Use of Electronic Health Records and Clinical Decision Support Systems for Antimicrobial Stewardship

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Electronic health records (EHRs) and clinical decision support systems (CDSSs) have the potential to enhance antimicrobial stewardship. Numerous EHRs and CDSSs are available and have the potential to enable all clinicians and antimicrobial stewardship programs (ASPs) to more efficiently review pharmacy, microbiology, and clinical data. Literature evaluating the impact of EHRs and CDSSs on patient outcomes is lacking, although EHRs with integrated CDSSs have demonstrated improvements in clinical and economic outcomes. Both technologies can be used to enhance existing ASPs and their implementation of core ASP strategies. Resolution of administrative, legal, and technical issues will enhance the acceptance and impact of these systems. EHR systems will increase in value when manufacturers include integrated ASP tools and CDSSs that do not require extensive commitment of information technology resources. Further research is needed to determine the true impact of current systems on ASP and the ultimate goal of improved patient outcomes through optimized antimicrobial use.

Keywords. antimicrobial stewardship; clinical decision support system; electronic health record.

Electronic health records (EHRs) and clinical decision support systems (CDSSs) are playing increasingly important roles in the delivery of healthcare services in the United States [1, 2], and show potential for furthering antimicrobial stewardship programs (ASPs). These forms of technology are gradually transforming the US healthcare system from one that is primarily paper based to one that uses electronic technology to provide clinicians with integrated information, enabling them to deliver higher-quality and more efficient care [3]. In fact, the Centers for Medicare and Medicaid Services (CMS) identifies EHRs as "the next step in continued progress of healthcare" [4].

The primary purpose of the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009 was to encourage US physicians and hospitals to adopt EHR systems [5]. An EHR is a longitudinal record of patient health information generated by 1 or more encounters in any care setting [6]. Through HITECH, the federal government may disburse up to $27 billion in incentive payments over a 10-year period, and may award up to $44 000 (through Medicare) and $63 750 (through Medicaid) to individual clinicians [5]. HITECH is also making financial incentives available to qualified institutions as they adopt, implement, upgrade, or show "meaningful use" of certified EHR technology by meeting several predefined objectives established by CMS [7]. Furthermore, the Institute of Medicine has identified EHR functions that are necessary for improving patient safety, supporting delivery of effective care, facilitating chronic disease management, and improving efficiency [8]. These include health information and data, results and order management, decision and patient support, electronic communication and connectivity, administrative processes and reporting, and population health.

Whether EHRs will meet the expectations for improvement in patient care is yet to be determined, and little literature has specifically evaluated the impact of

EHR introduction on antimicrobial use or appropriateness. Although the currently available EHRs offer many practical advantages, their impact on improving antimicrobial use and infectious disease–relevant patient outcomes has been limited, primarily owing to the paucity of included CDSS capability. Although the widespread use of EHRs is a relatively new phenomenon, third-party CDSSs have been used for many years to assist both ASPs and clinicians implement processes consistent with current clinical practice guidelines. CDSSs typically utilize individual patient data coupled with population statistics and computerized clinical guidance to provide patient-specific management recommendations either on clinician request or at the point of care. CDSSs have aided clinicians in selecting appropriate antimicrobial therapy for various infections as well as in avoiding preventable errors, and have been shown to improve the overall quality of care [5]. CDSSs that have been integrated into EHR platforms have been shown to enhance the quality of clinical care and improve patient outcomes [9–12].

The primary objective of this paper is to provide an overview of currently available EHRs and CDSSs, with an emphasis on their role in promoting ASPs. We will provide examples of how these systems can facilitate and enhance ASPs. We will also discuss barriers to implementing and using EHRs and CDSSs, and methods by which these barriers can be overcome.

CAPABILITY REVIEW OF COMMONLY USED EHR PLATFORMS

Today, Epic Systems Corporation (Verona, Wisconsin) and Cerner Corporation (North Kansas City, Missouri) are the EHR vendors with the largest US market share [13]. Until recently, these systems provided little in terms of entry-level options for ASP functionality, but offered tools allowing ASP teams and information technology (IT) departments to develop customized methods for improving antimicrobial use [13]. Given the growing national impetus to implement ASPs, Epic and Cerner are developing software with enhanced stewardship functionality.

The Epic EHR System
Epic Systems Corporation is currently the leading provider of hospital EHRs, and has been especially favored by large hospitals [13]. According to a 2012 report, Epic captured 65% (53 of 82) and 25% (75 of 300) of new-vendor contracts for hospitals with ≥200 and <200 beds, respectively [14, 15]. Of 2950 hospitals receiving federal payments for using "complete EHRs" for inpatients, Epic has almost 20% of the market share [16]. Of interest, in early June 2014, Apple announced a partnership with Epic to create a platform called HealthKit. This platform enables members of healthcare organizations who use Epic's software to link results from health and fitness applications they use, to alert their primary care providers [17].

