Expert Clinical Decision Support Systems to Enhance Antimicrobial Stewardship Programs

Insights from the Society of Infectious Diseases Pharmacists

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Health care–associated infections (HAIs) are a leading cause of in-hospital mortality and adverse events such as antimicrobial resistance. These infections place tremendous burdens on the health care system and create situations for misuse of antimicrobial drugs. Recognition of these factors has led professional societies, clinicians, and hospitals to develop programs to improve the management of HAIs and the use of antimicrobial drugs. The clinical literature is replete with examples of these programs, often referred to as antimicrobial stewardship. Traditionally, antimicrobial stewardship programs have relied on manual methods combined with clinical oversight and intervention. The advent of modern health care information technology offers the opportunity to expand the breadth and depth of these programs. Expert clinical decision support systems are the most promising of these information technology advances.

Key Words: clinical decision support, patient safety, antimicrobial stewardship, infectious diseases, antimicrobial resistance, informatics, computer-assisted therapy.

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OUTLINE

Management of infectious diseases in hospitalized patients is both a patient safety and a cost-of-care issue.[1–4] Health care–associated infections (HAIs) are a challenge at both the population and institutional level. These infections place a tremendous burden of illness on the entire health care system, as manifested by harm to patients, the environment, and the economy.[4–6] The compromises in patient safety that result from these infections are staggering. Approximately 2 million patients each year, or 6% of admissions, develop an infection in the hospital and 90,000 die as a result of the infection.[3, 6, 7] Furthermore, antimicrobial drugs are a leading cause of adverse drug events and thus are a target of patient safety efforts in improving drug use.[8–10]

Equally troubling is the observation that as much as 50% of antimicrobial drug use is inappropriate.[11–13] Suboptimal use of antimicrobial drugs, as well as other factors, has resulted in an alarming rise in resistant HAIs.[7, 14, 15] According to the Centers for Disease Control and Prevention, more than 70% of bacteria that cause HAIs are resistant to at least one of the drugs most commonly used to treat the infection.[15] Inadequate or inappropriate treatment of HAIs, particularly in the intensive care setting, is an important

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determinant of death in the hospital.[16, 17] Patients isolated for certain infectious processes are twice as likely to experience a noninfectious adverse event, of which 73% are preventable, compared with cohorts who are not in isolation.[18]

The financial burdens placed on the health care delivery system as a result of HAIs and misuse of antimicrobials are of great concern. Prevention and management of infections are major cost drivers in hospitals in the United States, with annual economic costs of $6.7 billion in 2002 dollars.[19] Economic models of various types of nosocomial infections have demonstrated substantial excess costs attributed to HAIs that occur in the hospital. A recent investigation reported that infections occurring during hospitalization were associated with 9.58 extra days and $38,656 in extra charges.[20] A study designed to measure attributable costs, rather than charges, found excess costs of $6767 and $15,275 for suspected and confirmed hospital-acquired infections, respectively.[21] Infections acquired during cardiac surgery can add $8200–42,000 to the cost of care, and surgical-site infections diagnosed after hospital discharge average excess costs of $5155/case.[22]

In addition to the extra costs attributed to the management of HAIs, additional extra costs are associated with adverse drug events that result from antimicrobials. Studies have demonstrated that the attributable excess cost of hospital-associated adverse drug events range from $2013 for actual events[23] to $4685 for preventable adverse drug events.[24] Likewise, there are costs associated with treating antimicrobial-resistant nosocomial infections. Recent estimates place annual costs in the United States at $4 billion.[25] Because of the potentially destabilizing economic consequences of antimicrobial resistance, both the Central Intelligence Agency and the World Bank have declared antimicrobial resistance as a national security risk for the United States.[25] In addition, systemic antiinfectives are the largest therapeutic drug class expenditure in nonfederal U.S. hospitals.[26]

Professional societies and individual authors have outlined strategies to prevent or manage the patient safety and economic burdens placed on the U.S. health care system as a result of HAIs and misuse of antimicrobials.[27–33] The plethora of programs to improve antimicrobial use have included formulary manipulations, antibiotic order forms, selective susceptibility reporting, academic counter detailing (education), restriction of pharmaceutical representatives, prior approval, concurrent review with feedback, antibiotic streamlining programs, and antibiotic cycling, to name the most popular. Most, if not all, of these strategies have demonstrated an initial impact; however, holding and sustaining the gains have been difficult.

