Use of computerized decision support systems to improve antibiotic prescribing

Karin Thursky

This decade will see the emergence of the electronic medical record, electronic prescribing and computerized decision support in the hospital setting. Current opinion from key infectious diseases bodies supports the use of computerized decision support systems as potentially useful tools in antibiotic stewardship programs. However, although antibiotic decision support systems appear beneficial for improving the quality of prescribing and reducing the costs of antibiotic prescribing, their overall cost–effectiveness, impact on patient outcome and antimicrobial resistance is much less certain. This review describes computerized decision support systems used to assist with antibiotic prescribing, the evidence for their effectiveness and the current and future roles.

John Naisbett, a well-known futurist, is famous for the phrase, “We are drowning in information, but starving for knowledge”. This is a remarkably apt description of the situation faced by the hospital clinician in the 21st Century, and explains the ‘knowledge–performance gap’ between best evidence and clinical practice. Clinical knowledge needs are often unmet at the time of decision making because existing means of obtaining comprehensive information is unsatisfactory [1–3]. These deficits in information storage and delivery then force the clinician to rely on human memory, another highly variable and inefficient storage and delivery system [2].

Computerized decision support may be defined as access to knowledge stored electronically to aid patients, carers and service providers in making decisions on healthcare [4]. Computerized decision support systems (CDSS) have the potential to bridge this knowledge–performance gap by organizing and presenting the appropriate information sources to the user so that they are able to make clinical decisions with reduced error and increased accuracy.

Antibiotic prescribing, particularly for the critically ill patient, requires a complex sequence of decisions based on uncertain and poorly structured information from a variety of sources [5]. In many cases, the decision to start antibiotic therapy is based on the clinical suspicion of infection, hence the clinician must use appropriate diagnostic criteria, consider the likely pathogen, as well as local patterns of common bacteria and antibiotic resistance (antibiogram). In the presence of an isolate they must consider the likely clinical significance (as colonizers are common in the intensive care unit [ICU]), then interpret the laboratory susceptibility data, choose an optimal antibiotic regimen based on best evidence, prescribe the correct dose (sometimes in the presence of organ failure) for an optimal duration, and consider potential drug interactions, contraindications and adverse reactions.

Sintchenko and colleagues evaluated the task complexity of antibiotic prescribing in the critical care setting. The aim of the study was to identify the cognitively demanding components that would benefit from automation using a decision support tool. Antibiotic prescribing for ventilator-associated pneumonia (VAP) was found to be more cognitively demanding than prescribing for sepsis or central venous line infection [6]. The ability to reduce the complexity of decisions is a cognitive behavior found in intensive care
physicians when compared with more junior staff [5]. This fact might suggest that clinical decision support is more likely to improve the quality of decision making in less experienced doctors. Another study designed to identify knowledge-performance gaps in the antibiotic management of bacterial isolates in an ICU found that inadequate antibiotic coverage was often observed for *Pseudomonas aeruginosa*, *Acinetobacter* spp., *Stenotrophomonas maltophilia*, *Staphylococcus aureus* and Enterobacteriaceae spp. [7]. Narrower spectrum antibiotic therapy was potentially available for 30% of isolates after sensitivity results were known. The authors identified various interventions that could have improved antibiotic prescribing such as availability of the unit antibiogram, improved communication with the laboratory and antibiotic prescribing guidelines.

The infectious diseases consultation influences antibiotic usage as well as diagnostic precision (differentiating colonization from infection) [8,9]. The infectious diseases physician is more likely to optimize antibiotic management by choosing appropriate empirical therapy, and switching from a broad-spectrum to a narrower spectrum antibiotic once culture results are available (de-escalation) [10]. They are also more likely to take into account pathogen- and patient-specific issues when making recommendations (an example might be the failure rate for treatment of a catheter-related infection if the catheter is not removed) [11]. Morbidity and mortality is decreased in patients with sepsis due to improved empirical and directed antibiotic prescribing [12–14].

In one questionnaire-based study evaluating the sources of information used by clinicians for antibiotic prescribing, 55% of clinicians reported the use of at least one external resource [15]. For antibiotic selection, the most common resources were advice from another physician or pharmacist. Nonhuman resources (such as handbooks and the internet) were more likely to be used for antibiotic dosing rather than selection. Over 85% of the clinicians felt that computerized decision support would optimize antibiotic prescribing.

It can also be argued that the role of CDSS is to perform the same role – that is, to improve or maintain decision quality under conditions of reduced cognitive resources [6] – computerized decision support for antimicrobial prescribing should be targeted to reducing task complexity. One area of potential intervention identified from the studies described above is assistance with the interpretation of *in vitro* susceptibility data and unit antibiogram. These systems must assist with antibiotic selection and dosing but ultimately attempt to minimize the overseuse/misuse of antibiotics.

**Computerized decision support systems for antibiotic prescribing**

CDSS are able to reduce the cognitive burden of medical decision making by bringing together patient-specific data and knowledge bases. Although there are many definitions, the following accurately describes the purpose of CDSS: “Clinical decision support is any software that directly aids clinical decision making in which characteristics of patients are matched to a computerized knowledge base for the purpose of generating patient-specific assessments or recommendations that are then presented to clinicians for consideration” [16]. This review excludes studies that simply present guidelines without patient-specific information (passive decision support) such as internet/intranet guidelines. Medline and Google were searched for systematic reviews of CDSS and any study relating to antibiotic DSS using the following text words or phrases: computerized, electronic, decision support, antibiotic and antimicrobial, in all possible combinations.

The three major components of a CDSS are knowledge bases, rules and software.

Knowledge bases are electronic storages of any information that may be used in the decision-making process. There are two types of knowledge used by the clinician – objective and subjective knowledge [17]. Objective knowledge represents ‘textbook’ knowledge that can easily be represented as rules. It might include locally developed knowledge based on expert opinion, commercial databases or clinical practice guidelines. Rule-based systems typically use ‘if’ and ‘then’ type statements. An example of this might be the recommendation of a non-β-lactam antibiotic if the patient is severely allergic to penicillin.

Subjective knowledge, on the other hand, represents experience and changes frequently over time. This knowledge may be represented by cases, so that with time, predictions may be made as patterns develop. One of the earliest expert systems developed in medicine was Mycin (1972–1980) [18], which was developed at Stanford in the 1970s. A large number of if-then rules were collected from experienced clinicians [19]. A logical reasoning computer used patient data and case-based reasoning to provide antibiotic advice for bacteremia and meningitis. The following is an English version of one of Mycin’s rules: “if the infection is primary bacteremia, and the site of the culture is one of the sterile sites, and the suspected portal of entry is the gastrointestinal tract, then there is suggestive evidence (0.7) that infection is bacteroid.”

Although the system was never used in clinical practice due to the immature state of the clinical information infrastructure at the time, it was the forerunner of many other expert systems. In a controlled setting, where Mycin recommendations were compared with the recommendations of nine human prescribers for ten test cases of meningitis, the program was correct 65% of the time as judged by experts compared with a rating of 42.5–62.5% for the humans [20].

There are several examples of the use of probability-based methods for the diagnosis and treatment of infectious diseases. The Antibiotic Assistant at the LDS Hospital in UT, USA uses predictive models developed from stepwise logistical regression models of the patient database [21,22]. These models provide population-based probabilities of infections in relation to specific variables. The prediction rule depends on an existing database, and is problematic if one or more variables are missing for a patient [19].

