Decision support systems for antibiotic prescribing

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Purpose of review
To explore recent developments in computerized evidence-based guidelines and decision support systems that have been designed to improve the effectiveness and efficiency of antibiotic prescribing.

Recent findings
The most frequently utilized decision support systems are electronic guidelines and protocols, especially for empirical selection of antibiotics. The majority of decision support systems result in improvement in clinical performance and, in at least half of the published trials, in patient outcomes. Despite the reported successes of individual applications, the safety of electronic prescribing systems in routine practice has been identified recently as an issue of potential concern. Bioinformatics-assisted prescribing may contribute to reducing the complexities of prescribing combinations of antimicrobials in the era of multidrug resistance.

Summary
The reemerging interest in prescribing decision support reflects the recent change in emphasis from support for diagnostic decisions towards support for patient management and from systems targeting a broad range of clinical diagnoses to task-specific and condition-specific decision aids.

Keywords
antibiotic prescribing, clinical decision support, evidence-based medicine, infectious diseases

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Introduction

Suboptimal decisions are the most common reason for inappropriate antibiotic prescribing in primary care and hospital settings, with the majority of errors occurring in the drug prescribing stage [1,2]. Even at university medical centres, the proportions of inappropriate antibiotic prescriptions range from 41 to 66% [2]. Errors result from 'system failures', such as lack of access to up-to-date information at the point of prescribing or poor communication, and/or faulty individual decisions. Misuse of antibiotics can result in unnecessary exposure of patients to medication, adverse drug events (ADEs), persistent or progressive infection and an increase in healthcare costs; it is also a major risk factor for the emergence and epidemic spread of infection due to multiresistant microorganisms, which are associated with a higher mortality than infection due to susceptible strains [3,4]. Antibiotic resistance is most likely to develop in situations in which there is a concentration of very sick patients at risk of infection (such as intensive care units) and extensive use of antimicrobials. Prevention of antibiotic misuse is the key to controlling antibiotic resistance [5]. However, appropriate empirical antibiotic selection is becoming increasingly complex. The most frequent reason for inappropriate empirical antibiotic selection is that the causative pathogen is resistant to the antibiotic chosen [6•]. As this situation is not uncommon in high-risk settings, it is apparent that clinicians need assistance in selection of antibiotics for their sickest patients.

Computerized evidence-based guidelines and decision support systems (DSS) have been promoted as the key to improving effectiveness and efficiency of clinical decisions [7]. DSS in healthcare can be defined as computer programs that are designed to help health professionals make clinical decisions. Clinical decision support means that relevant, objective, accurate and up-to-date information is readily available to healthcare providers. Furthermore, DSS aim to integrate individual patient data with the best available evidence, which may include local guidelines or protocols, patient-specific advice or interpretation of laboratory results and alerts or reminders to focus attention on specific problems [7].

There is growing interest in the effects of computerized guidelines and clinical DSS on antibiotic prescribing, especially in reducing practice variation and error [8]. Here, we review key contributions, highlight challenges and speculate on the future of clinical decision support.

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'Epidemiology' of prescribing errors

Despite recent trends that demonstrate reduced outpatient use of antimicrobial agents, prescribing in hospitals continues to exceed well tolerated levels. Studies [9,10] have demonstrated significant variations in prescribing patterns between different countries, healthcare systems, individual prescribers and within and between clinical specialties. These differences may be related partly to different patient populations, but they also reflect variations in doctors' attitudes, level of expertise, tolerance of uncertainty and personal styles of decision-making. For example, although microbiological investigations are the basis of appropriate management, clinicians express varying opinions about the relevance of laboratory results to decisions regarding antibiotic choice.

The incidence of prescribing errors has been reported to range from three to 99 errors per 1000 inpatient medication orders [11,12]. The majority occur on the day of admission and a large proportion are potentially preventable, as they are often attributable to inadequate knowledge or inappropriate application of prescribing rules. Up to one third of prescribing errors have been judged to be clinically significant and they are most frequently related to anti-infective medication orders [12]. Medication errors resulting in preventable ADEs most commonly occur at the ordering stage [2].