Various Epic software–based tools have been developed to enhance ASP functionality. Entry-level tools that are currently available include iVents, which can record and communicate ASP recommendations and interventions; antibiotic order forms; dose-checking decision support; a navigator that presents information needed to make an educated decision about patient therapy in one location; "best practice advisories"; 96-hour stop-date notifications; patient prioritization and monitoring forms; intravenous-to-oral algorithms; and order sets [18]. A retrospective analysis showed that iVents use was associated with more ASP recommendations, decreased antimicrobial utilization, significant reduction in nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infections, and a trend toward fewer *Clostridium difficile* infections [19] Moreover, a CDSS integrated with Epic reduced the administration of all antibiotics, anti-MRSA agents, and antipseudomonal agents [20].

A major benefit of Epic for ASP is its interoperability between health systems. The Care Everywhere tool is a secure application that only works with Epic-to-Epic EHR transfers, and it provides a complete account of a patient's medical records and results wherever a patient goes—locally, regionally, or nationally. This is an important tool because the patient's health information arrives immediately in an institution's EHR securely rather than being faxed hours later. Kaelber et al [21] recently showed the value of the Care Everywhere tool in Epic by evaluating providers' perceptions from an integrated tertiary care system in northeast Ohio. Among the 74 survey respondents: 93% agreed that health information exchange through Care Everywhere resulted in more efficient care; 85% agreed that the tool saved time; and 84% and 74% stated that the health information exchange decreased laboratory and imaging use, respectively.

Because Epic's ASP tools have been developed by individual hospitals that often have limited IT resources, more complex functionality, such as the ability to create an institutional antibiogram, has often been absent. An enhanced Epic version to be released in November 2014 will offer an infection control and stewardship module at an additional charge. This updated version will offer preprogrammed "drug–bug" mismatch decision support, improved days-of-therapy calculations (including the option to submit data to the National Healthcare Safety Network–Antimicrobial Use and Resistance [NHSN-AUR] module), and real-time antibiogram reporting. Additional modifications will likely reduce institution-specific configuration requirements for iVents and other existing Epic tools [18]. A significant limitation to the current version of Epic is that hospital-developed configurations cannot be readily shared among institutions.

The Cerner EHR System
Currently, the Cerner Corporation holds the number 2 position in the EMR market, and has been gaining market share. While Epic in the past has been favored by large hospitals, Epic's 5-to-1

advantage over Cerner in new installations in 2010 has shrunk to 2 to 1 in 2012 [13].

As with Epic, Cerner provides little entry-level functionality for ASP. However, the ability to locally customize the software has provided the opportunity for organizations with adequate IT resources to develop some useful tools to assist their local ASP [22]. Similar to Epic, locally developed stewardship enhancements cannot easily be shared with other institutions.

With both the Cerner and Epic systems, order sets that assist clinicians in selecting an appropriate antimicrobial and initiating diagnostic testing are often developed. However, developing and maintaining order sets is labor intensive, and the sets can be easily bypassed. Cerner and Epic software can be modified so that clinicians are required to use a drop-down box to enter antibiotic indications during order entry. This approach encourages prescribers to reflect on their choice of agent and provides the ASP with data that can be used for audits and possible interventions. A single-institution study using a Cerner system showed that indication selection accuracy exceeded 95% [23].

Cerner's customized alert-development feature permits creation of alerts that notify clinicians when they are ordering restricted agents. This feature can prompt the clinician to answer questions that will help to determine whether use of the restricted agent is appropriate, and it also facilitates ASP review of prescriber requests.

Another Cerner capability, M-page, allows custom-aggregated EHR data to be sent to an HTML (hypertext markup language) page. Data on previous antimicrobial treatment, previous culture results, and other diagnostic tests can be formatted so that the ASP can conduct a quick data review for 1 or multiple patients.

Cerner also offers dose-range checking at the point of initial order. However, this capability is rather rudimentary, as organ function is not considered, and there is no capability to react to organ-function changes over time. Also, without careful review and local modification, Cerner dose ranges may conflict with local dosing guidelines, potentially creating confusion among prescribers.

ADD-ON CDSSs

Although EHR systems are being implemented rapidly throughout the United States, they are primarily focused on clinical functionality and patient care, leaving decision-support functionality to be implemented by individual facilities. The scope of CDSS tools included in EHRs are typically limited to medication safety or to generating lists of patients who have specific characteristics or are receiving specific medications. Therefore, many third-party CDSSs have been developed to provide more advanced CDSS and case-finding functionality for ASPs.

Available third-party CDSSs are usually full "software as a service" programs with secure Web-based programs. All of them collate data from multiple sources, including microbiology and pharmacy, and may or may not include patient and coding data. The advantages of these systems are that they can be used without the need for customized builds after a period of interface development and data stream validation. Furthermore, the case-finding and logic capabilities of these programs are currently more robust than those of EHR systems.

Nevertheless, all CDSSs are dependent on their ability to interface with institutional data sources, such as microbiology reports and medication data, and the quality of EHR data. Interface and data quality issues can have a major impact on data fidelity.

Additionally, institutions that have already invested significant capital in implementing an EHR system are reluctant to invest in CDSSs. Therefore, ASPs and infection control departments must often make the case that current EHR systems do not meet their needs and that third-party CDSSs offer major improvements in efficiency and flexibility.

We will provide a brief description of the most commonly used CDSSs today in the following paragraphs. Table 1 summarizes key characteristics of these systems.