The future of sustainable antimicrobial stewardship programs appears, like all of health care, to rely heavily on information technology. In fact, the prime directive for effectively improving behavior and working conditions is to embrace technology.[14] Clinical decision support (CDS) systems have been identified to meet this directive in the areas of HAIs and antimicrobial stewardship. In fact, others have stated, "the most innovative and promising approach to the use of antiinfective therapy may be the use of computer-assisted prescribing—user-friendly, expert systems available at the point of use."[32]

Role of Informatics

The current U.S. health care system is often described as undergoing an information revolution. The rapid expansion of scientific and clinical knowledge has changed the health care landscape so that no longer is the question—how much of clinical practice is based in evidence?—but rather—how much of the available evidence is applied at the front lines of patient care? The U.S. National Library of Medicine archives 1500–3500 citations each day Tuesday–Saturday.[34] Much of the evidence (knowledge) is unfiltered and in that state is often unreliable or irrelevant to daily practice.[35] Point-of-care connectivity between the relevant evidence base and patient data is often nonexistent, providing for innumerable delays in decision making and thus subjecting patients to potential harm. Research indicates that if evidence was properly filtered and combined with patient data at the time of clinical decision making, 30–60% of decisions would be different.[35–39] Further complicating the situation is that the unaided human mind has a limited ability to process and incorporate information into decision making; information theory states that 4–7 simultaneous data constructs can be processed before sensory overload occurs.[36, 39]

This human limitation, the explosion of medical knowledge, and the complexities of illness contribute to wide variations in clinical practice, to clinical error, and to poor compliance with guidelines. It is simply unrealistic to believe that modern health care can continue to be delivered without the adoption of information technologies. Research in the field of clinical informatics (an application subfield of medical informatics) has led to the development of health care information technology that enhances decision making by improving the connectivity between patient data and knowledge.[40, 41] Clinical decision support systems are the primary clinical informatics technologies at the nexus of patient-specific and knowledge-based information.

Clinical Decision Support Systems

In a seminal article in the field of clinical informatics,[42] the foundations, goals, and challenges of CDS systems were summarized. In the broadest sense, these applications are tools that focus attention, manage information, and provide for patient-specific consultation. More specific, a CDS system is software that uses individual patient data, population statistics, and computerized clinical knowledge to offer real-time, patient-specific information management, assessment, and recommendations. Six major generic uses (levels) of CDS systems have been defined: alerting, interpreting, assisting, critiquing, diagnosing, and managing decision support.[43]

Clinical decision support systems intelligently filter clinical knowledge and patient-related information and present alerts, interpretations, critiques, and recommendations at the appropriate time. Clinical decision support systems operate on a continuum that includes accessing intelligently filtered information, prompting when appropriate, offering guided choices to enhance care, and providing feedback of outcomes analysis. Another key distinction is the mode used by the CDS system to interact with clinicians, that being active or passive CDS.

Active and Passive Modes

Active CDS systems silently process data and information, automatically communicating with clinicians when current data indicate the need for intervention. Active CDS systems provide guidance and decision support as a by-product of monitoring or data management activities. This mode of the CDS system offers the greatest appeal to busy clinicians since little or no data entry is required of the clinician. Such capability requires that CDS systems have embedded clinical knowledge and that the technology seamlessly interfaces or integrates with a comprehensive patient database (electronic medical record) or all relevant ancillary clinical databases.

The power of active "knowledge-embedded" CDS systems is that they operate in real-time and knowledge is brought to bear immediately without clinicians having to seek it. All six generic uses of CDS systems can be accommodated in an active system. Active CDS systems require careful design, and particular attention to detail is necessary so that the systems are not intrusive and noisy (e.g., generating false-positive alerts). Outputs should be actionable, pithy or concise, patient specific, disease or task specific, and available at the time of care.