Decision support to optimize antibiotic utilization

Common types of DSS for antibiotic prescribing are listed in the Table 1 [13,14••,15–24,25•,26]. The most frequently utilized are electronic guidelines and protocols, especially for empirical selection of antibiotics. Many prescribing applications provide information on pathogens, diagnosis, medication and treatment. They include, among others, ePocrates ID (part of ePocrates Rx Pro), the Johns Hopkins Division of Infectious Diseases Antibiotic Guide, the Sanford Guide to Antimicrobial Therapy and Infectious Diseases and Antimicrobials Notes, which were reviewed elsewhere [18]. They can be downloaded onto portable handheld computers or personal digital assistants used by health professionals for a variety of purposes, including patient tracking and medical reference [27,28••]. Surveillance data can be helpful for empirical antibiotic choice if infection is suspected, because delay in providing appropriate therapy while awaiting results of diagnostic investigations can lead to suboptimal patient outcomes. Although regional or national data may provide a sense of the magnitude of resistance to a given antimicrobial agent, local and preferably unit-specific data are of greater value to clinicians [28••]. Hospitals should have active programs for surveillance of rates of bacterial resistance to common antibiotics and should analyse antimicrobial usage and resistance trends.

The implementation of DSS and compliance with recommendations depends on an ability to achieve significant, appropriate and sustainable behaviour change. The passive dissemination of guidelines and consensus-derived recommendations is unlikely to influence clinicians' behaviour [29,30]. Implementation of interactive clinical guidelines through an electronic medical record has been more effective in changing decision-making patterns of clinicians. However, there is a perception that better,

Table 1 Task-specific decision support for antibiotic prescribing

Task	Subtask	Decision support type	References
Microbiology result-independent (empirical) prescribing	Infection risk assessment	Probability calculators, often linked to provider-entered, patient-specific information	[13,14••,15]
	Assessment of possible antibiotic resistance profiles	Interactive interface providing local cumulative antibiotic resistance data	[16,17]
	Choice of therapies	Electronic protocols and guidelines (no link to electronic records or laboratory information systems)	[16,18]
	Approval for prescribing and auditing use of 'restricted' antibiotics	Automated antibiotic approval for common evidence-based indications	[19,20]
	Ordering	Computerized physician order entry systems, usually linked to medication lists, electronic protocols and pharmacy databases	[21]
Microbiology result guided prescribing	Initiation of therapy and therapy adjustment	Real-time access to laboratory results through portable computers or smart pages	[15]
		Computer-assisted monitoring: alerts to critical laboratory results, potential drug interactions	[22,23]
		Interactive interface (e.g. 'microbiology browser') providing interpretative reporting of culture results	[22]
	Choice of therapies	Electronic protocols and guidelines linked to electronic records or laboratory information systems	[23,24]
	Monitoring of therapies	Reminders about discrepancies between prescribed antibiotics and culture susceptibility results	[25•,26]

