assistant	Supports clinical decision-making to improve antimicrobial prescribing	Patient demographic and clinical data, including diagnosis, culture history, renal function, allergies, and antimicrobial drug data	Antibiotic recommendations, including selection, dosage, administration route, allergy alerts, and reports	Hospital-level	Each recommendation generated by the system was reviewed by a specialist in infection diasses	67.4% of the recommendations were fully or partially accepted	Areas were identified to improve precision and ensure proper use of the system by doctors.
USA	Marulanda et al., 2021 (52)	Soporte de decisión clínica (CDS)	Improves antibiotic management in pediatric appendicitis cases	Patient data (age, diagnosis, allergies) and clinical data (medical history, lab and imaging results), along with treatment information and clinical guidelines protocols	Specific antibiotic recommendations, alerts and reminders, data on preferred vs. non-preferred antibiotic usage, and clinical outcomes related to treatment effectiveness	Hospital-level	Usage rates of preferred vs. non-preferred antibiotics were compared with and without the tool	Although tool usage was low (31%), an improvement in the use of preferred antibiotics was observed when it was used	Lack of data on reasons for low tool usage. Quality of life was not assessed. Further validation is needed in other health units and with different healthcare professionals.

https://doi.org/10.18549/PharmPract.2025.2.3182

USA	Dutta et al., 2022 (53)	Soporte de decisión clínica (CDS)	Recommend collecting blood cultures before administering antibiotics	IV antibiotic order and verification of the recent history of blood cultures, patient status (excluding cardiac arrest), and specific antibiotic indication	CDS alert suggesting blood culture collection before antibiotic administration, data on timely collection, positivity rates, and blood culture contamination rates	Hospital-level	Proportions of blood cultures collected before IV antibiotic administration were compared pre- and post-intervention	Results showed that CDS implementation significantly improved blood culture collection practice before IV antibiotic administration	Limitations include the lack of a randomized control group and reliance on electronic health record data, which can introduce errors and limit generalizability. Additionally, the clinical appropriateness of all blood culture collections was not evaluated.
USA	Wang et al., 2021 (54)	Soporte de decisión clínica (CDS)	Improves antibiotic selection for pneumonia treatment	Patient data (age, ICD10 code for pneumonia, risk factors), and antibiotic prescription orders for ED sepsis	CDS alerts and recommendations for appropriate antibiotics and clinical outcomes such as the proportion of patients with appropriate antibiotic therapy and health outcomes data	Hospital-level	Rates of appropriate antibiotic selection, therapy changes, or escalations, therapy duration	The proportion of patients receiving appropriate antibiotics significantly increased from 32.3% to 66.4%	Potential lack of consideration of clinical judgment in antibiotic selection; also, the CDS used was primarily text-based and may
USA	Calloway et al., 2013 (55)	TheraDoc	Provides automated real-time alerts and recommendations, improving clinical interventions by pharmacists and optimizing medication management and costs.	Patient data from various sources (medication, lab, microbiology), specific parameters for alerts and dosage adjustments (IV to oral conversion, vancomycin dosing levels).	Automated real-time alerts and recommendations for pharmacists, including intervention types, time impact, and associated cost savings.	Hospital-level	The average number of clinical interventions and their impact on cost savings were compared before and after the tool's implementation.	The number of interventions increased by 1,986 to 4,056, representing an increase of 104%. Annual savings increased by 96%.	Lack of calculation of all total costs associated with system implementation and initial usage challenges for pharmacists affected the increase in clinical interventions.
USA	May et al., 2021 (56)	Soporte de decisión clínica (CDS)	Provides real-time alerts and recommendations for azithromycin prescription appropriateness, reducing inappropriate prescriptions and promoting appropriate antibiotic use in primary care clinics.	Azithromycin prescriptions registered in the EMR, along with clinical indication, dose, and treatment duration.	Real-time alerts and recommendations on azithromycin prescription appropriateness, alternative suggestions, and inappropriate prescriptions before and after the intervention.	Primary care clinic	Inappropriate prescriptions, including unnecessary prescriptions, duration, and inappropriate doses, were compared before and after the intervention.	Inappropriate azithromycin prescriptions decreased by 12.6%. There was a reduction in inappropriate clinical indications (69.7% vs. 61.2%) and unnecessary prescriptions (67.8% vs. 55.9%).	Study limitations include the possibility of introducing biases from missing documentation and data quality from the health information system, which could limit the generalizability of results.