Passive CDS systems require more clinician effort compared with active systems. First, clinicians need to recognize when consultation would be useful, and second, they must make a specific request of the system before receiving advice. Passive CDS systems usually operate under three generic styles of use: critiquing, assisting, or diagnosing decision support. Most of the clinical use of passive CDS systems occurs when clinicians want to use the technology as a sounding board for their own ideas or to rule out or limit competing alternatives. Poorly designed passive CDS systems require significant data inputs by the user before generating advice; clinician acceptance is often suboptimal. Thus, like successful active CDS systems, clinically accepted passive CDS systems must interface or integrate with an electronic medical records system or all applicable ancillary databases.

Design Features

Consideration of usability and design issues is paramount to the acceptance and adoption of any technology.[44] Clinical informatics research has identified eight design features of a CDS system that lead to successful adoption of these systems in hospitals[9]:

- Software that makes the clinician's job easier. Clinicians are always looking for easier ways to perform daily tasks and will adopt technology that meets this objective. To accomplish this goal, CDS systems must fit into the clinical workflow and use an intuitive, configurable user interface. Maximum time-saving benefits are realized when active CDS is deployed.
- Educational component to foster user acceptance. Providing literature references as well as important caveats within the application increases adoption and acceptance of

CDS systems as convenient, credible, and trusted knowledge sources.

- Patient-specific consultation, with intelligent filtering of knowledge and patient data. A convenient scorecard for evaluating this feature is the extent to which a CDS system addresses the "5Ws." The CDS software that focuses attention and adds patient context to content (evidence base) allows clinicians to focus on *who* they need to see, *what* data or information they need to look at, *what* course of action (recommendations) to take, *why* that action should be taken (evidence or literature), and *what* should be documented to complete the intervention.
- Real-time operation at the point of care.
- Online feedback and documentation within the application. Online feedback is equally important for both the user and the designer; this feature allows for prompt identification and resolution of critical issues whether they are logical oversights in the knowledge base or software bugs.
- Evidence-based clinical choices. Removing high-end knowledge workers such as physicians and pharmacists from the decision-making process is a mistake. They will resent or reject the system if it challenges their role. Outputs of the CDS system should be recommendations rather than mandates. The recommendations should be supported with appropriately filtered referential material and patient data, thus preserving clinical autonomy. Likewise, when an anticipated choice is contra-indicated, presenting it in proper context, explicitly indicating that it is contraindicated secondary to patient-specific issues, fosters trust and acceptance of the technology. Choice further enhances user acceptance because it recognizes the role of tacit knowledge in any decision-making process and guards against criticisms of "cookbook medicine" and loss of clinical judgment.[45]
- All six aforementioned generic uses. The CDS system that provides alerting, interpreting, assisting, critiquing, diagnosing, and managing decision support demonstrates maximum flexibility and has the broadest user appeal.
- Mandatory adherence to standards for messaging and clinical terminology (vocabulary). Standards are the backbone of technology, ensuring consistency between and interoperability of disparate information systems; standards are fundamental for accuracy and usability.[46]

Messaging and Terminology Standards and Technical Architecture

Standards provide for two main levels of interoperability: functional and semantic. Functional interoperability is accomplished through messaging standards that allow two or more computer systems to exchange information so that it is human readable by the user. Semantic interoperability relies on terminology standards. When information shared by different computer systems is understood at the level of formally defined domain concepts, semantic interoperability occurs between two or more computer systems.

Within the health care system, the major communication standard for functional interoperability is that of Health Level 7.[47] The Health Level 7 standard is a data-interchange standard built on protocols established in March 1987. These protocols define the message format of health care computing interfaces. Version 1.0 was published in September 1987 and, on February 8, 1996, was approved by the American National Standards Institute as the first health care data-interchange American National Standard. The current version of Health Level 7 is 2.5, with version 3 under development.

A variety of clinical terminology standards exist in the health care system, giving meaning to raw data and allowing for semantic inter-operability. Systemized Nomenclature of Medicine (SNOMED)[48] clinical terms are one example of a clinical reference terminology that provides for semantic interoperability. The SNOMED terminology is the most comprehensive international and multilingual clinical reference terminology available in the world. It serves as a taxonomy for a specific set of concepts (e.g., organisms, allergies, device procedures, symptoms) with distinct meaning; the current core terminology contains more than 357,000 health care concepts. Without strict adherence to standards, CDS systems likely would not function properly or satisfy the first design feature, let alone the other six.

