Effects of Computerized Physician Order Entry and Clinical Decision Support Systems on Medication Safety

A Systematic Review

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Background: Iatrogenic injuries related to medications are common, costly, and clinically significant. Computerized physician order entry (CPOE) and clinical decision support systems (CDSSs) may reduce medication error rates.

Methods: We identified trials that evaluated the effects of CPOE and CDSSs on medication safety by electronically searching MEDLINE and the Cochrane Library and by manually searching the bibliographies of retrieved articles. Studies were included for systematic review if the design was a randomized controlled trial, a nonrandomized controlled trial, or an observational study with controls and if the measured outcomes were clinical (eg, adverse drug events) or surrogate (eg, medication errors) markers. Two reviewers extracted all the data. Discussion resolved any disagreements.

Results: Five trials assessing CPOE and 7 assessing isolated CDSSs met the criteria. Of the CPOE studies, 2 demonstrated a marked decrease in the serious medication error rate, 1 an improvement in corollary orders, 1 an improvement in 5 prescribing behaviors, and 1 an improvement in nephrotoxic drug dose and frequency. Of the 7 studies evaluating isolated CDSSs, 3 demonstrated statistically significant improvements in antibiotic-associated medication errors or adverse drug events and 1 an improvement in theophylline-associated medication errors. The remaining 3 studies had nonsignificant results.

Conclusions: Use of CPOE and isolated CDSSs can substantially reduce medication error rates, but most studies have not been powered to detect differences in adverse drug events and have evaluated a small number of "homegrown" systems. Research is needed to evaluate commercial systems, to compare the various applications, to identify key components of applications, and to identify factors related to successful implementation of these systems.

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MEDICATION ERRORS and adverse drug events (ADEs) are common, costly, and clinically important problems.[1-7] Each year, an estimated 770 000 people are injured or die in hospitals from ADEs, which are injuries resulting from drug use.[4,5,8] Adult hospital incidence rates of ADEs have ranged from 2 to 7 per 100 admissions,[2,4,9,10] although determination of a precise national estimate is difficult because studies have used varying definitions.[11] Approximately 28% of ADEs are associated with a medication error and therefore are judged to be preventable.[2] Of preventable ADEs, 56% occurred during drug ordering.[2]

Two inpatient studies, 1 in adults[2] and 1 in children,[7] found that medication errors occurred at rates of more than 5% and that approximately half of all medication errors occurred at the stage of drug order-ing. The principal types of medication errors include missing a dose and incorrect medication doses, frequencies, or routes.[2] The frequency and type of medication errors found depend on the method used to detect them. Other studies,[1] which used a direct observation method to assess how accurately orders are carried out, found high rates of drug administration errors.

Analysis of medication errors suggests that prevention strategies targeting systems rather than individuals are most effective in reducing errors.[12] Computerized physician order entry (CPOE) and clinical decision support systems (CDSSs) are promising interventions that target the ordering stage of medications, where most medication errors and preventable ADEs occur. Despite growing public mandates and the obvious theoretical advantages of these systems, organizational adoption of CPOE and CDSSs has been limited. The much publicized Institute of Medicine

Table 1. Hierarchy of Study Designs*

Level	Study Design	Description
1	Randomized controlled trials	Includes quasi-randomized processes such as alternate allocation
2	Nonrandomized controlled trials	Includes prospectively planned studies with predetermined eligibility criteria and outcome measures or prospective cohort studies that include intervention and control groups
3	Observational studies with controls	Includes retrospective, interrupted time series (a change in trend attributable to the intervention), case-control studies, cohort studies with controls, and health services research that includes adjustment for likely confounding variables
4	Observational studies without controls	Includes cohort studies without controls and case series

*Systematic reviews were assigned the highest to lowest level of study design included in the review, followed by an "A" (eg, a systematic review that included 1 randomized controlled trial and several observational studies with controls was designated "Level 1A-3A").

report *To Err Is Human*[13] drew attention to this "digital divide" between health care and other industrial sectors and called for more widespread adoption of information technology solutions to improve medication safety. Results of recent surveys[14,15] of US hospitals indicate that only 4.3% to 15.0% of hospitals have an electronic medication order-entry system in place. If partially implemented systems and institutions in the process of acquiring systems are included, this figure may be as high as 30%.[14,15] The degree to which health care has lagged behind other sectors in automating complex and hazardous processes is striking. For example, adoption of information technology interventions such as bar coding and automated drug delivery systems to reduce drug administration errors has also been slow. Therefore, we undertook this study to systematically review the cumulative evidence on the effects of CPOE and CDSSs on medication safety.

METHODS

DEFINITION OF CPOE AND CDSSs

Computerized physician order entry refers to a variety of computer-based systems that share the common features of automating the medication ordering process and that ensure standardized, legible, and complete orders. Clinical decision support systems are built into almost all CPOE systems to varying degrees. Basic clinical decision support provides computerized advice regarding drug doses, routes, and frequencies, and more sophisticated CDSSs can perform drug allergy checks, drug–laboratory value checks, and drug-drug interaction checks and can provide reminders about corollary orders (eg, prompting the user to order glucose checks after ordering insulin) or drug guidelines.[16]

Clinical decision support systems may also be implemented without CPOE. Basic CDSSs often assist in tasks such as drug selection, dosing, and duration, and more refined CDSSs can incorporate patient- or pathogen-specific information. The ordering physician may view such advice and then proceed with a conventional handwritten medication order.