TheraDoc

TheraDoc (Hospira, Inc, Lake Forest, Illinois; recently acquired by Premier), one of the first CDSSs, developed out of the highly successful antimicrobial system used at LDS Hospital, Salt Lake City [9, 10]. TheraDoc can be used for ASPs, infection control, clinical care, and medication and adverse drug event monitoring. In contrast to other commonly used CDSSs, it offers access to treatment guidelines. In terms of its patient outcome management and reporting capabilities, the system provides the ability to track unit-based and prescriber utilization as well as drug and unit trends in organism susceptibilities.

TheraDoc has many useful ASP tools, including antimicrobial agent and dose selection assistance, tracking and flagging of resistant pathogens, and tracking antimicrobial utilization (including submission to the NHSN-AUR module). Hospital-wide antibiograms are easily generated. Unit-specific antibiogram data are also available, although limited, and are dependent upon the chosen strategy to account for duplicate isolates.

ASP functionality is primarily accomplished through real-time alerts, which are updated as new culture results become available or antimicrobial agents change. Alerts can be viewed on a computer monitor or transmitted to an e-mail address or pager. Prebuilt alerts include use of specific agents, isolation of resistant pathogens, redundant therapy, antimicrobial de-escalation, and drug–bug mismatch, and customized alerts can easily be created to target specific situations. Alerts can be set up for the entire institution or specific units and include links to pertinent clinical, microbiology, radiology, and medication data, making data review more efficient.

Table 1. Electronic Health Records and Clinical Decision Support Systems Currently Available in the United States

Feature	EHRs		CDSSs				
	Epic	Cerner	TheraDoc (Premier)	SafetySurveillor (Premier)	QC PathFinder (Vecna)	Sentri7 (Pharmacy OneSource)	MedMined (CareFusion)
EHR integration	NA	NA	Yes	No	Yes	Yes	No
Treatment guidelines	Order sets	Order sets	Yes	No	No	Yes (via embedded hyperlinks)	No
Real-time alerts	Yes	Yes (with IT customization)	Yes	Yes	Yes	Yes	Yes
Delayed alerts[a]	Yes	No	No	Yes	Yes	Yes	Yes
Customizable alerts	Yes	Yes (with IT customization)	Yes	Yes	Yes	Yes	Yes
Clinical information	Yes	Yes	Yes	Yes	No	Yes	Yes
Infection control software	Yes	No	Yes	Yes	Yes	Yes	Yes
Institutional antibiogram	Yes	No	Yes	Yes	Yes	Yes	Yes
Unit antibiogram	Yes	No	Yes	Yes	Yes	Yes (available in June 2014)	Yes
Prescriber metrics	Yes	No	Yes	Yes	No	No	Yes
Patient outcome tracking and reporting capabilities	No	No	No	No	No	No	No
Product cost	++++	++++	++++	+++	+++	+++	+++

Abbreviations: +++, >$100K; ++++, >$500K; CDSS, clinical decision support system; EHR, electronic health record; IT, information technology; NA, not applicable.

[a] With the delayed-alert feature, alerts do not occur in real time but 2–3 times a day, depending on how data from the hospital warehouse are uploaded to the server.

Patient interventions can be tracked and reported, and patient rosters generated and utilized by various practitioners. TheraDoc is limited in that patient outcomes reporting is only available for healthcare-associated infections documented in the infection control component. TheraDoc's CDSS can be utilized for medications other than antimicrobials, noninfectious clinical syndromes, and other hospital departments, such as the pharmacy [24]. A limitation of this and most other CDSSs is that data fidelity is essential and small data stream changes may compromise functionality. For example, a change in the code for a medication included within an alert can prevent the alert from functioning.

SafetySurveillor
SafetySurveillor (Premier, Inc, Charlotte, North Carolina) is a system that supports ASP and infection prevention. Like other CDSSs, it integrates microbiology laboratory data with inpatient pharmacy data and has many prebuilt alerts. SafetySurveillor also provides antimicrobial utilization and antibiogram reporting capabilities. Similar to TheraDoc, as there is no feedback loop into the EHR from any CDSS intervention or recommendation, the patient's EHR must be open before any recommendations can be addressed. The University of Wisconsin Hospitals and Clinics created a "best practices alert" tool in the EHR that allows for bidirectional communication between the ASP team and the patient care team based on patients identified by the CDSS [20].

In a randomized 3-month clinical study comparing patient management with the SafetySurveillor to standard management without a CDSS, the ASP team intervened in the cases of 359 patients in the SafetySurveillor arm compared with 180 patients in the control arm [11]. CDSS use reduced the ASP team's workload by 1 hour per day and resulted in antimicrobial cost savings of $84 000. No changes in mortality or hospital length of stay were observed.

SafetySurveillor is currently upgrading all customers to a more comprehensive CDSS platform called SafetyAdvisor. Although the capabilities of SafetyAdvisor do not differ substantially from those of SafetySurveillor, it is easier to perform ASP-related tasks, such as setting up alerts. Similar to TheraDoc, SafetyAdvisor enables the stewardship team to monitor non–infectious disease–related issues.