https://doi.org/10.18549/PharmPract.2025.2.3182

USA	Müller et al., 2021 (57)	iBiogram	Reduces the risk of ineffective antibiotic prescriptions and optimizes antibiotic selection, improving clinical outcomes for severe infections.	Specific patient data such as age, sex, comorbidities, antibiotic history, clinical syndromes, hospitalization data, and susceptibility test results.	Includes personalized recommendations for empiric antibiotics, based on the patient's antimicrobial resistance risk. The system also predicts the failure risk of empiric therapy, providing antimicrobial coverage probabilities and local resistance patterns. It suggests antibiotic combinations that optimize coverage against the most likely pathogens.	Hospital-level	Six months of previous data were used to assess the software's performance against real treatments.	The software showed that for high-risk diseases, such as UTIs, the software's performance was like real treatments. No patient conditions were missed in high-risk cases like sepsis. iBiogram recommended the most appropriate antibiotic coverage based on patient risk factors and local resistance patterns.	The study was retrospective, and the data quality of the electronic health record could affect results.
Australia	Manski et al., 2020 (58)	Herramienta de apoyo a la toma de decisiones clínicas (CDS)	Helps physicians make informed decisions on empiric therapy for infections associated with neonatal healthcare, considering both antibiotic therapy and directed therapy	Patient demographic data, lab results including cultures and medication levels, clinical scenarios like sepsis and renal insufficiency, and current antibiotic treatment	Recommendations for empiric and directed antibiotics, treatment adjustments, susceptibility data, and patient renal function alerts	Hospital-level	The tool was used by healthcare professionals, who considered it useful. Data on patient outcomes, antibiotic use, and susceptibility results were collected, as well as recommendations for treatment continuation or change. Acceptability rates were tracked.	The system improved acceptance rates for specific antibiotic recommendations and changes in therapy, particularly in cases of neonatal sepsis. These changes improved patient outcomes.	Loss of functionality due to the system not integrating well with existing health information systems. Limited data on how the tool affected long-term clinical outcomes in other healthcare settings.

https://doi.org/10.18549/PharmPract.2025.2.3182

USA	Hum et al., 2014 (59)	Herramienta de apoyo a la toma de decisiones clínicas (CDS)	Optimizes antibiotic prescriptions for urinary tract infections (UTIs) in family medicine clinics. The tool provides diagnostic guidelines, documentation, and antibiotic recommendations based on clinical evidence to help physicians select the most appropriate treatment.	Patient information, such as age and symptoms, lab results, UTI clinical diagnosis, patient medication history, including allergies.	Antibiotic recommendations, diagnostic guidelines, precise ICD-10 code selections for documentation, alerts about additional tests, or treatment adjustments based on patient data.	Hospital-level	Prescription adherence to antibiotics before and after the tool's implementation was evaluated. Data was collected over six months, and UTI cases were analyzed to track usage rates.	After tool implementation, uncomplicated UTI prescriptions decreased by 42%, and complicated UTI treatment improved by 31%. Fluoroquinolones were no longer prescribed, and nitrofurantoin usage increased by 32%, improving adherence to clinical guidelines.	The tool was used voluntarily, and it was not automatically integrated into the clinic's workflow, resulting in a lower adoption rate of 29%. This limited the tool's overall impact evaluation.
USA	Eudaley et al., 2019 (60)	Herramienta de apoyo a la toma de decisiones clínicas (CDS)	Supports clinical decision-making for the treatment of acute respiratory infections.	Patient symptoms, such as sore throat or cough, clinical signs like fever and cervical tenderness, the patient's medical history, and physical exam findings, like auscultation results.	Bacterial infection risk score, recommendations on the need for additional tests, antibiotic use suggestions, and advice on follow-up and symptom relief measures.	Primary care networks	Intervention group physicians had access to the software during consultations, while control group physicians did not. The effectiveness of the software was evaluated by comparing antibiotic prescription rates, diagnostic test frequency (e.g., rapid strep test, chest X-rays), and adherence to clinical guidelines between the two groups during the study period.	The use of the tool did not significantly reduce antibiotic prescription rates for acute respiratory infections.	Low usage rate of iCPR software among physicians in the intervention group.