STUDY IDENTIFICATION AND SELECTION

Studies were identified by searching the US National Library of Medicine MEDLINE electronic bibliographic database and the electronic Cochrane Library. The MEDLINE search strategy was performed using the following MeSH terms: *hospital information systems*; *decision support systems, clinical*; and *drug therapy, computer-assisted*. In addition, we searched for key title words related to computerized order entry and combined the results of these searches with MeSH terms capturing adverse events and medical errors: *medical error*, *iatrogenic disease*, *sentinel surveillance*, and *safety*. The Cochrane Library was searched using similar key terms and title words. Reference lists from all relevant articles, including 2 systematic reviews,[17,18] were reviewed to identify additional primary studies.

Specifically, we sought articles describing computerized systems for per-

forming general order entry or CDSSs for guiding physicians in the order-writing process. Computerized programs that screen for potential ADEs were not included, unless they interact with users during the order-writing process,[10,19,20] and neither were CDSSs built into programmable intravenous infusion pumps.[21-23] Although both of these practices play a role in improving medication safety, they do not affect the stage of order writing, which is the focus of this review.

STUDY EVALUATION

Two of us (R.K. and K.G.S.) reviewed all the articles to determine the level of evidence for practice effectiveness using frameworks developed by the University of California San Francisco–Stanford Evidence-Based Practice Center for the evaluation of study design (**Table 1**) and measured outcomes (**Table 2**).[24] This classification scheme was developed because of the heterogeneous nature of the studies evaluating CPOE and CDSSs. The scheme incorporates features of existing frameworks and recommendations for evaluating and synthesizing evidence.[25-31] We included articles with a minimum level 3 study design (observational studies with controls) and level 2 outcomes (surrogate clinical outcomes). Studies that reported a mixture of level 2 and level 3 outcomes (outcomes with an indirect or unestablished connection to the target safety outcome) were included, as had been decided prospectively. Disagreements were resolved by discussion.

OUTCOME DEFINITIONS

Medication errors are errors in the process of ordering, transcribing, dispensing, administering, or monitoring medications. One example is an order written for acetaminophen without a route of administration. Medication errors include a mixture of errors with differing potentials for patient injury.

Potential ADEs are medication errors with significant potential to harm a patient that may or may not actually reach a patient. An example of an intercepted potential ADE is an order written for a morphine overdose that is noticed and corrected by a pharmacist before the drug is administered. An example of a noninterrupted potential ADE is an administered overdose of morphine to a patient who does not have any sequelae. Medication errors and potential ADEs were considered surrogate outcomes (level 2).

Adverse drug events are injuries resulting from drug use and therefore con-

stitute clinical outcomes (level 1). Adverse drug events associated with a medication error are considered preventable, whereas those not associated with a medication error are considered nonpreventable. An example of a preventable ADE is the development of a rash after the administration of penicillin to a known penicillin-allergic patient. In contrast, a nonpreventable ADE is the development of a penicillin-associated rash in a patient with no known previous allergies.

Nonintercepted serious medication errors include nonintercepted potential ADEs and preventable ADEs (ie, medication errors that either have the potential to or actually cause harm to a patient). Errors that are not intercepted and have the potential to or actually cause injury are the most important from the perspective of patient safety.

DATA EXTRACTION AND ANALYSIS

Studies were grouped into 2 categories: those evaluating CPOE with CDSSs and those evaluating CDSSs alone. No studies were found assessing CPOE alone. We did not quantitatively score the quality of the studies owing to the recognized difficulties in quality scoring in general[29,32] and especially for a heterogeneous group of studies such as those included in this review. Nonetheless, both reviewers abstracted each study for prospectively determined elements pertaining to methodological quality.[33] In addition, the reviewers described the study design, setting, outcomes, and results. Other extracted information included data regarding potential harm from the practice and issues regarding cost and implementation.

RESULTS

STUDY DESIGN AND SETTINGS

Twelve studies met the inclusion criteria for study design and measured outcomes. The 5 studies listed in **Table 3** evaluated CPOE with CDSSs.[34-38] In the first study,[34] investigators at the Regenstrief Institute for Health Care (affiliated with the Indiana University School of Medicine, Indianapolis) conducted a randomized controlled trial of 2181 patients evaluating the effects of CPOE on corollary order prescribing.[35-38] The remaining 4 studies[35-38] evaluated the CPOE system at Brigham and Women's Hospital

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Table 2. Hierarchy of Outcome Measures