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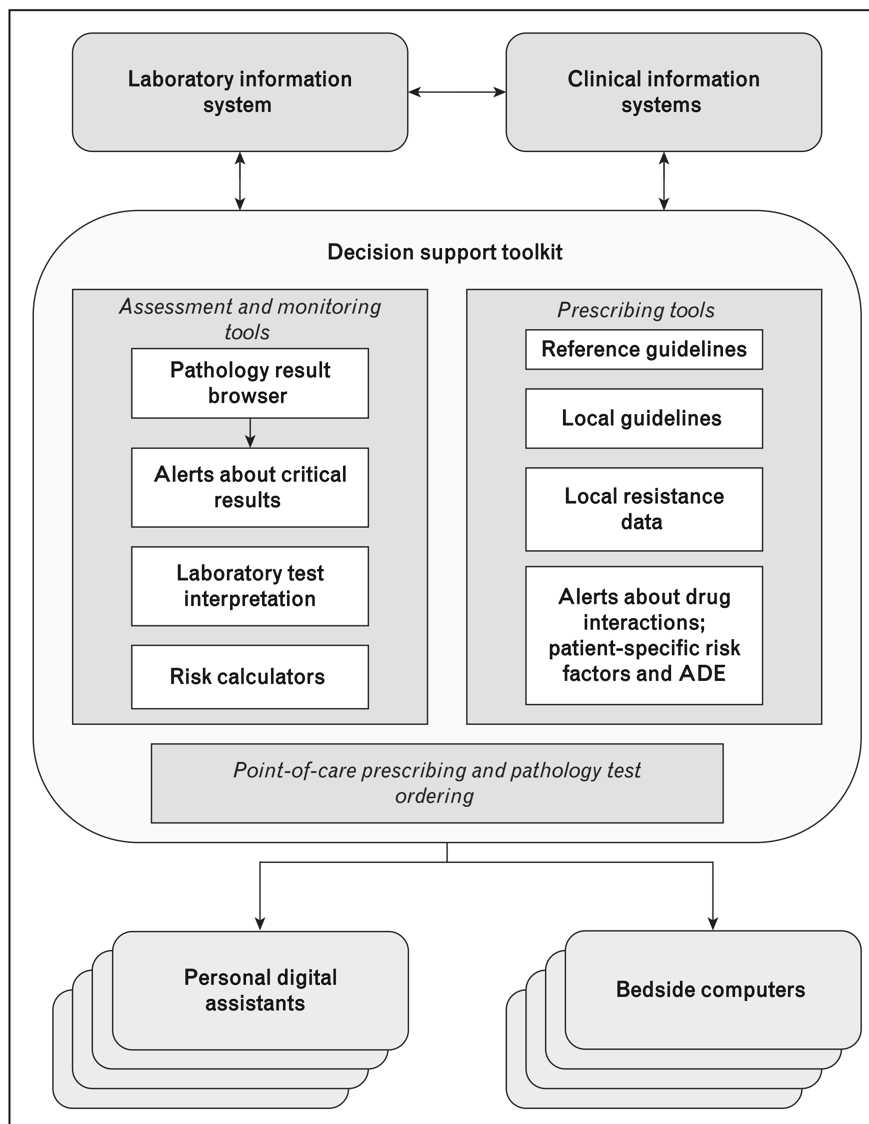
Figure 1 Standard decision support toolkit for antibiotic prescribing



ADE, adverse drug event.

quicker and easier access to evidence will automatically lead to more effective clinical management. One of the major barriers to successful implementation of computerized DSS in healthcare is the fact that current models of collation and distribution of evidence are still relatively primitive and need substantial development [30]. Figure 1 illustrates how decision support for prescribing could be integrated with laboratory and clinical information and pharmacy systems. It should provide clinicians with secure and immediate access from bedside computers and hand-held personal digital assistants through the local healthcare network.

Risk assessment tools, which utilize patient-specific data entered by the user, vary in their level of sophistication and usability. For example, artificial neural networks have been used to help clinicians estimate patient outcomes; knowledge-acquisition tools have been applied to ventilator therapy management; and an antibiotic therapy adviser has been developed using case-based reasoning methods [17]. The latter system provided advice on management of critical care unit patients with hospital-acquired infections, based on similar previously documented cases. However, despite the promise of improvement in prescribing decisions, none of these systems has so far been evaluated in clinical trials [31]. They may be of particular benefit to junior clinicians as educational tools and to rural practitioners with limited access to consultation and subspecialty services. To date, however, there have been few studies to assess whether the use such devices can improve patient-specific decisions at the point-of-care, or clinical outcomes [13].