The minimum required technical architecture for CDS systems includes a communication engine to access disparate data, a vocabulary engine to accomplish semantic interoperability, a decision support–optimized patient database, a modular knowledge base, and inference engines that interpret and filter patient data and knowledge. Clinicians access and receive alerts, reminders, and guidance from CDS systems through a variety of mechanisms such as e-mail, secure paging, handheld personal data assistants, and Web browsers.

Historic Barriers to System Adoption

The historic barriers to widespread adoption of CDS systems are well known.[49–51] The following seven primary historic barriers have been identified:

- Lack of an health care information technology infrastructure uniformly using Health Level 7 as the communication standard for functional interoperability.
- Slow adoption of clinical terminology standards for semantic interoperability.
- Cost of implementation.
- A health care information technology infrastructure that is optimized for transaction processing.
- Perceived increase in liability risks.
- Suboptimal models for embedding, sharing, and maintaining knowledge.
- Fundamental development or design knowledge has been the purview of a few academic groups.

Significant reductions in implementation costs can be realized if standards for functional and semantic interoperability are widely adopted. This is particularly true for electronic microbiology data, which tend to vary widely in quality and integrity from institution to institution. Most laboratory information systems do not require discrete microbiology data, and as such this creates a significant cost issue when implementing CDS systems in the domain of infectious diseases. Ancillary information systems (such as laboratory and pharmacy information systems) as well as electronic medical record systems are optimized to process large volumes of transactions on a day-to-day basis, often called online transaction processing. The business operations of individual departments and the institution at large are heavily reliant on the capability of these systems to process transactions. Technically and operationally, it is difficult for online transaction processing systems to deliver the six generic uses of CDS systems. Successful CDS systems are optimized to automatically analyze all relevant data (regardless of the source) and process knowledge rather than transactions; an in-depth discussion of these issues is beyond the scope of this discussion.

Skeptics have traditionally resisted adopting CDS systems because of the perception of increased risks of liability if the system is not accessed or the advice is not followed. With respect to the former, a growing body of scientific evidence supports the use of technology, particularly CDS systems, to improve patient safety and quality of care.[52] Computerized provider order entry is becoming the touchstone of patient safety initiatives.[53] The U.S. federal government has demonstrated a growing interest in fostering the development and diffusion of information technology to improve the delivery of health care.[54] In aggregate, these forces and the maturation of health care information technology are driving the standard of care. As health care information technology and CDS systems become more pervasive, negligence may arise from a failure to use these technologies to prevent patient harm—the Hooper principle applied to health care information technology.[55] The perception of increased liability risks when advice is not followed can be mitigated by documenting within the CDS system the reasons for dismissing the alert and/or advice, assuming that those reasons are clinically justifiable. Furthermore, most CDS systems on the market are “open-looped” systems, which means that there is clinician intermediation before a recommendation is followed (e.g., prescribing a drug).

Improved knowledge-engineering techniques, as well as modern software development tools and architectures, have facilitated the development and maintenance of today’s CDS systems. Regardless of the individual barriers, the diffusion of innovations is a major challenge in all industries. Of reassurance, CDS systems, like all technologies, follow a predictable rate of spread called the technology adoption life cycle, based statistically on the number of standard deviations from the mean adoption time.[44] Sufficient evidence exists to support the use of CDS systems as tools for focusing attention, managing information, and augmenting clinical decision making to improve patient outcomes.[56] Historic barriers to adoption are systematically being dismantled as health care information technology redefines the base level of care.