Level	Outcome Measure	Description
1	Clinical outcome	Any measure of morbidity or mortality including adverse drug events as defined in the "Outcome Definitions" subsection of the text.
2	Surrogate outcome	Observed errors, intermediate outcomes (eg, laboratory test results) with a well-established connection to the clinical outcomes of interest (usually adverse events)
3	Other	Other measurable variables with an indirect or unestablished connection to the target safety outcome (eg, pretest/post test after an educational intervention and compliance with "optimal" or "recommended" prescribing practice)
4	None	No outcomes relevant to decreasing medical errors or adverse events (eg, the study describes an approach to detecting errors but reports no measured outcomes)

Table 3. Studies of Computerized Physician Order Entry (CPOE) With Clinical Decision Support Systems (CDSSs)

Source	Study Description	Study Design	Study Outcomes	Results
Overhage et al,[34] 1997	Impact of faculty and physician reminders (using CPOE) on corollary orders for 2181 adult inpatients in a general medical ward at a public teaching hospital affiliated with the Indiana University School of Medicine	Level 1 (RCT with physicians randomized to receive reminders or not)	Level 2 and 3 (errors of omission in corollary orders)	25% Improvement in ordering of corollary medications by faculty and residents ($P<.001$)
Bates et al,[35] 1998	CPOE with CDSSs for 6771 adult inpatients on medical, surgical, and intensive care wards at BWH, a tertiary care center affiliated with Harvard University	Levels 2 and 3 (2 study designs)	Level 1 (ADE rates) and level 2 (serious medication errors)	55% Decrease in nonintercepted serious medication errors ($P = .37$) and 17% decrease in preventable ADEs ($P = .37$)
Bates et al,[36] 1999	CPOE with CDSSs for 1817 adult inpatients in 3 medical units at BWH	Level 3 (retrospective time series)	Level 1 (ADEs) and level 2 (main outcome measure was medication errors)	81% Decrease in medication errors ($P<.001$) and 86% decrease in nonintercepted serious medication errors ($P<.001$)
Teich et al,[37] 2000	CPOE with CDSSs for all adult inpatients at BWH	Level 3 (retrospective before-after analysis)	Levels 2 and 3 (changes in 5 prescribing practices)	Improvement in 5 prescribing practices ($P<.001$ for each of the 5 comparisons)
Chertow et al,[38] 2001	CPOE with a CDSS to adjust drug dose and frequency in 7490 adult inpatients with renal insufficiency at BWH	Level 1 (RCT with a crossover design)	Level 2 (inappropriate drug dose and frequency)	13% Decrease in inappropriate dose ($P<.001$) and 24% decrease in inappropriate frequency ($P<.001$)

Abbreviations: ADE, adverse drug event; BWH, Brigham and Women's Hospital; RCT, randomized controlled trial.

(BWH). The first BWH study[35] was a cross-sectional analysis of 6771 patients comparing an intervention period of CPOE with CDSSs with a historical period, the next 2 BWH studies[36,37] were time series analyses, and the final BWH study[38] was a randomized controlled trial with a crossover design of 7490 patients.

Table 4 lists 7 studies[39-45] that evaluated isolated CDSSs; 6 were randomized controlled trials and 1 was a prospective before-after analysis. All of these studies were conducted in the inpatient setting. Burton et al[39] assessed the use of a computerized aminoglycoside dosing program for 75 patients at the Dallas Veterans Affairs Medical Center in Texas. Evans et al,[40,41] at LDS Hospital, Salt Lake City, Utah, performed 2 studies on antibiotic CDSSs: a randomized controlled trial[40] of empiric antibiotic drug selection using CDSSs with 451 patients and a cross-sectional analysis[41] comparing an intervention period of a computer-assisted anti-infective drug management program with a historical control period for 1136 patients in the intensive care unit. Casner et al[42] and Hurley et al[43] performed randomized controlled trials of computerized theophylline dosing programs with 17 and 48 patients, respectively. Mungall et al[44] evaluated a heparin dosing program for 25 inpatients, and White et al[45] evaluated a warfarin dosing program for 39 inpatients. In summary, many of the CDSS studies had small sample sizes and consequently were underpowered.

Table 4. Studies of Clinical Decision Support Systems (CDSSs)