Quality Compass PathFinder
Funding to develop the Quality Compass (QC) PathFinder (Vecna Technologies, Inc, Cambridge, Massachusetts) came from a National Institutes of Health/National Institute of Allergy and Infectious Diseases grant. The initial version was an electronic infection surveillance software package that reported infection rates to the NHSN, generated healthcare-acquired

infection alerts, created institutional or unit-specific real-time antibiograms, and reported pharmacy-related safety events.

The current version of QC PathFinder offers expanded capabilities, including documentation of ASP interventions; drug–bug mismatch, drug-no-bug or bug-no-drug alerts; and advanced reports based on patient-specific susceptibilities, drug profile, and laboratory values. The "advanced report" feature permits intuitive customization using Boolean operators and simplified retrospective and prospective report generation. The system facilitates various ASP strategies, such as prospective audit with intervention and feedback, regimen streamlining or de-escalation, dose optimization, and intravenous-to-oral conversion. Limitations are the inability to incorporate additional clinical information, such as patient temperature, and failure to use evidence-based treatment guidelines to guide antimicrobial use.

Sentri7

Sentri7 was developed by Pharmacy OneSource (Bellevue, Washington), a company acquired by Wolters Kluwer Health in 2011. Sentri7 was conceived as a real-time patient surveillance system to aid in healthcare interventions and improve quality performance by integrating data from EHR platforms.

Sentri7 capabilities help users implement Infectious Diseases Society of America (IDSA)/Society for Healthcare Epidemiology of America (SHEA) ASP guidelines. Similar to other CDSSs, Sentri7 supports the creation of a real-time antibiogram and supports antimicrobial management by triggering real-time alerts that may be selected from a collection of >150 prebuilt rules. Sentri7 offers antibiotic review when culture and susceptibility reports come back, identifying susceptible and resistant drug–bug combinations.

The distinguishing feature of Sentri7 is that users can easily customize and modify alerts and reports. After issuing an alert, the system provides a "suggested action" field to guide the response based on predefined input. As with TheraDoc, users can program urgent alerts to be sent as e-mail notifications and text messages. Similar to Epic's patient prioritization functionality, a user-defined list enables the ASP team to prioritize their workflow by characterizing patients according to the severity of their condition.

Because it is manufactured by a subsidiary of Wolters Kluwer Health, Sentri7 is integrated with UpToDate, a Wolters Kluwer Health division that produces evidence-based medicine summaries. Sentri7 is also linked to an interventions documentation application, Quantifi, which enables clinicians to document, monitor, and analyze clinical interventions, medication errors, adverse drug reactions, time spent for clinical activities, and associated costs.

A notable limitation of Sentri7 is that reporting drug use, such as defined daily dose or days of therapy, cannot be done

quickly. An upgrade to this function, which would facilitate the reporting of NHSN-AUR data to the Centers for Disease Control and Prevention (CDC), is now under consideration. The current version of Sentri7 does not have significant patient outcome reporting features.

Medmined

Medmined (CareFusion Corporation, San Diego, California) originated at the University of Alabama as a data-mining infection surveillance monitoring service. Today, Medmined can be used to integrate antibiotic utilization data with the medication delivery data maintained by the Pyxis system. Like other third-party CDSSs, Medmined offers real-time alerts, provides customizable alerts, generates ASP reports (such as bug–drug mismatches, restricted antimicrobial alerts, utilization by prescriber and intravenous-to-oral alerts), and creates customizable antibiograms by unit and time period.

VigiLanz and Other CDSSs

VigiLanz (VigiLanz Corporation, Minneapolis, Minnesota) offers a dynamic monitoring suite that includes infection control, adverse event reporting, and an ASP. Similar to other programs, it offers a real-time alert system for ASPs to use and allows tracking and reporting of interventions. The program is customizable, generates reports on costs and patient safety, and can be used for non–antibiotic prescription monitoring.

With so many vendors now in the CDSS market, an institution's choice of provider is based on programmatic needs and the direct and indirect costs of the system to the institution.

EHRs/CDSSs CAN FACILITATE AND ENHANCE ASP STRATEGIES

The IDSA/SHEA guidelines define prospective audit with intervention and feedback, and formulary restriction and preauthorization, as core strategies that provide the foundation for an ASP [25]. Among the supplemental strategies are guidelines, clinical pathways, and streamlining or de-escalation of therapy [25]. The following paragraphs describe the roles that EHRs and CDSSs currently play in carrying out these strategies.

Prospective Audit and Feedback

Prospective audit and feedback is generally accomplished through the review of lists of patients on antibiotics or the generation of alerts for combinations of specific antimicrobials and clinical or microbiology results. CDSSs have previously been relied on to provide the functionality to implement audit and feedback systems [26], but wide implementation of EHRs now offers improved efficiency by providing pertinent patient data in an easily accessible location. For example, the implementation of an EHR at a facility already using audit and feedback

increased the number of charts reviewed by 36.6%; increased the number of antimicrobial recommendations made by 98.1%, with a 124% increase in the number of recommendations accepted; and was associated with a 28.8% decline in antimicrobial use [27]. Both EHRs and CDSSs can assist in patient identification by providing lists of patients on specific antimicrobials for review. Implementation of such a system at a pediatric hospital that identified children on targeted antimicrobials for audit and feedback by the ASP team was associated with significant declines in both antimicrobial use and medication dosing errors [28, 29]. EHRs and CDSSs may also provide new methods for contacting clinicians with recommendations, as described with each software service previously in this article.