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Computerized physician-order-entry (CPOE) systems take advantage of the interface between electronic patient records and laboratory and pharmacy information systems, and have attracted the interest of healthcare managers as tools to enforce clinical protocols [32]. Such systems have the capacity to prevent the majority of medication ordering errors depending on specific CPOE system characteristics. For example, CPOE systems that deliver specific recommendations by matching individual patient characteristics to a knowledge base are more likely to mitigate ADEs [21]. DSS need to be able to take into account the patient's pathophysiological state, medical condition and pathological test results in order to present the physician with a prescribing recommendation, in addition to merely warning of a potential ADE.

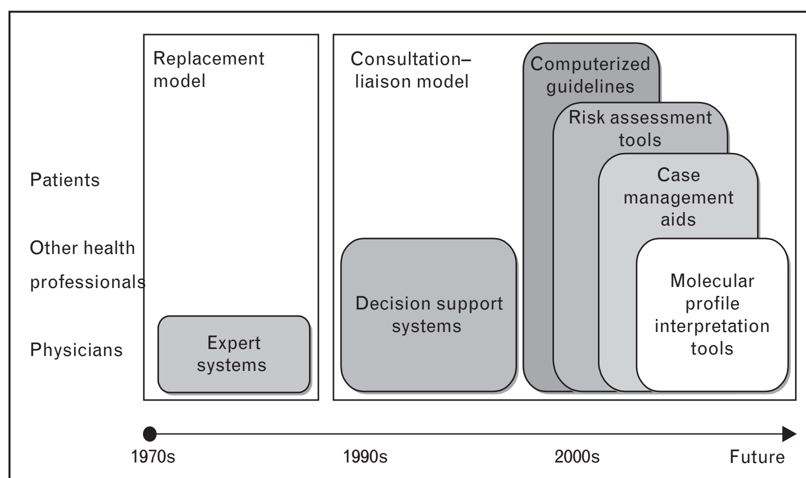
Restrictions on the use of particular classes of antibiotics have been used to limit inappropriate antimicrobial prescribing within an institution and many DSS have been employed to enforce and monitor such formulary-driven restrictions [19,20]. However, the consensus among medical professionals is that antimicrobial management programs should aim to promote the most appropriate use of antimicrobials rather than limiting choices. DSS are an integral part of antimicrobial management or 'stewardship' programs directed by multidisciplinary teams, which combine education with appropriate restriction of the use of some antimicrobials to specific indications [22]. The introduction of reliable, rapid diagnostic tests at the point-of-care can reinforce a strategy of prudent prescribing and in turn could transform prescribing practice from one of empiricism to one of greater precision. Evidence indicates that complex interventions that are built up from several components, including behaviour modification, are more likely to succeed.

New prescribing systems link electronic records, protocols and risk assessment tools

The concept of clinical decision support has evolved significantly over the last decade (Fig. 2). In contrast to stand-alone rule-based or 'expert' systems, that initiated the 'artificial intelligence' revolution and were seen as a potential threat to the medical profession, recent DSS have been promoted as tools that can aid decision-making, focus attention on specific risks and be integrated into clinical practice [31]. For example, DSS often have therapeutics information embedded in prescribing and dispensing software, which can be accessed at the point of decision-making. These systems can warn of potential interactions between the newly prescribed drug and others already listed in the medical record, check that the dose is within the recommended range, alert the clinician to known allergies, recommend relevant diagnostic tests and draw attention to significant results. Such systems often combine communication and advice functions and gather the basic clinical dataset necessary to make informed decisions about antibiotic therapy. This information can be supplemented with a set of therapeutic recommendations that conform to three criteria: that the anticipated pathogens are likely to be susceptible to the anti-infective agent chosen (based on local susceptibility data); that the recommended treatment course (drug, dose, route of administration and duration) accounts for patient variables, such as allergies and renal function, drug side-effects and potential to induce resistance; and that the least expensive of the clinically equivalent choices is suggested.