Modern computational methods are more suited to diagnostic decision support, as they are better at detecting patterns in biomedical data. These techniques are divided into...
CDSS for antibiotic prescribing

model-based methods such as Bayesian networks, and so-called ‘black-box’ methods that cannot be explained in terms of the logical relationships among variables [19].

The use of the theory of probabilistic networks (also called Bayesian networks) and decision theory allow the system to deal with uncertainty. Bayesian networks are built on the probability distributions of multiple variables taking into account conditional and independent relationships [19]. They are represented diagrammatically as a series of variables linked to each other by directional arrows. Examples of these systems include the ‘QID’ decision support system for empirical antibiotic therapy [23] and a Bayesian network for the diagnosis and treatment of VAP developed by Schurink and colleagues in Utrecht, The Netherlands [19]. The former is not in clinical use as much of the information required is not available in electronic databases and requires the clinician to enter the data, highlighting one of the barriers to successful implementation.

Artificial neural networks are capable of learning from a dataset. In a comprehensive review of this topic, Lisboa and colleagues extensively examined the benefits of neural networks in medical interventions [24,25]. Their use has been limited in the diagnosis or treatment of infections, perhaps because clinical data are often limited.

Antibiotic CDSS may function as nonintegrated (stand-alone) or integrated information systems [26]. Integrated antibiotic CDSS are embedded within other applications such as pharmacy dispensing systems or computerized physician order entry (CPOE). The majority of antibiotic decision support in commercial CPOE is limited to commercial drug interaction packages or drug databases. Almost all commercial CPOE systems are associated with front-end decision support such as default values, routes of administration, dose and frequencies, but may also include drug allergy checks, and drug laboratory value checks. The limitation of front-end alerts is the annoyance factor for the clinicians with frequent firing of rules during order entry [27]. Highly advanced systems such as the Antibiotic Assistant at the LDS hospital [22] are able to generate patient- and situation-specific recommendations based on data retrieved from the individual electronic health record.

Other antibiotic CDSS are asynchronous (do not provide decision support at the time of prescribing), utilizing knowledge-based expert systems that issue clinical alerts that are communicated to the clinicians after the antibiotic is ordered. An example of these are pharmacy-based antibiotic CDSS that monitor antibiotic prescriptions in relation to microbiology reports and generate reports of potential therapeutic mismatch [28–31].

Evidence for effectiveness of antibiotic computerized decision support systems

Evaluation of computerized decision support systems

Evaluation of CDSS is complex as standard clinical trial methodology is not practical or even possible. The gold standard is the randomized controlled trial (RCT) where the randomization occurs by practice or physician [32]. This approach is difficult in environments such as the ICU as cross contamination would occur between clinicians. The magnitude of this effect depends on the type of intervention. For example, interventions that require complex calculations by the decision support tool are less likely to cause contamination.

Kaplan performed a comprehensive review of evaluation methodologies for CDSS [33]. He found that most CDSS were evaluated in a clinical trial setting (such as RCTs, field tests or before and after design) so that little information is available about the performance of these systems in a real working environment. Few studies have reported assessments of speed or time costs and savings associated with the systems use. Most studies did not assess whether the CDSS supported organizational priorities or were aligned with the beliefs and financial interests of clinicians [34]. There is a paucity of qualitative studies, hence there is a profound lack of scientific information about why CDSS may or may not be effective. Other approaches to evaluation, such as ethnographic field studies, simulation, usability testing, cognitive studies, record and playback techniques, and sociotechnical analyses rarely appear in this literature.

The majority of antibiotic CDSS studies focus on intermediate outcomes such as the change in physician performance (e.g., change in antibiotic prescribing or adherence to guidelines) or antibiotic usage. Few studies have been able to demonstrate an improvement in patient outcome. The quality of studies reporting antibiotic interventions (including CDSS) is further compromised by inadequate study design. Ramsay and colleagues evaluated strategies used to improve antibiotic prescribing as part of a Cochrane review [35]. They found that only 18.3% of the literature conformed to acceptable methodological standards. The study designs that were considered acceptable included RCTs, and time–series analyses. Only three out of 68 studies included in their review used computers. There have been no studies designed to examine the impact of these systems on the development of antibiotic resistance.

Systematic reviews of effectiveness

There have been several systematic reviews evaluating the effectiveness of CDSS and CPOE [16,36–38]. A number of summary observations may be made from these reviews. CDSS appeared to be an effective measure to reduce medication error (Level I evidence), and increase physician guideline uptake/concordance (Level I evidence) [16,36–38]. The most effective CDSS were those that coupled to an electronic medical record and/or CPOE.

There are two meta-analyses of RCTs involving CDSS. Shea evaluated 16 computerized reminder systems for preventive care and reported mixed results [39]. The most extensive systematic review of 68 RCTs demonstrated benefits in DSS for drug dosing, preventive care and other medical care, but not diagnostic aids [36]. Overall, 66% of the computer-based systems improved clinical practice. Of all the studies, there were only two related to antibiotic prescribing, both of which were designed to assist with dosing recommendations for aminoglycosides [40,41]. Only six of 14 studies that measured patient outcome showed improvements.

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A systematic review of CDSS that aided drug dosing (e.g., anticoagulants, aminoglycosides) [38] demonstrated an overall benefit of these types of systems. Of 18 studies included, only two were related to antibiotic prescribing and both were CDSS for aminoglycoside prescribing [42,43]. This review was limited by the small number of patients included (671 patients in the 18 studies). The authors also identified that publication bias was likely to be an important factor limiting their conclusions, as studies with positive results were more likely to be reported. Johnston and colleagues reviewed 28 controlled trials of CDSS in both the in-patient and outpatient setting [32]. The majority of studies (except diagnostic DSS) demonstrated improved physician performance, however, only three of ten that evaluated patient outcome demonstrated improved outcome.

**Qualitative studies**

Kawamoto and colleagues performed a systematic review of 71 RCTs using CDSS with the aim of identifying the features of CDSS critical for improving clinical practice [34]. They evaluated each CDSS for the presence of features that could potentially explain why a system succeeded or failed. Many of these features relate to organizational, social and cultural issues correlating to doctor prescribing behavior.

Several leading authors in the field of medical informatics have identified several qualitative factors that make these systems successful [2,57,44]. Features of CDSS that are most likely to improve clinical practice are listed in TABLE 1.

**Computerized antibiotic decision support in clinical use**

Current opinion from the key infectious diseases bodies supports the use of antibiotic DSS as potentially useful tools in antibiotic stewardship programs [51,52,201]. The US Centers for Disease Control and Prevention (CDC) ‘campaign to prevent antimicrobial resistance in the healthcare settings’ supports the use of CDSS to improve the quality of antibiotic prescribing [52]. The 12-step campaign focuses on the prevention of infection, the effective diagnosis and treatment of infections, the practice of antimicrobial control and the prevention of transmission of infections. The campaign cites the success of the antibiotic CDSS at the LDS hospital [22] as the justification for the use of computerized decision support.