Traditionally, ASPs have focused on drug- or laboratory-based audit and feedback methods by reviewing patients who are taking certain agents or who have received specific laboratory results, but it is hoped the implementation of EHRs and CDSSs will facilitate a transition to disease-based audit and feedback. Then, rather than using specific agents or laboratory results to drive audit and feedback, the systems currently being implemented might eventually allow the identification of patients with clinical syndromes who would benefit from ASP intervention (eg, those with pneumonia, skin and soft tissue infection, or urinary tract infection). However, although EHRs supply all the needed data, the clinical decision support process to identify patients in this manner is in its infancy and is not reliably a part of any current EHR.

Additionally, EHR systems can assist in implementing strategies advocated by the CDC to broadly improve antimicrobial use: inclusion of indication and duration on all antimicrobial orders and an "antimicrobial time-out" at 48–72 hours [30]. Requiring an indication has several advantages, including prompting clinicians to consider the reason for ordering antimicrobials, providing a method for communicating the reason for antimicrobial prescribing (particularly useful with frequent provider transitions), and serving as a tool for ASP analysis. The implementation of prespecified indications in EHR within a preapproval system at a tertiary care center significantly improved efficiency and decreased the use of a number of broad-spectrum antimicrobials [31]. Antimicrobial time-outs can be incorporated by prompting or alerting clinicians, ASP, or floor pharmacists when culture results return or when antimicrobials have been active for >72 hours. It should be noted that CMS is currently piloting hospital surveyor worksheets, which include assessments for the implementation of antimicrobial indications and some form of antimicrobial time-out [32].

Formulary Restriction and Preauthorization
Formulary restriction and preauthorization is an IDSA/SHEA core strategy that requires selected antimicrobials to receive enhanced review at both the institutional level, through the

pharmacy and therapeutics committee, and at the patient care level, through informal consultation with an infectious disease specialist or adherence to criterion-based strategies [33].

Criterion-based antimicrobial restriction requires prescribers to select criteria from a predetermined menu before medication dispensing. Reed and colleagues [34] described their experience with this method in a study that used a computer-prescriber order entry system. Over the study period, use of doripenem decreased significantly compared with that of imipenem. Although no patient-specific data were presented, the impetus for the change to doripenem was the desire for pharmacodynamic optimization of carbapenem therapy.

Criterion-based antibiotic restriction may be as simple as requiring completion of an antibiotic order form that assigns an authorization code or documents the approving prescriber [18, 34]. An Australian ASP developed computerized stewardship software that required prescribers to provide an indication for all restricted antimicrobials [31]. The request was reviewed by an infectious disease–trained physician, and feedback regarding approval of the agent and the duration of therapy was provided to the prescriber. Under these circumstances, use of late-generation cephalosporins, glycopeptides, carbapenems, aminoglycosides, and fluoroquinolones decreased. Rates of MRSA and drug-resistant *Pseudomonas* infections also decreased.

Finally, formulary restriction occurs by selectively choosing regimens. Two neonatal intensive care units provided different empiric antibiotic regimens via order sets [35]. There was a significant difference between empiric regimens in the relative risk of subsequent colonization with resistant gram-negative bacilli. Through the creation of order sets, software developers can drive antibiotic prescribing toward a preferred regimen.

Incorporation of Evidence-Based Treatment Guidelines
Incorporating evidence-based treatment guidelines and best-practice pathways into CDSS and EHR platforms is a widely recommended and extensively adopted secondary ASP strategy [25]. Successful ASPs fully embed local clinician–derived consensus guidelines into their respective CDSSs as rules, algorithms, and predictive models [10].

Prompt Modification of Antimicrobial Therapy
The return of microbiology results or fulfillment of clinical criteria should prompt a review of antimicrobial therapy and consideration of whether it is appropriate to streamline or de-escalate therapy [25]. CDSSs can facilitate regimen changes by promptly alerting the infectious disease pharmacist and physician to test results [36, 37]. In one study, use of rapid diagnostic tools to identify *S. aureus* bacteremia, combined with immediate notification to an ASP team member, resulted in a 1.7-day reduction of time to appropriate antibiotic therapy ($P = .002$), a 6.2-day reduction in length of stay ($P = .07$), and a $21 387

reduction in hospital costs (P = .02) [37]. Similar results were demonstrated in studies that combined matrix-assisted laser desorption/ ionization time-of-flight (MALDI-TOF) identification with rapid ASP notification, which showed reductions in time to earlier appropriate therapy, reductions in hospital length of stay, and cost savings of >$20 000 per patient [38–40].

The development of rapid diagnostic tools has moved decisions about streamlining antibiotic therapy to earlier in the treatment course. Often, use of a rapid diagnostic tool is accompanied by use of a CDSS tool, such as an algorithm. It should be noted that the use of rapid diagnostics without systems such as ASP notification or specific CDSSs to prompt changes in therapy may not result in improvements in antimicrobial use [41]. Even in the absence of rapid diagnostics, streamlining can and should occur. In the study performed by Thursky and colleagues [42], a real-time CDSS tool evaluated current antibiotic prescription and microbiology results during patient care rounds and provided a recommendation for antibiotic modification. After deployment of the tool, third-generation cephalosporin utilization significantly decreased (P = .01).