Decision support consists of assessment and monitoring tools, prescribing decision aids and software for point-of-care prescribing and pathological test ordering.

Figure 2 Evolution of prescribing decision support



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Specifically, assessment and monitoring tools should include risk calculators for the most common or controversial indications for antimicrobial prescribing, such as community-acquired or ventilator-acquired pneumonias (VAP) [17], and a pathological result browser with alerts to critical results [22]. Clinicians have started to employ their patient datasets to train and test machine learning algorithms. For example, recently validated Bayesian network models can assist in predicting microbial causes of VAP and selecting antibiotic therapy using duration of admission and ventilation and microbial culture results [33•]. End users benefit from real-time access, at the point of prescribing, to all recent microbiology data including preliminary reports. Our experience indicates that prescribers in critical care place a particularly high value on timely microbiology results.

The use of situation assessment aids, as a form of computerized decision support, has also been advocated. Many such tools are based on scoring systems – that is, mathematical computations involving several key variables – to predict a particular patient's condition or outcome. Scoring systems have been used in medicine for nearly two decades but many clinicians still remain sceptical about using them in their practice. Successful scoring systems match with the decision-maker's mental model of the task and/or are highly integrated and deliver information in an unsolicited and easily accessible way [34••].

Information sources that assist with more common but less complex prescribing decisions would also be beneficial to prescribers. They include local (preferably hospital-specific or even unit-specific) antibiotic prescribing guidelines and antimicrobial susceptibility data. Observations suggest that prescribers in critical care consult with reference guidelines for possible drug–drug interactions or adverse effects more often than in other clinical settings [35]. Incorporation of self-education programmes such as a series of simulated cases, to which the novice user can apply the system and receive feedback on his or her performance, has been perceived as the additional value of DSS.

The dichotomy between the proliferation of evidence, such as clinical practice guidelines, and its low uptake in practice indicates that clinicians are already struggling with information oversupply and concomitant competition for their attention [30]. This has led to the suggestion that the notion of the 'best evidence' should be replaced with a more complex notion of the 'most effective evidence delivery', which takes into account both the inherent potential of evidence to improve clinical decisions, as well as the likelihood that its mode of delivery will be adopted [30].

Decision support can improve the quality and safety of prescribing

DSS can lead to better access to and use of evidence, more appropriate clinical decision-making and improved quality of care [31,32]. Several systematic reviews of DSS trials have demonstrated that, in the majority, the use of DSS resulted in improvements in clinical performance and, in at least half of the published trials, in patient outcomes [7,31,32]. Furthermore, studies relating to the impact of prescribing DSS, on the efficiency of healthcare delivery and medication management, have demonstrated cost savings due to fewer medication errors, ADEs and nosocomial infections, as well as increased efficiency of patient care and reduction in physician time spent on administrative tasks [22].

The use of prescribing DSS significantly improves compliance with clinical protocols and guidelines [28••]. It has been suggested that the use of guidelines may reflect the level of complexity of individual decisions [36]. For example, more complex cases are often associated with a significantly lower quality of, and confidence in, prescribing decisions which are more cognitively demanding. The complexity of a clinical decision has been shown, experimentally, to influence the type of information or decision support chosen. Prescribing guidelines are more likely to be used for decisions of 'lower' complexity, whereas computerized decision supports with laboratory data are accessed more often for those of 'higher' complexity [36].

The greatest benefits are produced by DSS in critical care, in which prescribing decisions are frequent and costly [31]. Recent studies indicate that the use of DSS in critical care can contribute to the reduction of patient length of stay. It also leads to changes in prescribing patterns such as a decrease in frequency of administration of vancomycin and β-lactamase resistant penicillins, which are extensively utilized in critical care units to provide 'broad-spectrum cover' for suspected infection. These antibiotics are among the most overused in hospital practice [37] and prescribing is likely to be reduced by interventions that increase physician confidence, without risk to patients. For example, the introduction of a real-time microbiology browser for isolate-directed antibiotic prescription led to a reduction in both total and broad-spectrum antibiotic use and to an increase in the number of switches to narrower spectrum antibiotics [22]. Seven of 13 studies aiming to reduce vancomycin prescribing in hospitals reported statistically significant reductions in acquisitions of vancomycin-resistant enterococci. Studies of wards with the most seriously ill patients were more likely to report positive results than studies of an entire hospital [38••]. However, the effectiveness of such interventions and

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their sustainability remain poorly defined because of the heterogeneity and low-quality designs of studies [31,39].