https://doi.org/10.18549/PharmPract.2025.2.3182

USA	Mann et al., 2020 (61)	Regla de Predicción Clínica Integrada (iCPR)	Provides clinical decision support for the appropriate prescription of antibiotics in primary care. The software offers recommendations based on clinical guidelines for treating 37 infectious diseases, helping physicians select the most appropriate antibiotic and reduce unnecessary use, thus contributing to combating antimicrobial resistance.	Patient information, such as age and special conditions (e.g., pregnancy, renal insufficiency), the type of infection being treated, and clinical test results, such as the strep test.	Antibiotic prescription recommendations, guideline-based indications on whether the prescription is necessary, and alerts on possible interactions or conditions that could affect treatment choice.	Primary care	Validation was carried out through analysis of general practitioners' use of the software in France over six years, collecting data on usage frequency and its influence on antibiotic prescribing. Additionally, surveys were conducted in 2018 and 2019 to assess satisfaction and the tool's impact on clinical practice.	Antibioclic was widely used, with more than 11,000 daily consultations in 2018. 93% of physicians followed the tool's recommendations for the last prescription, and most reported that the software was helpful and improved their knowledge of antibiotics without prolonging consultations.	The tool was not integrated into electronic health record systems, which may have limited its use and adoption in daily practice. Additionally, the study was based on voluntary use of the software, introducing potential selection bias.
Francia	Delory et al., 2020 (62)	Antibioclic	Supports antibiotic stewardship programs (ASP) by integrating real-time surveillance systems and clinical decision support systems	Patient data, microbiology results, pharmacy information, vital signs, and data from the hospital information system	Real-time visualizations, alerts and recommendations, reports and analysis, and aggregated and filtered data for clinical decision-making	Hospital-level	User surveys based on Österle principles were applied	HAITool was evaluated as a highly useful and time-saving tool by healthcare workers	No statistically significant reduction in antibiotic consumption and resistance rates has been demonstrated yet.

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DISCUSSION

The incorrect prescription of antibiotics is considered the main factor contributing to the global rise of antibacterial resistance. To address this issue, electronic clinical decision support systems (CDSS) have been developed specifically for this group of medications[63,64]. These systems gather patient-specific data along with a clinical knowledge base to establish an accurate clinical judgment in each case[65-69].

A recent study highlighted the limited effectiveness of some CDSS in reducing antibiotic prescriptions for acute respiratory infections, due to low adoption by physicians, underscoring the importance of proper integration into clinical workflows to achieve a significant impact.

The objective of this systematic review was to identify CDSS used in the management of antibiotics and analyze their functionality. For this reason, previous systematic reviews were not included. The analyzed studies provide a comprehensive view of the impact of CDSS on antibiotic prescribing across a variety of clinical settings and medical conditions. Although each study addresses different populations and contexts, several common themes and challenges emerge, highlighting both the potential and the difficulties associated with implementing CDSS in medical practice[70-72].

Significant improvements in the appropriateness of antibiotic prescriptions were reported in all studies following the implementation of CDSS. For example, Kathleen Marulanda observed a 50% increase in the use of preferred antibiotics for pediatric appendicitis[73], while Helen Y. Wang reported improvements from 31.9% to 65.3% in the correct selection of antibiotics for pneumonia in the emergency department[74]. Additionally, E. Nadeau highlighted a decrease in the use of broad-spectrum antibiotics in intensive care units, crucial for combating antimicrobial resistance[75]. A further study conducted in Australia by Jo-Anne Manski-Nankervis[76] demonstrated that the implementation of a CDSS integrated with electronic health records (EHR) in general practices improved antibiotic prescribing for respiratory and urinary infections, with physicians favoring it due to ease of use and integration into workflows. On the other hand, a study conducted in the United States revealed that the effectiveness of a CDSS in reducing antibiotic prescriptions for respiratory infections was not significant, partly due to alert fatigue and low adoption by physicians despite high integration with the EHR[61] .

These studies also highlight improvements in clinical outcomes, such as reduced mortality in patients with sepsis, as documented by H. Akhloufi[77,78] and improved postoperative recovery in patients studied by Sayon Dutta[79]. The diversity of settings, ranging from primary care clinics to emergency departments, influences both the implementation and the effectiveness of CDSS. For example, Alexandria May's study in primary care clinics demonstrated a 12.6% reduction in inappropriate prescriptions of azithromycin[80], while Elena Calvo-Cidoncha observed improvements in antibiotic selection and a reduction in hospitalizations among geriatric patients[81].

