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Unexpected Increased Mortality After Implementation of a Commercially Sold Computerized Physician Order Entry System

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ABSTRACT. *Objective.* In response to the landmark 1999 report by the Institute of Medicine and safety initiatives promoted by the Leapfrog Group, our institution implemented a commercially sold computerized physician order entry (CPOE) system in an effort to reduce medical errors and mortality. We sought to test the hypothesis that CPOE implementation results in reduced mortality among children who are transported for specialized care.

Methods. Demographic, clinical, and mortality data were collected of all children who were admitted via interfacility transport to our regional, academic, tertiary-care level children's hospital during an 18-month period. A commercially sold CPOE program that operated within the framework of a general, medical-surgical clinical application platform was rapidly implemented hospital-wide over 6 days during this period. Retrospective analyses of pre-CPOE and post-CPOE implementation time periods (13 months before and 5 months after CPOE implementation) were subsequently performed.

Results. Among 1942 children who were referred and admitted for specialized care during the study period, 75 died, accounting for an overall mortality rate of 3.86%. Univariate analysis revealed that mortality rate significantly increased from 2.80% (39 of 1394) before CPOE implementation to 6.57% (36 of 548) after CPOE implementation. Multivariate analysis revealed that CPOE remained independently associated with increased odds of mortality (odds ratio: 3.28; 95% confidence interval: 1.94–5.55) after adjustment for other mortality covariables.

Conclusions. We have observed an unexpected increase in mortality coincident with CPOE implementation. Although CPOE technology holds great promise as a tool to reduce human error during health care delivery, our unanticipated finding suggests that when implementing CPOE systems, institutions should continue to evaluate mortality effects, in addition to medication error rates, for children who are dependent on time-sensitive therapies. *Pediatrics* 2005;116:1506–1512; *administration,*

computer software, health care delivery/access, interhospital transport, outcome.

ABBREVIATIONS. CPOE, computerized physician order entry; CHP, Children's Hospital of Pittsburgh; ADE, adverse drug event; PRISM, Pediatric Risk of Mortality; OR, odds ratio; CI, confidence interval.

In their landmark report *To Err is Human: Building a Safer Health System*, members of the Institute of Medicine estimated that medical errors contributed to between 44 000 and 98 000 deaths annually in the United States.¹ As a result of this report, subsequent congressional hearings, and extensive media exposure, the issue of patient safety has quickly risen to a position of highest priority among many health care organizations. Sparked by this "safety initiative," many hospitals have looked toward emerging medical information technologies, specifically computerized physician order entry (CPOE) systems, as a potential tool to reduce human error during health care delivery.

Founded by The Business Roundtable, a national association of Fortune 500 CEOs who are committed to improving public policy, the Leapfrog Group (www.leapfroggroup.org) has embraced CPOE, citing its beneficial role in reducing medication error² as well as improving hospital resource utilization.³ With patient safety as its stated mission focus, the Leapfrog Group now actively promotes widespread CPOE implementation as 1 of its 4 benchmarks for patient safety standards.

In response to the Institute of Medicine's report and safety initiatives promoted by the Leapfrog Group, the Children's Hospital of Pittsburgh (CHP) implemented hospital-wide a commercially sold CPOE system in October 2002 to become 1 of the first children's hospitals in the United States to attain 100% CPOE status. Upperman et al⁴ recently reported that consistent with the experience at many other institutions, CPOE implementation at our hospital resulted in significant reductions in harmful adverse drug events (ADEs) during a 9-month study period.

However, despite CPOE's ability to reduce medication error rates, a few investigators have begun to question whether CPOE implementation necessarily results in improved patient outcome and have raised concerns regarding the Leapfrog Group's CPOE di-

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rective.⁵ Some have proposed that under certain circumstances, CPOE may actually foster “unintended consequences,”⁶ a concept recently supported by a study that described the role of CPOE in facilitating medication error risks through “systems integration failure” and “human-machine interface flaws.”⁷ In light of reemerging uncertainty and discussion regarding the impact that CPOE might have on patient outcome, we examined mortality rates among children who were admitted via interfacility transport before and after CPOE implementation, testing the hypothesis that patient outcome would improve after this intervention.

METHODS

Study Population

Institutional Review Board approval for this study was obtained from the Human Rights Committee of CHP. CHP is a 235-bed regional pediatric referral center with ~12 000 annual admissions (including ~3000 annual ICU admissions) and ~60 000 patient-days. We retrospectively examined demographic, clinical, and mortality data, extracted in accordance to Health Insurance Portability and Accountability Act regulations, for all children who were admitted to CHP via interfacility transport for specialized, tertiary-level care during an 18-month period from October 1, 2001, to March 31, 2003, using CHP’s Critical Care Transport Team interfacility transport database. We chose to study this patient population because they represented a “first encounter” cohort of patients to the hospital system, requiring immediate processing of admission and stabilization orders. Severity of illness for each patient was assessed by a Pediatric Risk of Mortality (PRISM) score, which then was used to calculate cumulative, predicted mortality rates for the study population.⁸ Changes to health care team dynamics and the manner by which bedside care was delivered were additionally noted post hoc.