Despite the reported successes of individual software applications, the safety of electronic prescribing systems in routine practice has been identified recently as an issue of potential concern [40]. Electronic medication management systems could potentially cause new types of error because of unfamiliarity with new user-interface designs, or constant interruptions in the healthcare workplace that may distract users. Other potential sources of DSS-related errors are automation biases. These include errors of omission, in which users miss important data because the system does not 'flag' them, and errors of commission, in which users follow what the decision aid suggests, even when it contradicts their training and other available data. Online DSS may also cause errors because clinicians assess the evidence incorrectly, possibly in part because of cognitive biases [41].

Genomics and prescribing

There is increasing evidence of the value of rapid molecular profiling of pathogens as an aid to communicable disease control. The body of knowledge on molecular profiles and epidemiology of pathogens, which is accumulating in databases and the biomedical literature, is expanding rapidly. Pathogens with epidemic potential may produce virulence factors or specific genotypes associated with more severe disease or complications. This information could potentially revolutionize the choice of antibiotics and the duration of antimicrobial therapy [39]. Such targeted antimicrobial prescribing will be reinforced by genotypic information about host factors such as the presence or absence of single nucleotide polymorphisms in genes significantly associated with variations in individual susceptibility to infection and in drug response including ADEs [40].

The diversity of antimicrobial resistance mechanisms further complicates the choice of optimal therapies. To support clinicians in this task, a range of bioinformatics tools for predicting drug resistance or response to therapy from the genotype and local epidemiology of resistance markers have been pioneered [39,42]. They have been developed using either statistical approaches, in which the model inference and prediction are treated as regression problems, or machine learning algorithms, in which the model is addressed as a classification problem. The statistical learning approach to ranking therapy choices often relies on a direct correlation between the microbial profile, the therapy decision and the response to treatment. However, these developments so far are limited to viral infections such as HIV and hepatitis B. For example, several susceptibility scores have been implemented for combination antiretroviral drugs that take into account specific resistance mutations and sum up the activities of individual drugs in the regimen [42]. Computer-assisted therapy appears to show an attractive way to reduce the complexities of prescribing combinations of antimicrobials. It has highlighted the need for wide-ranging databases containing appropriately quality-controlled data from genotypic resistance assays, treatment regimens and short-term and long-term outcomes, to correlate mutational patterns, local resistance epidemiology and specific treatments with laboratory and clinical outcomes.

Conclusion

Antibiotic misuse appears to be caused more by inadequate information than by inappropriate behaviour. Therefore, making useful information available at the point-of-care and assisting physicians in the more efficient use of data in their daily work have been suggested as focal points for optimizing antibiotic utilization. Although the use of DSS has accelerated in recent years, little progress has been made towards developing a widely accepted model of system uptake and acceptance. It has been assumed for a long time that the characteristics of the technology determine the rate and speed of its adoption and uptake, regardless of the task and decision-maker characteristics. However, more sophisticated change management programs that are built up from several components, including behaviour modification, are more likely to succeed. The growing interest in prescribing decision support reflects current shifts in emphasis from providing support for diagnostic decisions towards support for patient management and away from DSS targeting a broad range of clinical diagnoses to task-specific and condition-specific decision aids. Bioinformatics-assisted prescribing may also assist in reducing the complexities of prescribing combinations of antimicrobials in the era of multidrug resistance.

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