Infectious Diseases–Specific Systems

The management of infectious diseases crosses all specialty boundaries, involves a multitude of causative pathogens and hundreds of generic antiinfective compounds, and usually requires management by clinicians without special training in infectious diseases. Antiinfective agents are usually chosen in a setting of incomplete knowledge of the causative pathogen and a lack of appreciation for the distinct pharmacokinetic and pharmacodynamic properties of the drugs. Antimicrobial misuse most often results from inadequate information rather than inappropriate behavior. Health care information technology and expert CDS systems offer the greatest potential to improve clinical knowledge management and identify situations of antimicrobial misuse. Clinical decision support systems have been shown to improve the empiric, therapeutic, and surgical prophylactic use of antimicrobials.[9, 57–69]

The hallmark of these systems is the capability to address patient-specific problems while accounting for institutional and individual variances. The CDS systems that target infectious diseases and antimicrobial drug use as their focus must adhere to the eight aforementioned design features, as well as to domain-specific requirements. The infectious diseases domain-specific components include organism and drug name hierarchy lexicons, intrinsic and cross-resistance rules, automated antibiograms, antibiotic selection rules, mitigating factor rules, equivalent and alternative agent rules, contraindication rules, drug interaction rules, formulary matching rules, dosing rules, duration-of-use rules, explicit logic and caveat statements, literature references and structured feedback tailored at the syndrome, disease, and recommendation levels. Some of these components are technically trivial, whereas others require sophisticated architectures and design.

The mandatory adherence to organism and drug name hierarchy lexicons (clinical terminology standards) is critical for semantic interoperability. Sophisticated inference engines of CDS systems are required to automatically handle redundant antimicrobial spectra drug combinations and to automatically recognize resistance patterns based on microbial phenotypes. Early systems were designed to examine the susceptibility results of individual antibiotics; more advanced modern expert systems reason across susceptibility results, analyze the data, and infer resistance patterns by predicting the underlying mechanism(s) of resistance. The advantage of the latter approach is that anomalous combinations of phenotypes and organisms can be considered, which allows for more precise predictions of antimicrobial drug choice.

The target functional requirements for a comprehensive CDS system in infectious diseases should be the Centers for Disease Control and Prevention 12-step program to prevent antimicrobial resistance among hospital patients (Table 1).[15] The CDS systems that meet these functional requirements should generate vaccination reminders (step 1) and catheter extended-use alerts (step 2). The computer algorithms of CDS systems should be able to automatically screen for and alert on inconsistencies between patients' antimicrobial drug therapies and their microbiology susceptibility test results, in addition to generating alerts that narrow drug spectrum when appropriate (step 3). To further meet the spirit of step 3, these technologies should contain sophisticated inference engines that can analyze data to infer infectious processes, prompting for proper selection, dosage, and administration of drugs.

The CDS systems should recognize the limitations of their knowledge bases and the complexities of patient factors, recommending human expert consultation in these scenarios (step 4). Parenteral-to-oral antimicrobial switch alerts, automated formulary checking, and evidence-based recommendations for prophylaxis and treatment of defined infections should be standard functions (step 5).

Infectious disease–specific CDS systems should also automatically produce institutionwide and location-specific antibiograms that conform to the latest performance standards of the Clinical and Laboratory Standards Institute (formerly the National Committee for Clinical Laboratory Standards), currently the M39-A guidelines.[70] The technology should use local antimicrobial resistance data derived from CDS system–generated antibiograms to guide empiric drug selection and track emerging resistance (step 6). Well-designed inference engines[71, 72] can discriminate between contaminated and colonized microbiology test results, suggesting interventions other than drugs when contamination or colonization occurs (steps 7 and 8). Target-drug alerts for vancomycin (step 9), as well as alerts for duration of therapy or prophylaxis (step 10), are well within the functional capabilities of CDS systems. Finally, comprehensive CDS systems in the domain of infectious diseases management should include components that alert and recommend for

Table 1. Functional Requirements of Infectious Diseases–Specific Clinical Decision Support Systems in Relation to the Centers for Disease Control and Prevention 12-Step Program to Prevent Antimicrobial Resistance Among Hospitalized Adults