**Table 1. Features of computerized decision support systems likely to increase clinician uptake.**

<table>
<thead>
<tr>
<th>Features</th>
<th>Ref.</th>
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<tbody>
<tr>
<td>The primary determinant of user satisfaction is speed</td>
<td>[45]</td>
</tr>
<tr>
<td>They should automatically provide decision support as part of</td>
<td>[34]</td>
</tr>
<tr>
<td>clinician workflow (i.e., integrated with clinical practice)</td>
<td></td>
</tr>
<tr>
<td>Usability is very important</td>
<td>[44]</td>
</tr>
<tr>
<td>The system should provide alternate recommendations rather than just</td>
<td>[34]</td>
</tr>
<tr>
<td>an assessment (i.e., promotes action rather than inaction)</td>
<td></td>
</tr>
<tr>
<td>Physicians will often override reminders/suggestions if they have</td>
<td>[22,46]</td>
</tr>
<tr>
<td>strong beliefs about the medication or clinical situation</td>
<td></td>
</tr>
<tr>
<td>The system should require documentation of reasons for not following</td>
<td>[37,47]</td>
</tr>
<tr>
<td>the recommendations</td>
<td></td>
</tr>
<tr>
<td>There should be justification of decision support via provision of</td>
<td>[1,48]</td>
</tr>
<tr>
<td>reasoning and research evidence</td>
<td></td>
</tr>
<tr>
<td>Simple interventions work the best</td>
<td>[44]</td>
</tr>
<tr>
<td>Additional information should only be requested from the user if</td>
<td>[49,50]</td>
</tr>
<tr>
<td>necessary. Clinicians are poor at entering data elements for</td>
<td></td>
</tr>
<tr>
<td>advanced decision support. Arduous data entry results in poor system</td>
<td></td>
</tr>
<tr>
<td>acceptance</td>
<td></td>
</tr>
<tr>
<td>The impact should be monitored and performance feedback should</td>
<td>[44]</td>
</tr>
<tr>
<td>be provided to clinicians</td>
<td></td>
</tr>
<tr>
<td>The systems should provide incentives to use such as paper-based output;</td>
<td>[44]</td>
</tr>
<tr>
<td>complex calculations or feedback to users</td>
<td></td>
</tr>
<tr>
<td>There should be an alignment of incentives between guideline developers</td>
<td>[44]</td>
</tr>
<tr>
<td>and users (rather than be driven by profits)</td>
<td></td>
</tr>
<tr>
<td>There should be local user involvement in the development process and</td>
<td>[44]</td>
</tr>
<tr>
<td>local guideline development or adaptation</td>
<td></td>
</tr>
<tr>
<td>Computerized decision support systems should be accompanied by</td>
<td>[67]</td>
</tr>
<tr>
<td>conventional education</td>
<td></td>
</tr>
</tbody>
</table>

Table 1 lists examples of computer-assisted interventions that target each step.

The following section will describe existing expert systems that assist with antibiotic prescribing and in a hospital setting. Outcomes of studies of antibiotic DSS in clinical use in the hospital setting are shown in TABLES 2, 3 AND 4. These are divided into three groups – those interventions that were embedded into CPOE (or front-end); asynchronous pharmacy-based antibiotic DSS and other programs used by physicians utilizing technologies that are more novel such as the Internet or hand-held devices.

Diagnostic DSS for infectious diseases are within the scope of this review, but the reader is referred to a systematic review by Bravata [53]. The usefulness of these systems for decision making, such as in early detection systems for bioterrorism, are limited because false-positive and false-negative rates are unknown for most systems.

There are several examples of DSS that assist with the identification of patients at high risk for nosocomial infection using data from the electronic patient record, microbiology, pathology and radiology results [21,25,54,55]. These DSS have medical dictionaries that can deal with semantics and clinical vocabulary so that information can be used from all these data sources. These systems facilitate early infection prevention and surveillance activities.

In summary, although antibiotic DSS appear beneficial for improving the quality of prescribing and reducing the costs of antibiotic prescribing, their overall cost-effectiveness, impact on patient outcome and antimicrobial resistance is much less certain. They are most likely to be successful as part of a multidisciplinary antibiotic stewardship program [66].
Computerized decision support utilizing computerized physician order entry

A substantial body of literature about CDSS and antibiotic DSS originates from just two institutions in the USA – the LDS hospital in Salt Lake City, UT, USA and the Brigham and Women’s Hospital in Boston, MA, USA. Both institutions have advanced hospital information systems that offer clinicians sophisticated decision support in common. Both information systems were developed over many years, and driven by local experts and clinicians at these institutions.

The LDS hospital’s Health Evaluation through Logical Processing (HELP) system has been in clinical use for over 25 years and uses local clinician-derived consensus practice guidelines to provide continuous surveillance and computerized decision support. They have been able to develop such highly sophisticated programs due to comprehensive clinical databases and the fully computerized nature of the medical workflow (such as electronic order entry, electronic medical records and bedside computers in each patient room). They have consequently published extensively on a wide range of CDSS tools for the management of infections, infection control surveillance, surgical prophylaxis and adverse drug events (ADEs) [67–74].

The antibiotic management program is available at the bedside, and provides advanced decision support for antibiotic prescription during the process of prescribing. The decision support logic uses patient-specific data from the electronic health record such as clinical observations, white cell count and other laboratory data, microbiology and radiology data, and clinical details such as admission diagnosis. Local epidemiological data and variables from matched patients from the previous 5-year period are used if clinical data are incomplete or unavailable.

The results of the antibiotic management program were reported in the *New England Journal of Medicine* in 1998 [22] and the study is widely quoted in the literature for antibiotic control as the benchmark for CDSS [52]. The before and after study was performed in the 12-bed intensive care service from 1992 to 1995 and evaluated the impact of the Antibiotic Assistant on antibiotic usage patterns, susceptibility mismatches, allergy alerts, excess doses, ADEs and costs. These outcomes were adjusted for patient factors including illness severity. There was a significant reduction in antibiotic mismatches, drug alerts, ADEs and hospitalization costs in patients in whom the program was followed compared with the historical cohort, or patients in whom the program was overridden. One of the striking findings of this study was that only 46% of antibiotic recommendations were followed, compared

### Table 2. The 12-step CDC campaign to prevent the development of antimicrobial resistance and examples of studies using computerized decision support that target the steps.