CPOE System

The CPOE system (PowerOrders; Cerner [a member of The Leapfrog Group], Kansas City, MO) that was purchased by CHP is a commercially sold “add-in” application module that operates within the software architecture of a medical information technology clinical applications platform developed by the same vendor (Millennium; Cerner). Additional modules may be integrated into the platform as they are developed and become commercially available and according to the specific needs of a particular institution.

Approximately 3 months before CPOE implementation, all hospital health care personnel were trained through a mandatory 3-hour computer tutorial and practice session. Hospital-wide implementation of CHP’s CPOE system (along with its clinical applications platform) occurred over a 6-day period, reaching full operation by October 29, 2002. Designated CPOE experts were present to provide “hands-on” consultation support during the immediate postimplementation period, after which support was reduced to telephone consultation. This CPOE program provides physician “point-of-care” and decision support with alerts and reminders regarding potential drug–drug, drug–allergy, and drug–food interactions in addition to potential medication errors. Physician orders are entered primarily through selecting from various order “menus” and “sub-menus” that require completion of requisite fields before orders are accepted. For example, to place an order for “cefotaxime 500 mg iv q6hr × 7 days,” the physician begins by first securely logging into the CPOE system at an open computer terminal, identifies the intended patient from the patient menu, opens the order window and chooses medications, and then selects (or types) cefotaxime from the orderable search menu. Confirmation of this selection then opens a series of sub-menus that request specific fields to be filled: the dose (500), the dosing unit (mg), the route of administration (iv), the dosing frequency (q6hr), the duration (7), and the duration unit (days). Incomplete order entry fields prompt the physician to fill the missing fields before continuation of the order. After all requisite fields have been entered, the order is processed for decision support, point-

of-care analysis, and potential medication errors, after which the physician is requested to confirm, override, modify, or cancel the order. The ordering of continuous intravenous infusions, respiratory therapies, laboratory studies, radiographic studies, and other clinical directives proceeds in a similar manner. All new medication orders require activation by the nurse before the pharmacist receives the actual order for processing. To facilitate the order entry process, this CPOE software program can be modified so that repetitive or frequently executed order algorithms can be saved as preprogrammed favorites, and multiple-order algorithms can be bundled into preprogrammed “order sets” that come with default selections for requisite order fields. However, no ICU-specific order sets had been programmed at the time of CPOE implementation but instead were developed over time after CPOE implementation.

Statistical Analysis

Differences between groups (before vs after CPOE implementation and survivor vs nonsurvivor) were determined by Mann-Whitney rank sum test for continuous data and by χ^2 or Fisher’s exact tests for categorical data. Differences between observed and predicted mortality rates were determined by *z* statistics. To determine which factors might be independently associated with mortality, all variables whose *P* values were <.25 in univariate analysis were entered into a stepwise logistic regression model that also accounted for significant interactions between variables. Because incorporation of PRISM score with some of its component variables in the same model might create potential collinearity, 2 separate models, with and without the PRISM score, were fit to address this possibility. Mortality odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using standard mathematical formulas. Data were analyzed using SPSS statistical software program (version 12.0; Chicago, IL).

RESULTS

During the 18-month study period, 1942 children were admitted to our hospital via interfacility transport, representing ~10% of the annual admissions for the period. Demographic and clinical characteristics for this study population are shown in Table 1. The median age of these patients was 9 months, and 55.7% were male. The most common clinical conditions for admission were airway/respiratory (42.6%), infectious disease (34.9%), and central nervous system/neuromuscular (19.4%) related. Reflecting the tertiary-care referral nature of this transport population, 1102 (56.7%) children initially were admitted to an ICU, which represented ~25% of the annual ICU admissions for the period.

A total of 1394 admissions occurred during the 13 months before CPOE implementation, and 548 admissions occurred during the 5 months after CPOE implementation. Demographic and clinical characteristics of the patients for these 2 periods are also shown in Table 1. In general, the frequencies of clinical conditions did not substantially differ before and after CPOE implementation, except for central nervous system/neuromuscular-related diseases (20.7% [before] vs 16.2% [after]; *P* = .031, χ^2).