Although many third-party CDSSs, such as TheraDoc, Sentry-7, and SafetySurveillor, can prompt the ASP when de-escalation may be appropriate, this information does not appear in the patient's EHR, and the change must be entered in the EHR if and when the change has been made. ASP recommendations regarding antibiotic de-escalation were accepted >80% of the time in a study in which providers were directed to a navigator that presented all of the information needed to make a decision regarding de-escalation [20]. Prescribers could provide feedback if their recommendation was declined.

The ability to monitor drug dosing in patients with altered renal function is a desirable feature of EHRs and CDSSs. The Epic system can generate a report that shows renal function trends over time or identify patients with a change in renal function over time [18]. M-page in Cerner can be utilized to provide similar data [22]. CDSSs have the capability to follow trends in renal function and alert the clinician when significant changes occur, allowing appropriate alterations in drug dosing to be made in a timely manner. Vendors have implemented these alerts using methods as simple as a defined increase in serum creatinine over a 24-hour period or as complex as the rate of change in the serum creatinine level over a defined period of time. Custom alerts allow the user to define renal function parameters and to associate them with individual drugs or various therapeutic classes.

Ralph et al [43] implemented a custom alert in TheraDoc that identifies patients who are receiving vancomycin and have a ≥30% serum creatinine increase over a 24-hour period. This alert was implemented as an early warning for patients with declining renal function so that vancomycin doses could be adjusted proactively to prevent further worsening of renal insufficiency. The effectiveness of this alert was evaluated by comparing the number of significantly elevated vancomycin trough concentrations (>25 mg/L) in the 6-month period before implementation of this alert with those observed during the 9-month time period after alert implementation. A statistically significant decrease was found in the number of supratherapeutic troughs after alert implementation. An evaluation is currently under way regarding the impact of this alert and subsequent intervention on the incidence of renal insufficiency occurring during vancomycin therapy.

Both EHRs and CDSSs can be used to identify patients who may be eligible for intravenous-to-oral conversions through their alerting feature. Medication profiles of patients who are receiving the parenteral dosage form of drugs that have been identified as targets for conversion are examined for orders for other oral medications. Once a patient has been identified, the stewardship pharmacist or another member of the ASP evaluates whether there are any extenuating circumstances that would prevent the intravenous-to-oral switch. Because this type of alerting mechanism produces many false-positive alerts, the clinician must carefully evaluate each one before initiating an intravenous-to-oral conversion.

BARRIERS AND CHALLENGES TO EHRs AND CDSSs

Challenges of System Implementation and Maintenance

Implementing EHRs and CDSSs is a challenging process for vendors, institutions, and clinicians [44]. Major barriers to implementing these systems include system costs; administrative, ethical, and legal issues; and ineffective implementation because of "alert fatigue."

In the current healthcare market, cost containment is a constant concern for institutions. The global EHR market is projected to reach $22.3 billion by the end of 2015, with the United States accounting for 45% of this amount [45]. In a CDW Healthcare study [46], 200 physician group practices not using an EHR system were surveyed about their primary concerns regarding EHR adoption. Among the respondents, 66% identified hardware and software costs as their chief concern. Moreover, in a study conducted by the Commonwealth Fund [47], estimated EHR costs during the first year after implementation averaged $44 000 per full-time provider and $8500 each additional year per physician. Ninety-one percent of this cost was related to hardware replacement, vendor software maintenance and support fees, and payments for information technology staff or external contractors.

Amatayakul and Hodges [48] examined unforeseen cost issues and observed that "plans for change management, process and workflow improvement, comprehensive training, user support and system ownership are all critically important to EHR

success and require funding, but without the right people and the right team, the initiative can wander—and may very well fail." Another major barrier to implementation of a CDSS both within and external to an EHR is a lack of IT personnel available for development. Creation of decision support within an existing EHR requires many hours to develop, build, and test so that it is both functional and efficient. Many facilities lack the personnel or are unable or unwilling to prioritize the creation of CDSSs to improve antimicrobial use. Although EHR implementation can be expensive, once the systems are fully executed, patient workflow efficiencies could produce up to $150 000 in additional annual revenue and can greatly increase the effectiveness and efficiency of ASP personnel [46]. However, few of these financial gains accrue to the institution (that makes the initial investment), but rather to the third-party payers in the form of avoided errors and improved efficiencies, which translate into reduced claims payments.

Administrative, Ethical, and Legal Issues

Prescribers may regard the adoption of a CDSS to coordinate antimicrobial use with clinical management as subjective and controlling. Providers often fear loss of autonomy in the decision-making process, particularly in cases involving a switch from intravenous to oral therapy, de-escalation strategies, and the use of restricted antibiotics.