Source	Study Description	Study Design	Study Outcomes	Results
Hurley et al,[43] 1986	Use of a computerized theophylline dosing program for 48 inpatients at Preston and Northcote Community Hospital, Northcote, Victoria	Level 1 (RCT)	Level 1 (clinical manifestations of theophylline toxicity; level 2 (toxic serum theophyliline levels)	2 Patients with clinical toxicity in control group vs none in study group ($P = .13$) Lower rates of toxic levels in intervention patients (18.9%) vs controls (37.8%) ($P = .04$)
White et al,[45] 1987	Use of a computerized warfarin dosing program for 39 inpatients at Veterans Administration Medical Center, Palo Alto, Calif, or the University of California, Davis, Medical Center	Level 1 (RCT)	Level 1 (bleeding complications); level 2 (overanticoagulation)	None of the intervention patients had bleeding complications vs 3 control patients (8%) ($P = .07$) Fewer intervention patients were over anticoagulated (5% vs 17%) ($P = .11$)
Burton et al,[39] 1991	Use of a computerized aminoglycoside dosing program for 75 inpatients at the Dallas Veterans Affairs Medical Center, a 680-bed tertiary care center in Texas	Level 1 (RCT)	Level 2 (toxic serum aminoglycoside levels)	Lower rates of toxic levels in intervention patients (5.6%) vs controls (9.3%) ($P = .40$)
Casner et al,[42] 1993	Use of a computerized theophylline dosing program for 17 inpatients at the Thomanson General Hospital, El Paso, Tex	Level 1 (RCT)	Level 1 (clinical manifestations of theophylline toxicity); level 2 (subtherapeutic or supratherapeutic serum theophylline levels)	No significant differences in any outcome. One patient (6%) in study group exhibited signs of toxicity vs none in control group ($P = .30$). One patient in each group had a toxic level ($P = .90$); proportions of patients with subtherapeutic levels was 23.5% for study group and 16.7% for control group ($P = .60$)
Evans et al,[40] 1994	Use of a computerized antibiotic drug selection consultant for 451 inpatients at LDS Hospital, a 520-bed community teaching hospital and tertiary referral center in Salt Lake City, Utah	Level 1 (RCT with a crossover design)	Level 2 (1 of 5 primary outcomes was pathogen susceptibility to prescribed antibiotic regimens)	17% Greater pathogen susceptibility to an antibiotic drug regimen suggested by a computer consultant vs physicians ($P<.001$)
Mungall et al,[44] 1994	Use of a computerized heparin dosing program for 25 inpatients at McLaren Regional Medical Center in Flint, Mich, and Midland Regional Medical Center, Midland, Mich	Level 1 (RCT)	Level 1 (bleeding events)	Fewer intervention patients bled (4.2%) vs controls (7.7%) ($P = .6$)
Evans et al,[41] 1998	Computer-based anti-infective drug management program for 1136 patients from a 12-bed ICU at LDS Hospital	Level 2 (prospective before-after analysis)	Level 1 (one primary outcome was ADEs due to anti-infective agents)	70% Decrease in ADEs caused by anti-infective agents ($P = .02$)

Abbreviations: ADE, adverse drug event; ICU, intensive care unit; RCT, randomized controlled trial.

STUDY OUTCOMES

Most of the included CPOE studies primarily measured level 2 and level 3 outcomes because level 1 outcomes are significantly less frequent. Therefore, larger and longer studies are necessary to measure the effects of an intervention on ADE rates, and the costs of such studies are very high. The first 2 BWH studies[35,36] primarily measured nonintercepted serious medication errors (level 2) and medication errors (level 2) but also included ADEs as a secondary outcome (level 1). The other 3 CPOE studies reported level 2 and level 3 outcomes (ie, prescribing practices,[37] corollary orders,[34] and appropriate drug dose and frequency[38]). Corollary orders (level 2 and level 3 outcomes) are orders needed to detect or ameliorate potential effects of a trigger order, for example, ordering regular laboratory tests of coagulation status after starting a patient on intravenous heparin therapy.

Similarly, the studies evaluating CDSSs report level 1 and level 2 outcomes, with level 1 outcomes often a secondary end point. Burton et al[39] reported rates of toxic serum aminoglycoside levels (level 2). Evans et al determined rates of pathogen susceptibility to an antibiotic drug regimen (level 2)[40] and rates of anti-infective drug–associated ADEs (level 1).[41] Casner et al[42] and Hurley et al[43] reported rates of toxic serum theophylline levels (level 2). Mungall et al[44] and White et al[45] reported bleeding complications (level 1), and White et al[45] also reported overanticoagulation rates (level 2).

CPOE AND MEDICATION SAFETY

The first BWH study[35] assessing the impact of CPOE with CDSSs demonstrated a 55% decrease in nonintercepted serious medication errors ($P=.01$). As a secondary outcome, this study found a 17% decrease in the preventable ADE rate, which was not statistically significant ($P=.37$). The CPOE application at the time of this study included only basic decision support, with limited checking for allergies and drug-drug interactions. The second study,[36] a time series analysis, evaluated medication error rates before CPOE and in the 3 years subsequent to its implementation. It demonstrated an 81% decrease in medication errors and an 86% decrease in nonintercepted serious medication errors ($P<.001$ for both). This study found a decrease in the rate of ADEs per 1000 patient-days from 14.7 to 9.6 during the study ($P=.09$) and a decrease in the number of preventable ADEs from 5 to 2 ($P=.05$).

The remaining 3 studies assessed more specific types of medication errors. Overhage et al[34] demonstrated a greater than 25% improvement in the rates of corollary orders with implementation of computerized reminders. Teich et al[37] demonstrated 5 prescribing improvements in types, doses, and frequencies of drug use with the implementation of computerized clinical decision support. Finally, Chertow et al[38] demonstrated a 13% decrease in inappropriate dose and a 24% decrease in inappropriate frequency for nephrotoxic drugs in patients with renal insufficiency ($P<.001$ for both).