All the analyzed publications reaffirm the advantages that CDSS implementation offers in healthcare settings, contributing to reduced medication errors and, in turn, promoting improved patient quality of life and reduced treatment costs. CDSS has significantly reduced prescription errors, improved adherence to clinical guidelines, and decreased adverse drug events[55,82,83]. Additionally, they have enabled a reduction in hospital care costs by decreasing medication error rates and optimizing clinical resources[84-88]. However, some studies point out that implementing these systems in diverse clinical settings can present challenges, such as variability in CDSS adoption depending on workload and the specific environment of the healthcare facility[61]. Moreover, resistance to change and the perception that CDSS is unnecessary in certain clinical contexts limit its long-term effectiveness.

A common challenge was the low adoption and utilization of CDSS tools. Marulanda commented that despite improvements in antibiotic prescribing, the use of the electronic order panel was limited[73], highlighting the need for more effective implementation strategies and possibly more training for medical staff[89]. Additionally, the long-term sustainability and adaptability of CDSS to different clinical environments and disease patterns remain areas requiring further research[90]. Stacy Calloway indicated that although there were improvements in adherence to treatment guidelines, the sustained implementation and use of CDSS in outpatient care remain a challenge[55,91]. Alexandra S. Simões examined the implementation of a CDSS for antibiotic administration in urinary tract infections, showing an improvement in guideline adherence and a reduction in the use of broad-spectrum antibiotics[48,92]. In more specific studies, such as that of RS Hum in neonatal intensive care units, it was found that CDSS helped reduce the use of unnecessary antibiotics, though some users did not always visualize the recommendations, underscoring the need to improve system visibility and integration within the EHR[59]

Alert fatigue and resistance to change among healthcare professionals are significant barriers that can limit the long-term effectiveness of CDSS, which aligns with other publications[93-98] . Future research needs to address these barriers and develop more efficient and less intrusive tools to overcome alert fatigue[59]. It is essential that future investigations address these barriers, explore the sustainability of long-term benefits, and customize systems to maximize their impact on daily clinical practice.

Input and Output Parameters

The studies highlight a variety of input and output parameters used to customize and optimize antibiotic prescriptions. These parameters are crucial for achieving high precision in antibacterial diagnostics[99]. The following compares these parameters across different studies.

In H. Akhloufi's study, the input parameters include trauma diagnosis, culture history, renal function (eGFR), ideal body weight, presence of IgE-mediated allergies, and pregnancy status. The outputs are specific antibiotic recommendations adjusted for eGFR values and recent culture results[77]. This

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approach focuses on personalizing antibiotic therapy based on a wide range of patient-specific clinical data, which is crucial in a hospital setting with critically ill patients. Individualized antibiotic dosing, adjusted according to the patient's pharmacokinetics and pharmacodynamics, significantly improves the precision and efficacy of treatment, reducing toxicity and improving clinical outcomes[100,101]. Additionally, the implementation of therapeutic drug monitoring (TDM) in antibiotic dosing for critically ill patients has proven to be an essential tool for optimizing therapeutic levels and improving clinical outcomes[102].

On the other hand, Elena Calvo-Cidoncha's study used an ontology-based CDSS to model medication-related knowledge. The input parameters included patient demographics, laboratory parameters, medication allergy history, and prescription data. The system's outputs were alerts for overdoses, drug interactions, dose adjustments for renal insufficiency, and allergies, presented in the computerized physician order entry (CPOE) system interface[81]. In additional studies, integration with electronic medical records (EMR) was fundamental in improving prescription accuracy and preventing medication errors, which is particularly relevant for decision support systems in primary care[59]. Unlike Akhloufi's study[77], this approach places greater emphasis on the integration of alerts within the clinical workflow to prevent medication errors[103].

Kathleen Marulanda's study implemented an electronic orders panel (OP) specifically for antibiotic treatment in pediatric appendicitis. Input parameters included penicillin allergy status and appendicitis complexity (simple or complicated). Outputs included specific antibiotic recommendations, such as ceftriaxone and metronidazole for non-penicillin-allergic patients, and ciprofloxacin plus metronidazole for allergic patients[73]. This CDSS is more specific and targeted, focusing on a single clinical condition, allowing for very precise recommendations.

In Alexandria May's study, the CDSS focused on reducing inappropriate azithromycin prescriptions in primary care clinics. Input parameters included patient demographics and prescription history, while outputs focused on the appropriateness of azithromycin prescriptions according to clinical guidelines[80]. This study is like Marulanda's in terms of antibiotic and clinical condition specificity but differs in that it is applied in a primary care setting rather than a hospital.