<table>
<thead>
<tr>
<th>Step</th>
<th>CDC 12-step campaign</th>
<th>Examples of clinical studies using DSS</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Prevention of infection: pneumonia and influenza vaccination before hospital discharge</td>
<td>Automated alerts</td>
<td>[57]</td>
</tr>
<tr>
<td>2</td>
<td>Early removal and/or avoidance of catheters if not essential</td>
<td>Semi-automated email reminders</td>
<td>[52,58]</td>
</tr>
<tr>
<td>3</td>
<td>Target the pathogen: culturing the patient, targeting empirical therapy to likely pathogen or local antibiogram, targeting definitive therapy to known pathogen and susceptibility results</td>
<td>Antibiotic Assistant LDS, pharmacy-based review of cultures</td>
<td>[22,28–31, 59]</td>
</tr>
<tr>
<td>4</td>
<td>Accessing infectious diseases expertise</td>
<td>Antibiotic Assistant LDS</td>
<td>[22]</td>
</tr>
<tr>
<td>5</td>
<td>Practice antimicrobial control</td>
<td>Pharmacy-based computer monitoring, electronic approvals</td>
<td>[29–31,60, 61]</td>
</tr>
<tr>
<td>6</td>
<td>Use of local data such as the unit/hospital antibiogram</td>
<td>Antibiotic Assistant LDS</td>
<td>[22]</td>
</tr>
<tr>
<td>7</td>
<td>Treat infection not contamination – appropriate culturing techniques such as skin antisepsis before blood cultures, or taking cultures from peripheral sites rather than catheters</td>
<td>Diagnostic DSS for bacterial sepsis and VAP</td>
<td>[19,49,62–64]</td>
</tr>
<tr>
<td>8</td>
<td>Treat infection not contamination – need appropriate diagnoses for pneumonia, catheter-associated UTIs and bloodstream infections</td>
<td>Vancomycin guidelines during CPOE</td>
<td>[65]</td>
</tr>
<tr>
<td>9</td>
<td>Know when to say no to vancomycin</td>
<td>VAP risk calculator</td>
<td>[66]</td>
</tr>
<tr>
<td>10</td>
<td>Stop antibiotic therapy when infection is cured, infection is unlikely or not diagnosed</td>
<td>Electronic nosocomial infection surveillance</td>
<td>[21]</td>
</tr>
<tr>
<td>11</td>
<td>Isolate the pathogen standard infection control measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Prevention of transmission by staying home when sick and observing hand hygiene practices</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from [62]. CDC: US Centers for Disease Control and Prevention; CPOE: Computerized physician order entry; DSS: Decision support system; UTI: Urinary tract infection; VAP: Ventilator-associated pneumonia.
<table>
<thead>
<tr>
<th>Author/year</th>
<th>Decision support tool</th>
<th>Study type</th>
<th>Method of evaluation</th>
<th>Outcome</th>
<th>Cost/benefit (including development costs)</th>
<th>Comments</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pestotnik 1996 (USA)</td>
<td>Computerized AB decision support, order entry (LDS, UT, USA). Provides empirical therapy advice for syndromes/ unidentified isolates. Provides specific therapy for isolates. Provides cost–effectiveness of AB regimes. Utilizes pathology, admission diagnosis, WCC, temp, surgical data, radiology and antibiogram</td>
<td>Observational cohort study</td>
<td>Evaluated 63,759 patients from 1988 to 1994: Proportion receiving AB. Use of broad spectrum. Acquisition costs. AB costs per patient. Overall AB use. Mortality (corrected for case mix). ADEs</td>
<td>Patients receiving AB 32–53%. Broad-spectrum AB 24–47%. AB costs per patient US$123–52. AB use decreased by 22.8%. Mortality decreased from 3.65 to 2.65%. ADEs decreased 30%</td>
<td>AB costs per patient decreased from US$123 to 52. Acquisition costs 24.8–12.9% of drug expenditure budget</td>
<td>Homegrown system developed over decades. Limited transferability</td>
<td>[68]</td>
</tr>
<tr>
<td>Evans 1998 (USA)</td>
<td>Bedside computer-assisted management program with order entry in ICU (LDS)</td>
<td>Prospective before–after analysis</td>
<td>Pre and post study (1992–1995): AB use. Susceptibility mismatches. Allergy alerts. Excess dose. Adverse drug reactions. No doses of AB. Cost of AB. Adjusted for severity of illness</td>
<td>Patients receiving AB in 2-year reintervention period (n = 766; 67%) vs 1-year intervention period (n = 398; 73%). Significant reductions in mismatches, alerts, excess dose, ADEs reduced by 70% (28–4), no. doses ABs</td>
<td>Costs of ABs US$102 vs 340 (if always used intervention) Decreased cost of total hospitalization US$26,315 vs 35,283</td>
<td>Increased number of patients received AB during intervention. Only 46% of AB recommendations were followed compared with AB dosing suggestions (94%). Homegrown system developed over decades. Limited transferability</td>
<td>[22]</td>
</tr>
</tbody>
</table>

AB: Antibiotic; ADE: Adverse drug event; CPOE: Computerized physician order entry; DDD: Defined daily dose; ICU: Intensive care unit; RCT: Randomized controlled trial.
Table 3. Bedside computerized decision support systems with without associated computerized physician order entry (cont.).

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Decision support tool</th>
<th>Study type</th>
<th>Method of evaluation</th>
<th>Outcome</th>
<th>Cost/benefit (including development costs)</th>
<th>Comments</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shojania 1998 (USA)</td>
<td>Presentation of vancomycin guidelines at the time of initial order and after 72 h [CPOE] Physician use, bedside 720 bed</td>
<td>RCT (nonblinded) Clinicians randomized</td>
<td>396 physicians 1798 patients over 9 months Vancomycin orders Duration of therapy</td>
<td>32% decrease in vancomycin orders in the intervention group Duration 36% lower than control group Intervention did not significantly decrease amount of vancomycin dispensed</td>
<td>Projected savings of US$90,000 per year from annual cost of US$300,000</td>
<td>Vancomycin only Appropriateness of orders not assessed Secular trend decreasing during same period</td>
<td>[65]</td>
</tr>
<tr>
<td>Leibovici 1997 (Israel)</td>
<td>Problem-orientated database-driven DSS for empirical AB therapy</td>
<td>Prospective nonintervention comparative cohort</td>
<td>496 patients</td>
<td>Inappropriate empirical AB therapy for positive results Narrower spectrum for culture-negative patients</td>
<td>219 patients with positive culture/serological results Inappropriate empirical: physicians 42% vs DSS 23% (p &lt; 0.05) 277 patients with negative culture: narrower spectrum recommended by DSS in 27%</td>
<td>Not given</td>
<td>Not in clinical use</td>
</tr>
<tr>
<td>Heininger 1999 (Germany)</td>
<td>Interactive bedside DSS for AB therapy for registered infections in ICU Used data from patient (Carevue), microbiology (CLAB) and antibiogram databases (CAESER).</td>
<td>Prospective intervention study</td>
<td>447 patients in first 3 months of implementation Evaluation of empirical and directed therapy Calculation of rates of infections</td>
<td>102 infections 74% of empirical therapy covered isolated organisms 90% of directed therapy covered organisms</td>
<td>Not given</td>
<td>Interactive nature of program provided direct feedback to clinicians Provided means of estimating rates if ICU acquired infections</td>
<td>[56]</td>
</tr>
<tr>
<td>Thursky 2006 (Australia)</td>
<td>Interactive microbiology browser with rule-based decision support for isolate directed AB therapy in tertiary ICU – data used from pathology and antibiogram database</td>
<td>Prospective before and after analysis</td>
<td>524 admissions/6 months pre and 536 admissions/6 months post: Antibiotic use (DDDs) Change in broad-spectrum use (logistic regression) Susceptibility mismatches De-escalation to narrower spectrum</td>
<td>10.5% reduction of all ABs (166–144\ DDDs/100\ ICU\ bed\ days) 39% reduction carbapenems 42% reduction ceftriaxone 33% reduction vancomycin (\text{after}\ \text{risk}\ \text{adjustment}\ \text{for}\ \text{multiple}\ \text{factors}) Increased de-escalation Decreased AB mismatches during initial therapy (\text{OR}: 0.63, p = 0.02)</td>
<td>Development costs (AUS$350,000) not including full-time clinician researcher</td>
<td>Rapid uptake with 6028 episodes of use in first 6 months attributed to microbiology browser function</td>
<td>[93]</td>
</tr>
</tbody>
</table>

AB: Antibiotic; ADE: Adverse drug event; CPOE: Computerized physician order entry; DDD: Defined daily dose; ICU: Intensive care unit; RCT: Randomized controlled trial.
with 94% of antibiotic dosing suggestions. Clinicians were still able to order an antibiotic but were required to provide a reason in free text. Four years after this study was reported, a prospective study was performed to evaluate the concordance between physician’s orders and the recommendations made by the Antibiotic Assistant. Of 1078 physicians’ and Antibiotic Assistant order days, there was only 33% concordance. The authors attribute this fall in concordance due to insufficient monitoring of clinician satisfaction and/or acceptance of information, as well as education [75].