CDSSs AND MEDICATION SAFETY

Three of the studies assessing isolated CDSSs evaluated computerized antibiotic drug advice and demonstrated lower rates of toxic levels, improved pathogen susceptibility, and a decreased anti-infective drug–associated ADE rate. Burton et al[39] evaluated a computerized aminoglycoside dosing program and demonstrated lower rates of toxic levels in intervention patients, but the results were not statistically significant ($P=.40$). Evans et al[40] demonstrated a 17% greater pathogen susceptibility to an antibiotic drug regimen suggested by a computer consultant vs a physician ($P<.001$). In another study, Evans et al[41] reported a 70% decrease in ADEs caused by anti-infective agents through use of a computer-based anti-infective drug management program ($P=.02$).

Two other studies evaluated theophylline dosing. Casner et al[42] demonstrated no difference in rates of toxic serum levels. In contrast, Hurley et al[43] demonstrated significantly lower rates of toxic levels in intervention patients (18.9%) than in control patients (37.8%) ($P=.04$).

The final 2 studies evaluated anticoagulation agents. Evaluation of a heparin dosing system demonstrated lower rates of bleeding events in intervention patients (4.2%) vs control patients (7.7%), but without statistical significance ($P=.6$).[44] Similarly, evaluation of a warfarin (Coumadin) dosing program demonstrated lower rates of bleeding complications (0% vs 8%) and overanticoagulation rates (5% vs 17%), but neither result was statistically significant ($P=.11$).[45]

COMMENT

These studies provide evidence that the use of CPOE with CDSSs significantly decreases medication error and serious medication error rates at 2 institutions with "homegrown" systems. However, the effect on ADE rates has not been adequately tested because studies with sufficient power have not been performed. There is a strong correlation between medication errors and ADEs, so such applications will almost certainly reduce ADE rates. Nevertheless, medication errors have widely varying potential for harm, and it seems easiest to prevent those that rarely cause injury.[35,36]

Some of the CDSS studies,[40,41,43] particularly those evaluating antibiotic drug–associated programs, demonstrated focal reductions in medication errors with statistical significance as well as some decreases in ADE rates. Although other CDSSs tended to have statistically insignificant results, these studies[39,42,44,45] were underpowered, with sample sizes of 17 to 75 patients. Comprehensive applications, including CPOE and sophisticated decision support, will likely have the greatest effect.

One important question is whether the currently available data are sufficiently compelling that CPOE should be widely adopted or whether further research is required. We believe that further studies targeted at a few critical questions are desirable

but not a requirement before widespread adoption. For example, a multicenter study evaluating the impact of CPOE on ADE rates would cost tens of millions of dollars and would be hard to perform because CPOE is a complex application touching on so many parts of the clinical and information systems. Instead, research should focus on questions such as the following: What are the differences among various CPOE systems? What are barriers to adoption? What are the key decision support elements? How effective are specific pieces of decision support? How should these applications be implemented in community hospitals?

Most studies of CPOE have assessed only 2 internally developed (homegrown) systems. To date, dissemination of these systems has been limited for a variety of reasons. Most hospitals use commercial systems. Relatively few vendors have CPOE applications that have broad use at more than a handful of hospitals. As with evaluations of therapeutic agents, there is a reasonable expectation of a class effect[46] with many CPOE systems, but classes of CPOE remain to be established. For example, CPOE systems with no decision support will almost certainly decrease error rates less than systems with sophisticated decision support. Thus, one area for further research consists of developing tools to assess the extent to which a specific commercial CPOE application will reduce the medication error rate or the preventable ADE rate. Comparisons among such commercial products will likewise be informative.

Organizational adoption of CPOE has been limited. One survey[14] of 668 hospitals indicated that 15% had at least partially implemented CPOE. A more recent survey[15] of pharmacy directors at 1091 acute care hospitals in the United States (49% response rate) reported that 4.3% of hospitals had an electronic medication order-entry system in place.

Many barriers to CPOE adoption exist. Rogers[47] suggests that perceived attributes of an innovation and organizational social context strongly affect the innovation adoption rate. Perhaps most important, a health care institution must garner financial and organizational support before introducing CPOE with CDSSs. Computerized physician order entry requires large up-front capital investment with more remote, albeit substantial, returns. Such investment is especially challenging when organizations are losing money. In addition to the financial obstacles, implementing sophisticated new clinical information systems presents substantial organizational challenges owing to the impact on institutional culture and clinical workflow[48-51] and the need to accommodate existing institutional systems used for billing, laboratory, and pharmacy data.[52]

In addition, the efficacy of individual decision support elements warrants further investigation. Many of the CDSS studies included in this review produced nonsignificant results. Yet, it is difficult to draw definitive conclusions because of the small sample sizes. Larger studies need to be performed, as do studies identifying key, successful decision support elements.

COSTS AND BENEFITS OF CPOE AND CDSSs

Purchasing commercial CPOE systems is generally more expensive than is internally developing systems. Brigham and Women's Hospital has reported costs of $1.9 million for developing and implementing CPOE in 1992, with ongoing maintenance costs of $500 000 per year, although this was incremental to what was already a highly developed clinical system.[53] Fewer data are available regarding the cost of purchasing and implementing large commercial systems, but it may be on the order of tens of millions of dollars, especially if related clinical applications such as a clinical data repository must be upgraded. Several studies[34,37,54] report that only minimal resources are needed to introduce or maintain decision support programs into existing order-entry programs.