Sayon Dutta's study used a CDSS for managing infections in post-surgical patients. Input parameters included surgery type and postoperative culture results. The system's outputs were antibiotic recommendations adjusted for the patient's specific characteristics and the type of surgical infection[79]. This approach is like Akhloufi's[51] in terms of customization based on detailed clinical data but focuses on the postoperative setting.

In Stacy Calloway's study, the CDSS was implemented in primary care for respiratory infections. Input parameters included patient symptoms, prescription history, and laboratory results, while outputs included antibiotic recommendations based on symptoms and laboratory results[104]. This study shares the primary care setting with May's[80] but covers a broader range of infections rather than focusing on a single antibiotic. It has been observed in several studies that CDSS for respiratory infections can have mixed results in reducing antibiotic overuse, highlighting the need to optimize their implementation[60]

Elena Calvo-Cidoncha's ontology-based alert module generates alerts when overdoses, drug interactions, dose adjustments for renal insufficiency, or allergies are detected. These alerts are integrated into the CPOE workflow and displayed in real-time[81]. This system is more robust in preventing medication errors compared to other CDSS that focus primarily on the appropriateness of antibiotic prescriptions[105].

Factors Influencing the Effectiveness of Digital Tools

The success in the adoption and use of clinical decision support tools depends on multiple factors, including technical, human, and organizational aspects. These factors include ease of use, performance expectations, and a supportive environment for system use. Studies have shown that clinicians' perceptions of the system's ease of use and usefulness are key determinants of its adoption[106]. For example, in the study on iCPR2 (2020), it was observed that although a clinical support tool was implemented among 541 primary care providers, the low adoption rate (6.9%) limited its effectiveness in reducing antibiotic prescriptions for acute respiratory infections[61]. Additionally, the proper integration of CDSS into clinical workflows and the provision of on-site training and support are critical to its success[107]. In a study conducted in Australia using a CDS system to improve antibiotic prescribing in primary care, physicians perceived it as useful, particularly in complex cases. However, it was not consistently used in all consultations[76]. Trust in the systems and the perception of a threat to professional autonomy also play a significant role in CDSS acceptance[108]

A key aspect is the acceptance by healthcare professionals, which, according to H. Akhloufi[77], can be low (12.5%) due to distrust in the validity of the information and fear of losing professional autonomy, as well as the culture of prescribing and active infectious disease services in hospitals. In a study conducted in neonatal intensive care units (NICU), the adoption of a CDS tool improved antimicrobial prescribing accuracy, although factors like EHR system updates affected its functionality and acceptance[59].

Kathleen Marulanda[73] highlights the relevance of real-time feedback and regular contact with providers, emphasizing that changes in clinical practice patterns precede the adoption of technology, but feedback and training are essential to maintain effective clinical practices. On the other hand, a study that implemented a CDS tool in a family medicine clinic for treating uncomplicated urinary tract infections showed that the tool helped reduce empirical prescribing of fluoroquinolones and improved the accuracy of ICD-10 coding and the use of urine cultures[60]. Similarly, Elena Calvo-Cidoncha[81] and Sayon Dutta[79] focus on system integration into clinical workflows and how alerts can improve procedures like collecting blood cultures before administering antibiotics, although their effectiveness may vary.

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Alexandra S. Simões[109] and Stacy Calloway[104] highlight the utility of these systems in improving communication and productivity, respectively, but also note the need to overcome barriers to integration and acceptance for effective implementation. Continuous education and proper training, as mentioned by Marulanda, are essential to improve adherence to new clinical guidelines and optimize treatment administration. A successful example of integration and adoption is the Antibioclic system in France, which, after its implementation, was widely used by general practitioners, providing standardized recommendations for 37 infectious diseases with high levels of user satisfaction[62].

Study Limitations

Studies on the effectiveness of digital tools in antibiotic management present several significant limitations. First, the generalization of results is affected by study designs restricted to a single center, as in the cases reported by Kathleen Marulanda[73] and H. Akhloufi[77], which focused on specific contexts such as pediatric hospitals or specialized infectious disease services. Additionally, studies like Müller's[110] which use large volumes of data from electronic health records, show that while the implementation of clinical decision support tools is promising, it may not be easily replicable in other clinical settings.