Pestotnik and colleagues evaluated the clinical and financial outcomes of antibiotic practice guidelines implemented through the antibiotic CDSS at the LDS hospital [67]. Over a 7-year period from 1988 to 1994, measures of antibiotic use demonstrated significant reductions in antibiotic costs per treated patient, acquisition costs of pharmacy drug expenditure and antibiotic-associated ADEs, and an overall reduction in antibiotic use of 22%. During this period, antimicrobial resistance rates remained stable despite the increase in use of broad-spectrum antibiotics from 24 to 47% of all antibiotics used. The limitations of this study were its observational nature and other factors may have accounted for these changes, but it is the only study that describes the impact of a CDSS on the development of antimicrobial resistance.

### Table 4. Web-based and handheld antibiotic decision support systems.

<table>
<thead>
<tr>
<th>Author/ year</th>
<th>Primary user</th>
<th>Decision support tool</th>
<th>Study type</th>
<th>Method of evaluation</th>
<th>Outcome</th>
<th>Cost/benefit</th>
<th>Comments</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dayton et al 2000 (USA)</td>
<td>Physician</td>
<td>Web-based clinical guidelines for tuberculosis prophylaxis</td>
<td>RCT</td>
<td>Non-intervention study Clinicians randomized</td>
<td>Compared effectiveness of computerized guidelines with paper ones. 12 subjects in computer group and 17 in paper group</td>
<td>95.8% computer vs 56.6% paper recommendations correct</td>
<td>Not given</td>
<td>Did not use automated information from databases</td>
</tr>
<tr>
<td>Richards 2003 (Australia)</td>
<td>Physician</td>
<td>Web-based antimicrobial approval system for ceftriaxone</td>
<td>Before/after study</td>
<td>Change in rate of ceftriaxone use (as DDDs per 1000 OBDs) Concordance with national AB guidelines for ceftriaxone use</td>
<td>Sustained reduction in ceftriaxone Increased concordance from 25 to 51% (p &lt; 0.002) Increased gentamicin use (p = 0.0001)</td>
<td>Software US$6000 Postintervention audit 12 person weeks, maintenance and audit 1 person day per month</td>
<td>Multifaceted strategy-removed from wards, educational strategy Feedback provided to doctors Included trend data</td>
<td></td>
</tr>
<tr>
<td>Grayson 2004 (Australia)</td>
<td>Physician</td>
<td>Nonweb-based approval system for ABs</td>
<td>Before/after study</td>
<td>Number of approved courses 12 months before and 18 months after implementation Concordance with CAP guidelines in first 9 months</td>
<td>Replaced phone-based approvals by 48% Ceftriaxone usage increased initially (due to a dosage recommendation error) No reduction in ceftriaxone use or vancomycin use (stable)</td>
<td>Required up to 0.5 EFT for pharmacist</td>
<td>Third-generation cephalosporins and vancomycin</td>
<td></td>
</tr>
<tr>
<td>Sintchenko 2005 (Australia)</td>
<td>Physician</td>
<td>Hand-held DSS for AB prescribing in an ICU that provided microbiology reports, antibiogram, AB guidelines and VAP risk calculator</td>
<td>Before/after study</td>
<td>6 months before/6 months after. Change in rates of AB use System usage impact on length of stay</td>
<td>Reduction in total ABs 1925–1606 DDDs/1000 patient days (p = 0.04) Significant reduction in ceftriaxone and vancomycin. Most common reason for use: microreports 55%, guidelines 22.5%, antibiogram 19%, risk calculator 9%</td>
<td>Not given</td>
<td>Cannot determine which component influenced change in prescribing. Minimal use of risk calculator</td>
<td></td>
</tr>
</tbody>
</table>

AB: Antibiotic; CAP: Community-acquired pneumonia; DDD: Defined daily dose; DSS: Decision support system; EFT: Effective fulltime; ICU: Intensive care unit; OBD: Occupied bed-days; RCT: Randomized controlled trial; VAP: Ventilator-associated pneumonia.
<table>
<thead>
<tr>
<th>Author/year</th>
<th>Decision support tool</th>
<th>Study type</th>
<th>Method of evaluation</th>
<th>Outcome</th>
<th>Cost/benefit (including development costs)</th>
<th>Comments</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burton, 1991 (USA)</td>
<td>Program for aminoglycoside dosing using Bayesian PKs</td>
<td>RCT Patients randomized</td>
<td>Outcomes of aminoglycoside Rx: toxicity, LOS, response rates of clinical infection, duration of Rx</td>
<td>Toxicity 9.7 vs 5.1% (NS), LOS 20.3 vs 16 days (p = 0.028) – 26% reduction</td>
<td>Cost savings due to reduced LOS</td>
<td>Patients not clinicians randomized, no severity of illness data</td>
<td>[43]</td>
</tr>
<tr>
<td>Destache, 1990 (USA)</td>
<td>Program for aminoglycoside dosing</td>
<td>RCT Patients randomized</td>
<td>Response rates of clinical infection, toxicity</td>
<td>Increased patients with adequate trough levels Increased defervescence</td>
<td>Decreased cost of treatment (US$3578 vs 7102)</td>
<td>Not intention to treat, no severity of illness data</td>
<td>[42]</td>
</tr>
<tr>
<td>Schentag 1995 (USA)</td>
<td>Database extracted microbiology culture results and AB therapy, Identified cases for review by the clinical pharmacist. Recommended changes made to treating physicians</td>
<td>Prospective observational study</td>
<td>Dosage adjustment, parenteral change, redundancy, de-escalation, oral switch, diversion to clinical trial protocol, cost avoidance</td>
<td>266 patients over 7 months in 1989: 40% dose adjustment, 18% early discontinuation, 17% change to oral, 14% regimen change, 11% clinical trial protocol</td>
<td>Annual drug cost avoidance US$64,929. Administration cost avoidance US$16,226. Actual expenditure fell by &gt;US$200,000. Drug budget fell from 30.7 to 20.2%</td>
<td>Reduced time for manual review of 6–8 h per day. Program still heavily dependent on clinical pharmacists who had previously performed this role for several years</td>
<td>[90]</td>
</tr>
</tbody>
</table>

AB: Antibiotic; DDD: Defined daily dose; DRG: Diagnosis related group; ICU: Intensive care unit; LOS: Length of stay; PK: Pharmacokinetic; RCT: Randomized controlled trial.
**Table 5. Pharmacy-based antibiotic decision support systems (cont.).**