The beneficial effects of CPOE systems extend beyond medication safety and include reduced costs and quality improvement. These benefits have been achieved by providing feedback about the appropriateness and costs of laboratory and radiologic tests, easy implementation of clinical pathways, improved quality measurement, and improved coding and billing. Brigham and Women's Hospital estimated net savings of $5 to $10 million per year for the CPOE system.[55] In a randomized controlled clinical trial, Tierney et al[56] demonstrated that CPOE linked to a comprehensive electronic medical record system resulted in charges that were $887 (12.7%) lower per admission. Cost savings associated with averted ADEs may be considerable. For example, BWH, a 720-bed academic institution, estimated costs before CPOE implementation of $2.8 million annually for preventable ADEs.[57] Evans et al[58] reported a $100 000 per year cost avoidance with a computer-assisted antibiotic drug dosing program attributable to decreased antibiotic drug use and avoided ADEs.

POTENTIAL FOR HARM

As with any other technology, CPOE and CDSSs may introduce different types of medication errors. Incorrect default dosing or route suggestions may lead to potentially erroneous orders. For example, the first time series analysis[36] at BWH demonstrated an initial increase in intercepted potential ADEs attributable to the ordering screen structure for potassium chloride, which made it easy to order large doses of intravenous potassium. Once identified, this error was rectified, but this event underscores the importance of ongoing close scrutiny of CPOE and CDSSs. In general, as users become accustomed to CPOE and CDSSs, they are likely to accept computer suggestions with minimal reflection,[59] emphasizing the importance of testing decision support default settings and suggestions.

When CPOE systems are not electronically linked to computerized pharmacy systems, pharmacists must manually reenter orders into the pharmacy system, with a resultant increase in chance of error. Pedersen et al[15] found that 25.7% of surveyed hospitals with electronic prescribing lacked information system linkages to pharmacy systems.

The trigger level for computerized warnings must be set to the appropriate sensitivity. In situa-

tions with a potential for significant harm, it is important that providers receive warnings without being overwhelmed by alarms of marginal value. Hardware outages and software instability pose further risks. In particular, the reliability needed for CPOE is much higher than that required for systems that simply report laboratory test results. Finally, physicians can electronically write an order in the wrong patient's record, analogous to handwriting an order in the wrong patient's medical chart.

PRESENT LEGISLATION AND PUBLIC MANDATES

In the meantime, public and private groups are increasingly demanding implementation of CPOE and other information technologies. The Leapfrog Group, a consortium of companies that belong to the Business Roundtable, has endorsed CPOE in hospitals as 1 of 3 changes that would most improve patient safety in the United States.[60] A Medicare Payment Advisory Commission report[61] suggested instituting financial incentives for CPOE implementation. Legislation has also been introduced at the federal and state levels. United States Senators Bob Graham (D-Fla) and Olympia Snowe (R-Maine) recently introduced a bill, titled the "Medication Errors Reduction Act of 2001," to establish an informatics system grant program for hospitals and skilled nursing facilities.[62] At the state level, California recently enacted legislation stipulating that acute-care hospitals implement information technology such as CPOE to reduce medication-related errors.[63]

In conclusion, use of CPOE and isolated CDSSs significantly decreases medication error rates and provides other important benefits related to medication use. Funding constraints and public pressure to bridge the digital divide in health care make a large trial comparing paper ordering to sophisticated CPOE systems unlikely. However, a need exists for research evaluating commercial systems, the relative benefits of different classes of systems, and factors related to successful implementation of these systems.