Overall, 75 children died during the study period, accounting for an unadjusted mortality rate of 3.86%. Unadjusted mortality rate, however, increased from 2.80% (39 of 1394) before CPOE implementation to 6.57% (36 of 548) after CPOE implementation (*P* < .001, χ^2). Observed mortality was consistently better than predicted mortality before CPOE implementation, but this association did not remain after CPOE implementation (Fig 1). Demographic and clinical characteristics for survivors and nonsurvivors are

TABLE 1. Demographic and Clinical Characteristics of Patients Before and After CPOE System Implementation

Variable*	All Patients (N = 1942)	Before CPOE (N = 1394)	After CPOE (N = 548)	P†
Age, mo‡	9.0 (0.6–48.0)	9.0 (0.6–48.0)	10.0 (0.5–48.0)	.982
Male gender, n (%)	1082 (55.7%)	767 (55.0%)	315 (57.5%)	.352
Prematurity, n (%)	91 (4.7%)	60 (4.3%)	31 (5.7%)	.250
PRISM score‡	4 (0–7)	4 (0–7)	4 (0–7)	.292
Admitted to ICU, n (%)	1102 (56.7%)	790 (56.7%)	312 (56.9%)	.957
Airway/respiratory, n (%)	828 (42.6%)	578 (41.5%)	250 (45.6%)	.106
Infectious disease, n (%)	677 (34.9%)	489 (35.1%)	188 (34.3%)	.788
CNS/neuromuscular, n (%)	377 (19.4%)	288 (20.7%)	89 (16.2%)	.031
Surgical referral, n (%)	346 (17.8%)	252 (18.1%)	94 (17.2%)	.680
Gastrointestinal, n (%)	265 (13.6%)	191 (13.7%)	74 (13.5%)	.967
GCS score ≤8, n/N (%)	244/1927 (12.7%)	177/1386 (12.8%)	67/541 (12.4%)	.879
Metabolic/renal/ingestion, n (%)	221 (11.4%)	155 (11.1%)	66 (12.0%)	.618
Cardiovascular, n (%)	159 (8.2%)	109 (7.8%)	50 (9.1%)	.394
Shock, n (%)	156 (8.0%)	114 (8.2%)	42 (7.7%)	.778
Congenital/genetic, n (%)	93 (4.8%)	68 (4.9%)	25 (4.6%)	.861
Hematologic/oncologic, n (%)	57 (2.9%)	43 (3.1%)	14 (2.6%)	.636
Other diagnosis, n (%)	52 (2.7%)	40 (2.9%)	12 (2.2%)	.497
ECMO referral, n (%)	34 (1.8%)	24 (1.7%)	10 (1.8%)	.971

* Clinical categories are not mutually exclusive (eg, meningococemia = infectious disease and shock).

† P values reflect comparisons between “before” and “after” CPOE, as determined by Mann-Whitney rank sum test for continuous data and χ^2 or Fisher’s exact tests for categorical data. CNS, central nervous system; ECMO, extracorporeal membrane oxygenation; GCS, Glasgow Coma Scale.

‡ Continuous data are presented as median (interquartile range).

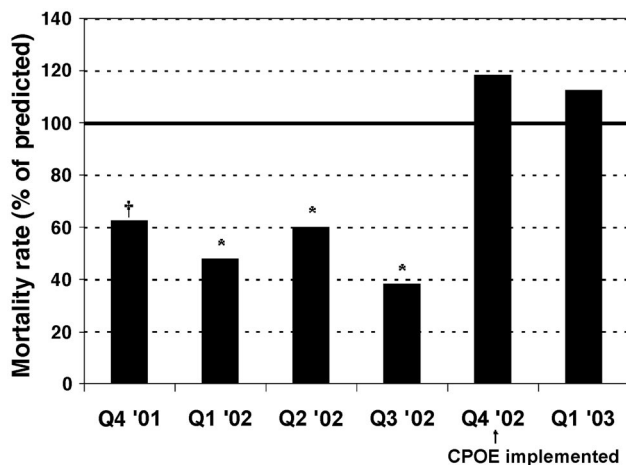


Fig 1. Observed mortality rates (presented as a normalized % of predicted mortality) during the 18-month study period are plotted according to quarter of year. Observed mortality rates were consistently better than predicted before CPOE implementation, but this relationship did not remain after CPOE implementation. * $P < .05$ and † $P = .07$, (observed vs predicted mortality, z statistic). Q, quarter.

shown in Table 2. Nonsurvivors were more likely to have been younger, been premature, been admitted directly to an ICU, had higher severity-of-illness scores, or been referred for surgery. Nonsurvivors were also more likely to have had severe coma, a cardiovascular-related condition, shock, or a congenital/genetic-related condition or been referred for extracorporeal membrane oxygenation support. Nonsurvivors were less likely to have had an infectious disease-related condition or metabolic/renal/ingestion-related condition.