Clinicians have safety and ethical concerns about interventions that may harm the patient. There are also concerns about the person who is ultimately responsible for changing therapy and whether intervention decisions can be tracked back to the prescriber or the ASP. Concerns about de-escalating therapy on the basis of electronic alerts must be weighed against what may be an even greater concern—harm caused by excessive antibiotic use. Members of the legal profession are showing greater interest in cases in which the failure to stop, narrow, or change antibiotic therapy results in an adverse event. However, institutions with an ASP should have an approved standard operating procedure in place to ensure that the ASP has team members who are trained and/or knowledgeable about antibiotic use. Also, it is important to ensure that electronic alerts are updated at least annually and that there is a safety net in place, to prevent a premature antibiotic discontinuation/de-escalation based on protocols. Individual patient circumstances should be considered, as patient safety is the ultimate ASP goal. This may mean deferring to provider preferences when unique or unforeseen clinical situations arise.

Given the ethical and legal issues surrounding antimicrobial use, administrators and providers should view CDSSs as quality improvement mechanisms that enhance patient safety and outcomes but never replace good clinical judgment. This outlook will change providers' focus from the "antibiotic police" to a quality of care initiative.

The Challenge of Excessive Alerts

Despite the usefulness of CDSSs' real-time alert-generation capabilities, it is challenging to deal with excessive numbers of alerts that are clinically impractical, even when they meet the criteria for an alert trigger [49, 50]. After implementation of a CDSS for antimicrobial stewardship, the Nebraska Medical Center found that approximately 76% of alerts were nonactionable [26]. ASP personnel can spend significant amounts of time reviewing these alerts. At the Nebraska Medical Center, for example, the review process took approximately 2–3 hours per day [26]. Excessive warnings can result in "alert fatigue," whereby the antimicrobial steward inadvertently disregards clinically relevant alerts, undermining the system's effectiveness and potentially leading to missed opportunities for appropriate interventions [51, 52].

To remedy alert fatigue, end users of CDSSs should provide vendors with continuous feedback about nonactionable alerts [52]. Local solutions include stratifying alerts to highlight only those of the greatest clinical importance and tailoring warnings to the user's clinical environment [52–54]. Vendors may be reluctant to modify alert systems owing to concerns about patient safety and fears about legal liability [55]. Ultimately, CDSS users must realize that clinical judgment cannot be replaced by electronic logic [26]. Clinical vigilance partnered with continuous process improvement can overcome the barrier of alert fatigue.

EHRs/CDSSs and Clinical Impact

The literature dealing with the consequences of using EHRs and CDSSs is currently very limited and has primarily evaluated CDSSs either alone or integrated into EHRs. The impact of EHRs alone on antimicrobial use has not been assessed. Table 2 summarizes the studies that have reported effects of clinical outcomes with CDSS use rather than EHR systems.

Published reports of CDSS studies have focused on 2 major areas of antimicrobial misuse: outpatient acute respiratory tract infections (ARTIs) and inpatient antimicrobial utilization. Studies that have assessed the effects of CDSS use on ARTI prescribing have had mixed results, with one showing a significant decline in inappropriate antibiotic prescribing in rural communities ($P = .03$) [56].

Although several other studies, which assessed the effect of integrating CDSSs directly into the progress note, showed small or nonsignificant changes in inappropriate and overall antibiotic prescribing [57–59]. However, each study found a relationship between access to a CDSS and decreased use of broad-spectrum antibiotics. One factor cited as responsible for the negative outcome was the infrequent use of CDSS forms, which were used only in 6% of ARTI visits in one study [60]. Reasons given by clinicians for not using the form included the need to actively invoke it at the start of the visit, change in workflow, and lack of flexibility once the form was in use.

Table 2. Clinical Decision Support Systems and Patient Outcomes

Reference Number	Study Design	Software	Setting	Results	Notes
[9]	Pre–Post	TheraDoc	ICU	Significant declines in antibiotic susceptibility mismatches, duration of excess drug doses, and orders for antibiotics to which the patient was allergic ($P < .01$). Also had a 70% reduction in ADE ($P = .018$).	No differences in mortality between groups
[10]	Prospective	TheraDoc	Inpatient	22.8% decline in antibiotic use, a $70 per-patient decrease in antibiotic costs, a decline in antibiotic adverse events, and a decline in hospital mortality over a 7-year period (3.65% to 2.65%, $P < .001$).	Time period evaluated was from 1988 to 1994
[56]	Cluster randomized	TheraDoc	Community clinics	Antibiotic prescribing rate declined from 84.1 to 75.3 prescriptions per 100 person-years ($P = .03$). Also reduced inappropriate antibiotic prescribing, from 32% to 5% ($P = .03$).	Macrolides reduced 28%, cephalosporins 7%, and penicillins 6%
[57]	Pre–post	Unknown	PPRnet— outpatients	Inappropriate antibiotic use declined 0.6% for ARI and 16.6% for broad antibiotics in adults.	Modest effect
[58]	Prospective interventional	Unknown	PPRnet	Antibiotic use did not change (+1.57%), decrease in broad antibiotic use for ARI (−16%).	Decreased broad antibiotic use
[59]	Retrospective observational	Unknown	Veterans Affairs— outpatients	Increase in antibiotic usage (0.63 to 0.72, $P = .001$).	No effect seen targeting ARI antibiotics
[60]	Prospective	Local program	Outpatients	Overall antibiotic prescribing 39% vs non-CDSS of 43%. ARI was 54% vs 59%.	CDSS form only used in 6% of ARI visits
[61]	Prospective	TheraDoc	Pediatrics	59% reduction in erroneous antimicrobial use, 28% decline in excess dose-days. No change in ADE or susceptibility mismatches.	
[62]	Cluster-randomized study	TREAT	Inpatient	Better empiric antibiotic therapy (70% vs 57%, $P < .001$). Length of stay and costs (−12%) also reduced.	No impact on mortality
[63]	Survival analysis	TREAT	Inpatient, single center	The ITT group 180-day survival in the control group was 68% vs 71% in the intervention group ($P = .1$). In the PP analysis, the survival percentages were 68% vs 74% ($P = .04$).	Analysis of only 1 center of whole study that analyzed 30-day mortality
[64]	Prospective	Antibiograms	ICU	Increased susceptibility to imipenem (18.3%/year) and gentamicin (11.6%/year).	No clinical outcomes data.