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REFERENCES

1. Barker KN, Mikeal RL, Pearson RE, Illig NA, Morse ML. Medication errors in nursing homes and small hospitals. *Am J Hosp Pharm.* 1982;39:987-991.
2. Bates DW, Cullen D, Laird N, et al. Incidence of adverse drug events and potential adverse drug events: implications for prevention. *JAMA.* 1995; 274:29-34.
3. Dean BS, Allan EL, Barber ND, Barker KN. Comparison of medication errors in an American and a British hospital. *Am J Health Syst Pharm.* 1995; 52:2543-2549.
4. Classen DC, Pestotnik SL, Evans RS, Lloyd JF, Burke JP. Adverse drug events in hospitalized patients: excess length of stay, extra costs, and attributable mortality. *JAMA.* 1997;277:301-306.
5. Cullen DJ, Sweitzer BJ, Bates DW, Burdick E, Edmondson A, Leape LL. Preventable adverse drug events in hospitalized patients: a comparative study of intensive care units and general care units. *Crit Care Med.* 1997;25:1289-1297.
6. Lesar TS, Lomaestro BM, Pohl H. Medication-prescribing errors in a teaching hospital: a 9-year experience. *Arch Intern Med.* 1997;157:1569-1576.
7. Kaushal R, Bates DW, Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. *JAMA.* 2001;285:2114-2120.
8. Cullen DJ, Bates DW, Small SD, Cooper JB, Nemeskal AR, Leape LL. The incident reporting system does not detect adverse drug events: a problem for quality improvement. *Jt Comm J Qual Improv.* 1995;21:541-548.
9. Bates DW, Boyle DL, Vander Vliet MB, Schneider J, Leape LL. Relationship between medication errors and adverse drug events. *J Gen Intern Med.* 1995;10:199-205.
10. Jha AK, Kuperman GJ, Teich JM, et al. Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. *J Am Med Inform Assoc.* 1998;5:305-314.
11. US General Accounting Office. *Adverse Drug Events.* Washington, DC: US General Accounting Office; 2000. Publication No. GAO/HEHS-00-21.
12. Leape LL, Bates DW, Cullen DJ, et al. Systems analysis of adverse drug events. *JAMA.* 1995; 274:35-43.
13. Institute of Medicine. *To Err Is Human: Building a Safer Health System.* Washington, DC: National Academy Press; 1999.
14. Ash JS, Gorman PN, Hersh WR. Physician order entry in US hospitals. *Proc AMIA Symp.* 1998; 235-239.
15. Pedersen CA, Schneider PJ, Santell JP. ASHP national survey of pharmacy practice in hospital settings: prescribing and transcribing—2001. *Am J Health Syst Pharm.* 2001;58:2251-2266.
16. Bates DW, Cohen M, Leape LL, Overhage JM, Shabot MM, Sheridan T. Reducing the frequency of errors in medicine using information technology. *J Am Med Inform Assoc.* 2001;8:299-308.
17. Walton RT, Harvey E, Dovey S, Freemantle N. Computerised advice on drug dosage to improve prescribing practice. *Cochrane Database Syst Rev.* 2001;1:CD002894.
18. Hunt DL, Haynes RB, Hanna SE, Smith K. Effects of computer-based clinical decision support systems on physician performance and patient outcomes: a systematic review. *JAMA.* 1998;280: 1339-1346.
19. Raschke RA, Gollihare B, Wunderlich TA, et al. A computer alert system to prevent injury from adverse drug events: development and evaluation in a community teaching hospital. *JAMA.* 1998;280:1317-1320.
20. Rind DM, Safran C, Phillips RS, et al. Effect of computer-based alerts on the treatment and outcomes of hospitalized patients. *Arch Intern Med.* 1994;154:1511-1517.
21. Theil DR, Stanley TE III, White WD, et al. Mid-

azolam and fentanyl continuous infusion anesthesia for cardiac surgery: a comparison of computer-assisted versus manual infusion systems. *J Cardiothorac Vasc Anesth*. 1993;7:300-306.

22. Ruiz R, Borches D, Gonzalez A, Corral J. A new sodium-nitroprusside-infusion controller for the regulation of arterial blood pressure. *Biomed Instrum Technol*. 1993;27:244-251.

23. Alvis JM, Reves JG, Govier AV, et al. Computer-assisted continuous infusions of fentanyl during cardiac anesthesia: comparison with a manual method. *Anesthesiology*. 1985;63:41-49.

24. Owens DK, Nease RF Jr. A normative analytic framework for development of practice guidelines for specific clinical populations. *Med Decis Making*. 1997;17:409-426.

25. Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med*. 2001; 20(suppl):21-35.

26. Guyatt G, Schunemann H, Cook D, et al. Grades of recommendation for antithrombotic agents. *Chest*. 2001;119:3S-7S.

27. Bucher HC, Guyatt GH, Cook DJ, Holbrook A, McAlister FA, for the Evidence-Based Medicine Working Group. Users' guides to the medical literature, XIX: applying clinical trial results, A: how to use an article measuring the effect of an intervention on surrogate end points. *JAMA*. 1999; 282:771-778.

28. Mulrow C, Langhorne P, Grimshaw J. Integrating heterogeneous pieces of evidence in systematic reviews. *Ann Intern Med*. 1997;127:989-995.

29. Juni P, Witschi A, Bloch R, Egger M. The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA*. 1999;282:1054-1060.

30. McKee M, Britton A, Black N, McPherson K, Sanderson C, Bain C. Methods in health services research: interpreting the evidence: choosing between randomized and non-randomized studies. *BMJ*. 1999;319:312-315.

31. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA*. 2000;283: 2008-2012.

32. Juni P, Altman DG, Egger M. Systematic reviews in health care: assessing the quality of controlled clinical trials. *BMJ*. 2001;323:42-46.

33. Shojania KG, Duncan BW, McDonald KM, Wachter RM. *Making Health Care Safer: A Critical Analysis of Patient Safety Practices*. Rockville, Md: Agency for Healthcare Research and Quality; 2001. AHRQ publication No. 01-E058.

34. Overhage JM, Tierney WM, Zhou XH, McDonald CJ. A randomized trial of "corollary orders" to prevent errors of omission. *J Am Med Inform Assoc*. 1997;4:364-375.

35. Bates DW, Leape LL, Cullen DJ, et al. Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. *JAMA*. 1998;280:1311-1316.

36. Bates DW, Teich J, Lee J, et al. The impact of computerized physician order entry on medication error prevention. *J Am Med Inform Assoc*. 1999;6: 313-321.