<table>
<thead>
<tr>
<th>Author/year</th>
<th>Decision support tool</th>
<th>Study type</th>
<th>Method of evaluation</th>
<th>Outcome</th>
<th>Cost/benefit (including development costs)</th>
<th>Comments</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glowacki 2003 (USA)</td>
<td>Pharmacy-based computer-assisted surveillance of redundant AB combinations. Pharmacist trained to review results and select patients for case review. Intervention consisted of written notes or contacting physician</td>
<td>Prospective nonrandomized interventional study</td>
<td>1182 (17%) patients received ≥2 ABs over 23 consecutive weekdays in 2001–192 (16%) included in study: costs of over-prescribing, potential cost savings, number or redundant AB days, cost of pharmacist time</td>
<td>77 episodes caused by physician prescribing error – 51% unintentional Usually for Gram positives or anaerobes. 76 episodes due to lapses in medication administration or ordering systems. 98% physicians accepted recommendations. Highest rate of error in ICU 6.5/100 patient-AB days</td>
<td>Annual potential cost savings US$60,000. Annual avoidance of 3500 redundant AB days. Pharmacy cost 0.33 h for case review and intervention. Net cost savings US$48,000 per year</td>
<td>Most common were piperacillin/tazobactam and cephalosporin, vancomycin and cephazolin and cephalosporin</td>
<td>[103]</td>
</tr>
<tr>
<td>Jozefiak 1995 (USA)</td>
<td>Identified therapeutic mismatch between isolate and prescribed AB, or if positive cultures were not associated with Rx. Managed by pharmacists. Results discussed with treating physicians Walkaway 40 (Dade microscan) and PharmLINK software 389 bed</td>
<td>Prospective nonrandomized Interventional study</td>
<td>1384 patients over 6 months 1. Number of interventions accepted. 2. AB as part of total expenditure. 3. Cost avoidance. Reports generated-assessment included chart review, and communication with treating unit. Notes put in patient chart</td>
<td>Interventions recommended for 348 patients (25%). IV to oral switch (115). Broad to narrow (100). Change b/c resistant (51). Stop (41). Adjust dose (18). Untreated isolates (19). Recommend ID cons (8). 83% accepted, 93% patient condition improved, 3% failed as a result of intervention</td>
<td>Lab purchased Walkaway 40. Pharmacy purchased PharmLINK at US$17,000 Full-time clinical pharmacist Training of pharmacists Cost avoidance US$32,164 for 6 months</td>
<td>Only functioned during day: Monday to Friday. Excluded orthopedics, pediatrics, gynecology and rehab (40% of patients) Timentin, ciprofloxacin, cefotetan, cefazidime</td>
<td>[30]</td>
</tr>
<tr>
<td>Barenfanger 2001 (USA)</td>
<td>Thera-trac2: links results from Vitek system to the pharmacy prescribing system. Pharmacist trained to interpret results. Intervention consisted of written notes or contacting physician</td>
<td>Nonrandomized controlled study</td>
<td>188 study, 190 control. Control group received same intervention Control group reviewed results of review of results. 24 interventions in control group, 52 in study group, 3 different analyses performed based on DRG</td>
<td>Acceptance of recommendations occurred in 76% of study group vs 71% of control group. No difference in comparison of outcomes and costs</td>
<td>Secondary analyses done with matching for DRG and adjustment for severity suggested cost reduction of US$1446 per patient with an intervention</td>
<td>Control and study groups not comparable (patients with surnames A-K, different pharmacists for each group)</td>
<td>[28]</td>
</tr>
<tr>
<td>Grau 1999 (Spain)</td>
<td>Identified restricted ABs (CA) and matched to microbiology results. Managed by pharmacists. Results discussed with treating physicians 450 bed</td>
<td>Before/after study</td>
<td>1. Collected DDDs of ABs and compared previous 3 years (1989–1991) with following 5 years (1992–1997). 2. Total expenditure. Adjustments made for case-mix. 3. Number CAs needing intervention. 4. Number accepted</td>
<td>12.5% CA needed intervention, 92% recommendations accepted. Numbers of CAs prescribed without micro decreased by half. No. DDDs per 100 occupied bed days increased during study. 11% failure rate of accepted interventions (AB changed)</td>
<td>Accepted interventions projected savings of US$83,359 per year. Total expenditure 39% (89–91) vs 29% (92–97). Time not measured. Full-time dedicated clinical pharmacist</td>
<td>AB were ciprofloxacin, cefonicid, ceftriaxone, imipenem</td>
<td>[29]</td>
</tr>
</tbody>
</table>

AB: Antibiotic; DDD: Defined daily dose; DRG: Diagnosis related group; ICU: Intensive care unit; LOS: Length of stay; PK: Pharmacokinetic; RCT: Randomized controlled trial.
Despite the remarkable success of the HELP system, many factors limited its transferability and applicability to other sites. The integrated database (the core component of the system that pulls together information from all other data stores) is ‘hospital based’ so that patient data cannot be shared between hospitals. In addition, the platform is outdated using a mainframe base rather than newer ‘windows’-type technologies [202]. The authors describe the extensive use of the HELP system as a research tool by medical informatics graduate students and that the close relationship between the clinicians and developers would not be possible with commercial vendor systems bound by strict IP contracts and service agreements. Although the system has resulted in significant improvements in antibiotic prescription, physicians only directly enter 1% of all in-patient medication orders highlighting the potential failure of CPOE [76].

The Women’s and Brigham Hospital’s clinical information system (Brigham Integrated Computing System [BICS]) is another example of an advanced CDSS that provides a wide range of data and applications including CPOE [77]. The BICS design emphasizes direct physician interaction and extensive clinical decision support. In contrast to the situation at LDS, physicians enter 85% of in-patient medication orders [76].

Studies of medication prescribing using the combined CPOE and CDSS have demonstrated a substantial reduction in medication errors. They found that 56% of errors occurred at the time of ordering the medication, with antibiotics the third most common drug after analgesics and sedatives. The estimated rate of ADE was 6.5 per 100 nonobstetric admissions [78]. In a time-series analysis over a 4-year period, the medication error rate fell 81% from 142 per 1000 patient days in the baseline period to 26.6 per 1000 patient days in the final period. There was a large impact on all types of medication errors (medication errors may be classified as dose errors, frequency errors, route errors, substitution errors and allergies) and in particular serious medication errors (those with the potential to cause injury) fell by 86% [78,79].

The ability to present antibiotic decision support at the time of prescribing was evaluated in a RCT in which physicians were randomized to receive information about vancomycin at the time of initial prescribing and at 72 h [64]. The information presented was a list of accepted indications based on the American Infection Control Association guidelines for vancomycin use. The primary outcome measures were vancomycin orders and duration of vancomycin use – the appropriateness of the orders was not assessed. There was a 32% reduction in vancomycin orders and a 36% reduction in duration in the intervention group, although there was a secular trend of decreasing whole hospital vancomycin use during the study period.