Abbreviations: ADE, adverse drug event; ARI, acute respiratory infection; CDSS, clinical decision support system; ICU, intensive care unit; ITT, intent to treat; PP, per protocol; PPRnet, Practice Partners Research Network.

This suggests that effective CDSSs should be incorporated into established workflows; data should be available to clinicians without requiring them to access a separate form, system, or window; and clinicians should be educated about CDSSs before and after their introduction.

In the inpatient setting, CDSSs have shown much greater effectiveness, with significant declines in antibiotic costs, antibiotic susceptibility mismatches, percentage and duration of excess drug doses, antimicrobial-associated adverse events, and orders for antibiotics to which the patient was allergic [9, 10, 61, 62]. Similarly, this has been demonstrated in pediatric and intensive care unit settings [9, 61]. Additionally,

implementation of CDSSs have also been associated with significant improvements in long-term mortality and gram-negative pathogen susceptibility [63, 64]. It should be noted that the CDSSs that provided these improvements were locally developed and provided point-of-care advice to treating clinicians based on local epidemiology and resistance patterns, making widespread implementation of such systems generally impractical.

Although the ultimate goal of ASPs is to improve patient outcomes, little evidence suggests that current EHRs and CDSSs have a major impact on these outcomes. Available EHRs and CDSSs focus on enhancing the process of care and reporting on process measures, such as intervention acceptance and

antibiotic utilization, but provide few data on patient outcomes. Although some systems report data on adverse events and rates of hospital-acquired infections (including those caused by *C. difficile*), their querying and reporting capabilities are modest to nonexistent. There is now an urgent need for a new generation of EHRs and CDSSs that can provide ASPs with patient outcomes data and that can play a role in improving patient outcomes.

Another desirable feature in future EHRs and CDSSs would be the capability to assist ASPs with diagnosis-based management, not merely drug-based management. As the goal of ASPs gradually evolves from optimal antimicrobial use to optimal management of patients with infectious diseases, it will be important for EHRs and CDSSs to be able to quickly identify patients with signs and symptoms of disorders such as urinary tract infection, pneumonia, and bacteremia, so that appropriate antimicrobial therapy can be initiated in a timely manner and patients will ideally experience improved outcomes.

CONCLUSIONS

This review discusses 2 of the most commonly encountered EHR systems and 6 of the available add-on CDSSs available to date, as well as the application of these systems to ASP. Although this is not a comprehensive review of all systems available, an overview of how EHRs and CDSSs have been utilized for ASP applications has been presented.

Although EHRs and CDSSs demonstrate the potential for promoting appropriate antimicrobial use, this potential for improvement remains relatively untapped. EHR adoption certainly can provide efficient review of pharmacy, microbiology, radiology, and clinical data, which allows ASPs the opportunity to provide a greater degree of impact on inappropriate antimicrobial use. Additionally, implementation of these technologies facilitates the promotion of patient care that is consistent with national and local clinical practice guidelines. Unfortunately, as highlighted above, few data exist linking the use of EHRs or CDSSs with demonstrable improvements in patient outcomes. It is hoped that as the administrative, legal, and technical barriers are overcome, the implementation of CDSS tools directly into EHRs will increase. Whereas ASPs will continue to play a key role in improving antimicrobial use, it is also hoped that the widespread integration of CDSSs within EHRs will have a much more profound effect, as these systems will be able to directly impact prescribing at the point of care. More research is warranted to assess the optimal design for EHRs and CDSSs to provide meaningful decision support and to improve the effectiveness of care while maintaining efficiency and provider autonomy. Additionally, we believe the value of EHR systems for ASPs will increase when manufacturers begin to directly integrate ASP tools within the systems, avoiding the need for extensive commitment of IT resources by the purchasing institution to develop them.

Although these systems provide clear benefit to ASP processes, there is almost no evidence to suggest that these process improvements actually improve patient outcomes. Additional research is needed to determine the true impact of current systems on ASP and the ultimate goal of improved patient outcomes through more appropriate antimicrobial use and a subsequent reduction in antimicrobial resistance. There is an urgent need for a new generation of systems with enhanced patient outcome management and reporting capabilities that can clearly be shown to positively impact patient outcomes.

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