37. Teich JM, Merchia PR, Schmiz JL, Kuperman GJ, Spurr C, Bates DW. Effects of computerized physician order entry in prescribing practices. *Arch Intern Med*. 2000;160:2741-2747.

38. Chertow GM, Lee J, Kuperman GJ, et al. Guided medication dosing for inpatients with renal insufficiency. *JAMA*. 2001;286:2839-2844.

39. Burton ME, Ash CL, Hill DP Jr, Handy T, Shepherd MD, Vasko MR. A controlled trial of the cost benefit of computerized bayesian aminoglycoside administration. *Clin Pharmacol Ther*. 1991; 49:685-694.

40. Evans RS, Classen DC, Pestonik SL, Lundsgaarde HP, Burke JP. Improving empiric antibiotic selection using computer decision support. *Arch Intern Med*. 1994;154:878-884.

41. Evans RS, Pestotnik SL, Classen DC, et al. A computer-assisted management program for antibiotics and other antiinfective agents. *N Engl J Med*. 1998;338:232-238.

42. Casner PR, Reilly R, Ho H. A randomized controlled trial of computerized pharmacokinetic theophylline dosing versus empiric physician dosing. *Clin Pharmacol Ther*. 1993;53:684-690.

43. Hurley SF, Dziukas LJ, McNeil JJ, Brignell MJ. A randomized controlled clinical trial of pharmacokinetic theophylline dosing. *Am Rev Respir Dis*. 1986;134:1219-1224.

44. Mungall DR, Anbe D, Forrester PL, et al. A prospective randomized comparison of the accuracy of computer-assisted versus GUSTO nomogram: directed heparin therapy. *Clin Pharmacol Ther*. 1994;55:591-596.

45. White RH, Hong R, Venook AP, et al. Initiation of warfarin therapy: comparison of physician dosing with computer-assisted dosing. *J Gen Intern Med*. 1987;2:141-148.

46. McAlister FA, Laupacis A, Wells GA, Sackett DL. Users' guides to the medical literature, XIX: applying clinical trial results, B: guidelines for determining whether a drug is exerting (more than) a class effect. *JAMA*. 1999;282:1371-1377.

47. Rogers EM. *Diffusion of Innovations*. New York, NY: Free Press; 1983.

48. Lorenzi NM, Riley RT, Blyth AJ, Southon G, Dixon BJ. Antecedents of the people and organizational aspects of medical informatics: review of the literature. *J Am Med Inform Assoc*. 1997;4:79-93.

49. Oostendorp A, Hoekstra S, Aarts J. Exploring factors required for successful implementation of healthcare informatics. *Stud Health Technol Inform*. 1998;51:146-151.

50. Berg M. Patient care information systems and health care work: a sociotechnical approach. *Int J Med Inf*. 1999;55:87-101.

51. Massaro TA. Introducing physician order entry at a major academic medical center, I: impact on organizational culture and behavior. *Acad Med*. 1993; 68:20-25.

52. Kleinke JD. Release 0.0: clinical information technology in the real world. *Health Aff (Millwood)*. 1998;17:23-38.

53. Glaser J, Teich JM, Kuperman G. Impact of information events on medical care. In: *Proceedings of the 1996 HIMMS Annual Conference*. Chicago, Ill: Healthcare Information and Management Systems Society; 1996:1-9.

54. Shojania KG, Yokoe D, Platt R, Fiskio J, Ma'luf N, Bates DW. Reducing vancomycin utilization using a computerized guideline: results of a randomized control trial. *J Am Med Inform Assoc*. 1998;5:554-562.

55. Teich J, Glaser J, Beckley RF, et al. Toward cost-effective, quality care: the Brigham Integrated Computing System. Steen EB, ed. *Proceedings From the Second Annual Nicholas E. Davies CPR Recognition Symposium*. Washington, DC: Computer-based Patient Record Institute; 1996:5-34.

56. Tierney WM, Miller ME, Overhage JM, McDonald CJ. Physician inpatient order writing on microcomputer workstations: effects on resource utilization. *JAMA*. 1993;269:379-383.

57. Bates DW, Spell N, Cullen D, et al. The costs of adverse drug events in hospitalized patients. *JAMA*. 1997;277:307-311.

58. Evans RS, Pestonik SL, Classen DC, Burke JP. Evaluation of a computer-assisted antibiotic-dose monitor. *Ann Pharmacother*. 1999;33:1026-1031.

59. Nadzam DM, Macklis RM. Promoting patient safety: is technology the solution? *Jt Comm J Qual Improv*. 2001;27:430-436.

60. Milstein A, Galvin RS, Delbanco SF, Salber P, Buck CR. Improving the safety of health care: the Leapfrog initiative. *Eff Clin Pract*. 2000;3:313-316.

61. Medicare Payment Advisory Commission. *Report to the Congress: Selected Medicare Issues*. Washington, DC: Medicare Payment Advisory Commission; 1999.

62. Medication Errors Reduction Act of 2001, S 824, 107th Cong, 1st Sess (2001).

63. California Senate Bill 1875, Chapter 816 §1339.63 (September 28, 2000).