The success of CPOE systems requires close integration of pharmacy and laboratory systems, as well as attention to the organizational and cultural changes that these systems bring. A site survey commissioned by the national taskforce (USA) found that 13% of 1050 hospitals had CPOE in 2001 [79], although this has now increased to approximately a third [80]. Interestingly, only 1% of physicians are required to interact with these systems, which would substantially reduce the efficacy of the associated DSS in reducing medication error [80]. The limited direct interaction of physicians with the order entry process will limit the success of triggers and alerts used to provide front-end decision support. The efficacy of commercial CPOE systems providing decision support is largely unknown, although there are emerging reports of systematic medication errors occurring with some systems [81,82]. Examples include pharmacy inventory displays being mistaken for guidelines, or antibiotic renewal notices being ignored when placed on the paper chart rather then on the electronic chart [82].

For CDSS developers there has been a major problem of lack of information technology (IT) infrastructure or support in the hospital setting. Many of the older hospital IT systems were transaction based and established for billing purposes rather than data capture or retrieval. In addition, there is a lack of coding standards including controlled medical vocabularies. Coding systems such as Snomed CT [203] are being increasingly utilized and has been provided freely to CDSS developers in the USA. As a result, many systems have been ‘home-grown’ using databases developed by local content experts and IT solutions tailored to the institution. The transferability of these systems and therefore generalizability of the results is limited due to their ‘home-grown’ nature.

The lack of leadership from physicians and medical schools, as well as control of information services in hospitals by IT departments and administrators without clinical expertise or input have been identified as major obstacles for the development of DSS [83]. Sites with successful advanced CDSS reported a common set of factors – very strong leadership with a clear long-term commitment, a commitment to improving clinical processes by enlisting clinician support and involving the clinicians in all stages of the development process. The strategies used met the institutions particular needs, goals and culture [76]. Further research is required to evaluate the impact of commercially available systems on antibiotic prescribing. This is important, as the institutions that have published their CDSS outcomes are generally those with strong institutional commitments to their system [79].

Pharmacy-based antibiotic computerized decision support
The second major group of antibiotic CDSS are those that link pharmacy and pathology information systems [28–31]. Several benefits to antibiotic prescribing can be achieved with effective communication between these systems such as [84]:

- Antibiotic choice (based on microbiology results)
- Antibiotic dosing and monitoring (based on pathology results)
- Improved clinician response time
- Broader quality improvement issues (antibiotic resistance and simultaneous microbiology surveillance)

These are also achieved using CDSS and CPOE as demonstrated in the studies described above, but may still be effectively achieved using stand-alone software applications.
Very few hospitals have linkages between pharmacy and laboratory databases, as these systems are usually commercial systems that are not compatible. Development of interfaces to link legacy databases is expensive and may not be a priority in a hospital institution with budgetary constraints. Changes can be achieved by improving communication between the pharmacy and the laboratory without specialized software [85].

Management of hospital antibiotic use by clinical pharmacists trained to overview microbiology results and antibiotic prescriptions is an effective way to improve antibiotic use and reduce costs [86]. In one institution that employed clinical pharmacy specialists to streamline and/or switch to oral antibiotics at days 2–4 when culture results are available, the savings exceeded US$2000–3000 per occupied bed compared with 17 other sites that employed pharmacists to monitor aminoglycoside and/or vancomycin doses only [87]. There are several studies that report on the results of commercial or in-house software programs reporting on antibiotic use in relation to patient microbiology results [31,88,89]. In all these studies, full-time, dedicated, trained pharmacists were responsible for reporting the results to the treating clinicians.

In one study, a program identified prescriptions of restricted antibiotics (ciprofloxacin, ceftriaxone and imipenem) and matched these to microbiology results [29]. Reports were generated for restricted antibiotics not associated with positive microbiology, and therapeutic mismatches. A before and after analysis compared whole hospital antibiotic utilization in the 3 years before and 5 years after the system was introduced. Antibiotic expenditure fell 10% from 39 to 29% of total drug expenditure. The prescription of restricted antibiotics prescribed without microbiology fell by half.

In a second study by Jozefiak, a commercial application identified therapeutic mismatches between microbiology and prescribed antibiotics, and identified positive cultures not associated with antibiotics [30]. During the 6-month study period, interventions were recommended for 25% of all patients. The most common interventions were recommendations to switch from intravenous to oral therapy, and to narrower spectrum antibiotics. The reports to physicians were only available on weekdays during working hours. They report that the infectious diseases physicians’ workload was not reduced, but rather increased influenced by their involvement in the development, training and peer-review processes associated with the program.

There are several examples of antibiotic DSS without CPOE used by clinicians at the bedside that provided rule-based and other pathology data [55,90,91]. These systems improved empirical and directed coverage of organisms, increased de-escalation to narrower spectrum antibiotics and in one study, significantly changed the pattern of antibiotic prescribing [90]. The advantage of these types of ‘front-end’ CDSS is that the physician receives immediate feedback rather than relying on the pharmacist action.

Web-/personal digital assistant-based decision support systems

The World Wide Web is evolving as a potentially useful tool for decision support owing to its open standards and its ability to provide concise, relevant clinical information at the location and time of need. Clinicians are now using the internet as an important professional resource as they can gain access to worldwide information sources. The internet was cited as the third most important source of antibiotic information after physicians and pharmacists, in one study looking at information resources used in prescribing antimicrobials [15]. One of the major limitations of the internet is the challenge of controlling the quality of information [92]. The intranet (which uses the same technology as the World Wide Web) is frequently used as a convenient and effective way to control and distribute information such as institutional clinical practice guidelines. However, there is no guarantee that providing guidelines in an electronic format makes it easier to retrieve the correct information [93,94].

The University of Iowa Department of Medicine, IA, USA has developed an internet-based DSS for the American Thoracic Society/CDC Tuberculosis Preventive Guidelines [95]. The DSS generates a recommendation for tuberculosis prophylaxis based on risk of infection and reactivation. This system functions independently of local patient/hospital databases by using an interactive format and requires the user to input particular patient clinical parameters. Although this limits the ability to provide automatic decision support, it avoids some of the technical problems related to database management and nonuniform data exchange. They compared the effectiveness of the internet-delivered DSS to paper-based resources using clinical scenario testing in a laboratory setting [92]. Two randomly selected groups of medical residents participated in this study. The computer group reached the appropriate recommendation in 92 out of 96 (95.8%) scenarios (eight scenarios × 12 subjects) compared with the scenarios by medical residents using the paper guidelines (77 out of 136; 56.6%; eight scenarios × 17 subjects).

The Royal Melbourne Hospital, Victoria, Australia introduced a web-based antimicrobial approval system in 2001. The system presented the user with accepted indications for ceftriaxone based on the Australian National antibiotic guidelines [96]. For the indication of community-acquired pneumonia, the system asked about the presence of chest X-ray abnormalities. Again, although this system retrieved the patient’s demographic details, it did not interface with any other hospital databases. Despite this, there was a dramatic and sustained reduction in ceftriaxone usage, and the concordance with the antibiotic guidelines increased from 25 to 51% [60].

Electronic (but not web-based) antibiotic approvals are also in use at the Austin Hospital in Melbourne, Australia. Although antibiotic usage rates remained stable during the 18-month evaluation period, there was good concordance with the guidelines for community-acquired pneumonia [97]. Both these systems required substantial education of the end-users to
maximize usage, and did not replace the traditional means of obtaining restricted antibiotics (by phone or referral to the Infectious Diseases Service).