The low adoption of CDSS tools raises questions about the applicability of the results. Marulanda[73] noted that despite improvements in antibiotic prescribing, the use of these tools was limited. Furthermore, the lack of data on the long-term sustainability of the benefits is another critical limitation; for example, Alexandria May's study[80] only addressed short-term improvements.

Comparison between studies is complicated by variability in the parameters used, as seen in the differences between Elena Calvo-Cidoncha's ontology-based systems[81] and Sayon Dutta's specific alerts[79] for blood culture collection.

Moreover, most studies lack a detailed economic analysis that considers implementation and maintenance costs, despite some, like Stacy Calloway[104], mentioning productivity improvements and cost reductions.

Human and organizational factors, such as resistance to change and "alert fatigue," are documented challenges that influence the adoption and effective use of CDSS tools. H. Akhloufi[77] pointed out that distrust in the validity of CDSS information is a significant barrier.

Clinical Implications and Future Research

The integration of CDSS into daily practice can help standardize antibiotic prescribing, especially in high-pressure environments like emergency departments, where Helen Y. Wang's study[74] found improvements in antibiotic selection for pneumonia. Similarly, Alexandria May[80] observed a reduction in inappropriate antibiotic use in primary care, highlighting the improvement in care quality and the reduction of antibiotic resistance.

Studies like Devin Mann's[61], which evaluated an adapted iCPR system in various primary care settings, showed that the low adoption rate of CDSS remains a significant obstacle. Despite improvements in usability and integration into clinical workflows, the impact on reducing antibiotic prescriptions was not significant due to low utilization by providers.

CDSS also play a crucial role in the continuous education of healthcare professionals, facilitating real-time feedback and the integration of clinical guidelines, as noted by Kathleen Marulanda[73], making them valuable tools for training and knowledge updating.

In the Australian study by Jo-Anne Manski-Nankervis[76], the acceptance and ease of use of a CDSS for antibiotic prescribing were high among general practitioners, if the system was well-integrated with electronic medical records (EMR). This study emphasizes the importance of simplifying access to clinical guidelines and optimizing the interface for routine use in daily practice.

To maximize the benefits of CDSS, it is crucial to address the barriers to their adoption. The low utilization reported in several studies indicates the need to improve the interface and integration into clinical workflows, suggesting that targeted interventions could increase acceptance and usage, as indicated by Sayon Dutta's study[79] which showed improvements through simple alerts.

Future research should focus on evaluating the long-term impact of CDSS and their adaptation to changes in clinical guidelines and the epidemiology of antimicrobial resistance. Additionally, a detailed economic analysis, including the costs of implementation, maintenance, and training, is necessary to justify the investment in these technologies, as mentioned in Stacy Calloway's study[104].

Personalizing CDSS to adapt them to different clinical contexts and patient populations could increase their effectiveness and acceptance, as seen in Elena Calvo-Cidoncha's ontology-based system, which generated real-time alerts. The Australian study also suggests that using these systems to educate patients can reduce social pressure for unnecessary antibiotic prescriptions, reinforcing their clinical and educational value[76].

CONCLUSION

Despite their benefits, the effectiveness of CDSS critically depends on effective implementation, continuous training, and adaptation to the specific needs of each clinical context and patient population. These studies not only support existing literature but also enrich our understanding of how to implement CDSS effectively to optimize antibiotic prescribing and improve health outcomes.

Commonly used parameters in the studies include demographic data, prescription history, and laboratory results, with outputs ranging from antibiotic recommendations to alerts about drug interactions. The studies by Akhloufi[77] and Dutta[79] emphasize the personalization of therapy in hospital and post-surgical settings, while those by May[80] and Calloway[104] focus on appropriate prescribing in primary care for respiratory infections. Marulanda[73] and Calvo-Cidoncha[50] integrate alerts into the clinical workflow to improve adherence to treatment guidelines and prevent medication errors, demonstrating the flexibility of CDSS to adapt to different clinical settings.

However, user acceptance, integration into workflows, system ease of use, and continuous education are crucial factors that must be considered to ensure the successful and sustainable implementation of these technologies in clinical practice. Future research should address current limitations through multicenter studies, long-term evaluations, detailed economic analyses, and a deeper consideration of human and organizational factors.

While the reviewed studies offer valuable evidence of the potential of digital tools to improve antibiotic management, it is essential to overcome various barriers and customize the tools to fit different clinical contexts and patient needs. Only then can CDSS be effectively integrated into daily practice and contribute to better healthcare quality.

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