Step and Description	Clinical Decision Support System Requirements for Each Step
Prevent Infections	
1. Vaccinate	Vaccination reminders
2. Remove catheters	Catheter extended-use alerts
Diagnose and treat infections effectively	
3. Target the pathogen	Drug-bug mismatch alerts
	Drug spectrum alerts
	Infer infections
	Timing-of-therapy alerts
	Timing-of-prophylaxis alerts
	Drug dosage alerts
4. Access the experts	Recommend infectious disease consultation when appropriate
Use antimicrobials wisely	
5. Practice antimicrobial control	Parenteral-to-oral switch alerts
	Automated formulary checking
	Automated recommendations for defined infections
	Automated recommendation for prophylaxis
	Evidence-based knowledge bases
6. Use local data	Automated antibiograms
	Automated empiric recommendations
	Track and alert on emerging resistance
7. Treat infection, not contamination	Infer contamination of specimens
8. Treat infection, not colonization	Infer colonization
9. Know when to say no to vancomycin	Target-drug alerts
10. Stop treatment when infection is cured or unlikely	Duration-of-therapy alerts
	Duration-of-prophylaxis alerts
Prevent transmission	
11. Isolate the pathogen	Patient isolation alerts
	Infection control precaution reminders
	Health care–associated infections case-finding alerts
	Patient-based location tracking
	Population-based location tracking
	Clonal detection and alerting
	Target-organism alerts
12. Break the chain of contagion	Hand-washing reminders
	Online infection control information

Adapted from reference 15.

infection control activities (steps 11 and 12).

The major technical limitation to accomplishing these target functional recommendations is the availability of electronic data from an electronic medical records system or ancillary information system. The minimum data for technical feasibility is admission, discharge, and transfer data; pharmacy data; and laboratory data, including microbiology. The availability of electronic surgery and radiology data enhances the clinical utility of an infectious diseases–specific CDS system.

Clinical Experience

Published clinical experience with CDS systems in infectious diseases has primarily come from one group[9, 13, 58–64, 71, 72]; however, other investigators[66–69, 73] have reported on their use of this technology to enhance antimicrobial stewardship programs and HAI surveillance. A wide variety of interventions are facilitated by applying the six generic uses of CDS systems. Alerting decision support has demonstrated benefit in increasing influenza vaccination rates,[65] improving the delivery time of preoperative antibiotics,[63] improving intraoperative dosing,[67] and reducing the duration of postoperative antibiotic use.[64] Alerts for parenteral-to-oral switching, discontinuation of therapy, and the need to change from broad-spectrum to specific therapy have enhanced the effectiveness of antimicrobial stewardship programs.[68] Alerting decision support has been shown to improve the capacity of clinicians to monitor for renal function changes that dictate dosage adjust-ments and pharmacokinetic monitoring.[60, 68] Clinical decision support systems have aided clinicians in monitoring microbiology data and managing inappropriate treatment approaches.[61, 65]

These systems are quickly becoming an essential element in the enlarging role of clinicians who specialize in infectious diseases, whether they are physicians or pharmacists. These tools and the documentation of the interventions that result from their use will enhance and support the role of clinicians in consultation and patient care. The technology will also allow clinical providers to demonstrate the value of their contributions in antiinfective management, patient safety, and detection and control of HAIs. The critical role of CDS systems in successful antimicrobial stewardship programs is self-evident: rather than replacing clinicians, they will greatly assist both the generalist and specialist by increasing their capacities and the reach of their influence.

Conclusion

The emergence of CDS systems as paradigm-shifting technologies that play a deterministic role in the selection of best practices is an encouraging development.[9, 52, 58] Clinical decision support systems have been shown to change behavior in a nonthreatening, defensible manner. These systems facilitate adherence to best practices and increase compliance with guidelines. Although they offer no panacea, such technologies offer the greatest potential to make care safer. Furthermore, the only effective means to control the rate of increases in health care costs is to address the decisions clinicians make about therapy.[74]

The heightened awareness of HAIs and antimicrobial stewardship as sentinel indicators of the quality and safety of patient care is a strong motivator for adopting such innovations. Providing reliable, efficient, and individualized infections management and antimicrobial stewardship requires a mastery of data, information, and knowledge that is achievable with the increased use of CDS systems. The design and functional requirements described in this article can be used to assess CDS systems for overall clinical use as well as antimicrobial stewardship. More than 2 decades ago, one author stated, "I recently proposed an eventual and ultimate solution to the perplexing problems confronting the medical practitioner in arriving at a tentative or definitive diagnosis and in selecting both initial empiric therapy and final definitive treatment for an infectious disease. This solution involves the development of a computer system that would store all of the known data on the clinical, etiologic, pharmacologic, therapeutic, and other aspects of all infectious diseases."[75] Perhaps at the dawn of the 21st century, his solution is becoming a reality.

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