The use of handheld computers or personal digital assistants (PDAs) has become increasingly more common in routine clinical practice with clinicians using them to access drug databases, electronic textbook and other information sources. These devices have the capacity to provide decision support at the point of care.

The Johns Hopkins (MD, USA) intranet-based Antibiotic Guide was evaluated in a study that examined the effectiveness of these guidelines in improving antibiotic prescribing for cellulitis, community-acquired pneumonia, bronchitis and meningitis [98]. In total, 100 junior medical staff were divided into four groups (‘firms’) and were provided with a PDA or advice from a pharmacist, both PDA and pharmacist or neither. A blinded chart review of compliance was performed. During the study period, 335 antibiotic decisions were included in the analysis. The use of the PDA was associated with a nonsignificant reduction in compliance (-3.0%). The infectious diseases knowledge of the medical staff was also tested before and 5 months after the introduction of the PDAs and did not improve. The failure of the PDA tool was attributed to its use in the in-patient setting. As the majority of prescribing decisions were made during ward rounds by more senior doctors, the impact on the junior staff was limited. In addition, providing guidelines in the absence of patient specific information reduces the incentive for use. PDAs are also problematic in that they have limited screen space that significantly affects their usability.

Sintchenko and colleagues used a web-based study to demonstrate that providing a DSS for the treatment of VAP in conjunction with microbiology results increased the agreement with decisions with those of an expert panel from 67 to 95%. The DSS tool (which provided a risk score for VAP) was more effective than electronic VAP guidelines or microbiology reports alone [63]. This experiment used eight simulated cases and evaluated the decision-making performance of 16 specialist infectious diseases and 15 intensive care physicians. Interestingly, the DSS tool was only utilized in a third of all decisions, and required significantly more time to use (average 245 s) than unaided prescribing (113 s), a factor that may impact physician adoption rates in the workplace.

The same group then evaluated the impact of a hand-held device on antibiotic prescribing in a before and after study in a single ICU over a 12-month period [65]. When the same information was provided as a hand-held tool the most frequent reasons for using the system were the microbiology reports (53%), followed by antibiotic guidelines (22%), antiobogram (16%) and VAP risk calculator (9%). Despite the infrequent use of the DSS compared with the large number of antibiotic prescribing decisions made, there was a significant impact on the pattern of prescribing, with a reduction in both total and broad-spectrum antibiotics. The intervention cohort had a reduced length of stay from a mean of 7.15–6.22 days, however, it is not possible to determine if the effect was due to the CDSS.

Cost–benefit analysis of antibiotic decision support
There are no rigorous cost–effectiveness or cost–benefit analyses in the antibiotic CDSS literature. Most published studies report cost avoidance or cost minimization figures. This is usually related to a reduction in antibiotic expenditure per patient or institution [22,30,64,67,99], reduction in the proportion of total drug expenditure [29,67], reduction in length of stay [22,43,65] or reduction in hospitalization costs [22,28]. Those studies with a reduction in institutional antibiotic expenditure reported savings of US$60,000–200,000 per annum.

The costs of development, implementing and maintaining antibiotic DSS are rarely reported in the literature. A few studies described cost in terms of personnel time required to manage the program. Two pharmacy-based systems required a full-time clinical pharmacist to run the program [29,30]. The real cost of advanced ‘home-grown systems’ where content is developed by clinicians who contribute time and expertise gratis, and where the software development is performed ‘in-house’ would be colossal. For example, the costs associated with the development and implementation of a CPOE system at Brigham and Women’s Hospital was US$4.4 million and US$500,000 per year in maintenance. The unrecovered costs were US$3.6 million despite savings of $1 million [79,100].

The high cost of CPOE and the challenges to get physicians to use these programs largely explains the low prevalence of these systems among hospitals both in the USA and Australia [100]. The Leapfrog group estimated that the 5-year projected costs of CPOE in a 200-bed hospital would be US$1.2–7.4 million [101,102]. Implementation of CPOE is time consuming, being in the order of 2 years for most hospitals. In Australia the majority of hospitals lack the foundations required for successful implementation and are in a state of transition between paper-based medical records and electronic medical records.

It would seem intuitive that CPOE would be more effective than other types of antibiotic DSS in improving antibiotic prescribing through alerts and triggers at the time of prescribing, and tracking orders through integration with pharmacy systems. However, this is as yet unproven. For most hospitals, the costs of implementing CPOE far exceed potential savings from drug cost avoidance and ADE avoidance [100]. Other types of antibiotic DSS such as pharmacy- or web-based systems have the potential to be much more cost effective due to the lower development costs, fewer integration requirements and easier implementation. Hence, in the current hospital environment there remains the role for lower cost, standalone antibiotic DSS.

Expert commentary
Although antibiotic DSS appear to be beneficial for improving the quality of prescribing by improving adherence to clinical guidelines and reducing medication error, there is insufficient evidence to show that they can improve patient outcome or prevent the development of antimicrobial resistance. In addition, while most interventions were effective in reducing the costs of antibiotic prescribing, little information is available about overall
Antibiotic DSS are most likely to be effective if they automatically provide decision support as part of the clinical workflow. Antibiotic DSS are heterogeneous but may be grouped into three major types – bedside CDSS that are used by physicians with/without associated computerized physician order entry; pharmacy managed CDSS and web-/personal digital assistant-based CDSS. Antibiotic DSS use many types of decision support logic including rule-based and case-based reasoning, probabilistic networks (Bayesian networks), artificial neural networks and fuzzy logic. Almost all reported antibiotic DSS demonstrate a reduction in costs associated with antibiotic use or length of stay, however, there is insufficient evidence to demonstrate that they prevent the development of antimicrobial resistance. Antibiotic DSS are most likely to be effective as part of a multidisciplinary antibiotic stewardship program. Antibiotic DSS are most likely to be effective if they automatically provide decision support as part of the clinical workflow. There is a need for appropriately designed longitudinal studies to examine the impact of antibiotic DSS (and antimicrobial stewardship programs) on the development of antimicrobial resistance.

References
Papers of special note have been highlighted as:
• of interest
  • of considerable interest
  • Comprehensive review of the current status of decision support systems (DSS) in the Australian and international healthcare setting, and government, institutional and physician-based factors that need to be addressed for the effective implementation of DSS.
10 Fluckiger U, Zimmerli W, Sax H, Frei R, Widmer AF. Clinical impact of an infectious disease service on the...


23 One of several publications about the LDS Hospital’s Health Evaluation through Logical Processing system. This study demonstrated significant reductions in antibiotic mismatches, costs and adverse drug events associated with the use of the antibiotic DSS in the intensive care unit.


34 **Limitations of CDSS literature, particularly the lack of qualitative studies.**


36 Describes features of CDSS likely to improve clinician uptake and practice.


41 **Systematic review of CDSS supporting drug dosing such as heparin, aminoglycosides and warfarin.**


44 Begg EF, Atkinson HC, Jeffery GM, Taylor NW. Individualised aminoglycoside dosage based on pharmacokinetic analysis is...
** A useful paper directed at clinicians outlining the key features of user-friendly DSS.  
• Comparison of performance of various diagnostic CDSS for infections.  
• Discussion about various strategies of antibiotic stewardship such as formulary management, clinical pathways, intravenous to oral conversion and approvals.  

**Websites**


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