Table 3 shows the results of the regression analyses that were performed to determine which factors might be independently associated with increased mortality. In the primary regression model that adjusted for PRISM score, shock was highly associated

with increased odds of mortality (OR: 6.24; 95% CI: 2.94–13.26), followed by CPOE (OR: 3.71; 95% CI: 2.13–6.46) and severe coma (OR: 3.43; 95% CI: 1.88–6.25). A metabolic/renal/ingestion-related condition was associated with decreased odds of mortality (0.12; 95% CI: 0.01–0.97; $P = .047$). Secondary analysis without PRISM score in the regression model revealed a more robust association with increased odds of mortality for severe coma (5.16; 95% CI: 2.95–9.00) and the appearance of an association with increased odds of mortality for ICU admission (4.68; 95% CI: 1.77–12.34) and extracorporeal membrane oxygenation referral (3.27; 95% CI: 1.14–9.40). CPOE’s association with increased odds of mortality (3.28; 95% CI: 1.94–5.55) persisted in this analysis. Additional regression analyses demonstrated that variable interactions were not significantly associated with outcome in either model (data not shown).

The usual “chain of events” that occurred when a patient was admitted through our transport system was altered after CPOE implementation. Before implementation of CPOE, after radio contact with the transport team, the ICU fellow was allowed to order critical medications/drips, which then were prepared by the bedside ICU nurse in anticipation of patient arrival. When needed, the ICU fellow could also make arrangements for the patient to receive an emergent diagnostic imaging study before coming into the ICU. A full set of admission orders could be written and ready before patient arrival. After CPOE implementation, order entry was not allowed until after the patient had physically arrived to the hospital and been fully registered into the system, leading to potential delays in new therapies and diagnostic testing (this policy later was rectified). The physical process of entering stabilization orders often required an average of ten “clicks” on the computer mouse per order, which translated to ~1 to 2 minutes per single order as compared with a few seconds

TABLE 2. Demographic and Clinical Characteristics of Survivors and Nonsurvivors

Variable*	Survivor (N = 1867)	Nonsurvivor (N = 75)	P†
Age, mo	10.0 (0.7–48.0)	1.0 (0.0–24.0)	<.001
Male gender, n (%)	1041 (55.8%)	41 (54.7%)	.946
Prematurity, n (%)	77 (4.1%)	14 (18.7%)	<.001
PRISM score	4 (0–6)	14 (4–26.5)	<.001
Admitted to ICU, n (%)	1032 (55.3%)	70 (93.3%)	<.001
CPOE, n (%)	512 (27.4%)	36 (48.0%)	<.001
Airway/respiratory, n (%)	788 (42.2%)	40 (53.3%)	.073
Infectious disease, n (%)	661 (35.4%)	16 (21.3%)	.017
CNS/neuromuscular, n (%)	365 (19.6%)	12 (16.0%)	.540
Surgical referral, n (%)	322 (17.2%)	24 (32.0%)	.002
Gastrointestinal, n (%)	258 (13.8%)	7 (9.3%)	.348
GCS score ≤8, n/N (%)	208/1853 (11.2%)	37/74 (50.0%)	<.001
Metabolic/renal/ingestion, n (%)	220 (11.8%)	1 (1.3%)	.009
Cardiovascular, n (%)	141 (7.6%)	18 (24.0%)	<.001
Shock, n (%)	138 (7.4%)	18 (24.0%)	<.001
Congenital/genetic, n (%)	84 (4.5%)	9 (12.0%)	.007
Hematologic/oncologic, n (%)	55 (2.9%)	2 (2.7%)	1.000
Other diagnosis, n (%)	50 (2.7%)	2 (2.7%)	1.000
ECMO referral, n (%)	27 (1.4%)	7 (9.3%)	<.001

* Clinical categories are not mutually exclusive (eg, meningococemia = infectious disease and shock). Continuous data are presented as median (interquartile range). Categorical data are presented as percentages of survivors and nonsurvivors.

† P values reflect comparisons between survivors and nonsurvivors, as determined by Mann-Whitney rank sum test for continuous data and χ^2 or Fisher's exact tests for categorical data.

TABLE 3. Factors Independently Associated With Increased Odds of Mortality

Variable	Mortality OR	95% Confidence Interval	P
Model adjusted for PRISM score*			
Shock	6.24	2.94–13.26	<.001
CPOE	3.71	2.13–6.46	<.001
GCS score ≤8	3.43	1.88–6.25	<.001
Surgical referral	3.29	1.73–6.28	<.001
Prematurity	3.28	1.56–6.91	.002
Cardiovascular	2.66	1.31–5.41	.007
PRISM score	1.11	1.07–1.14	<.001
Secondary analysis†			
Shock	6.74	3.37–13.51	<.001
GCS score ≤8	5.16	2.95–9.00	<.001
Admitted to ICU	4.68	1.77–12.34	.002
Surgical referral	3.84	2.04–7.26	<.001
Cardiovascular	3.63	1.84–7.16	<.001
Prematurity	3.51	1.71–7.20	.001
CPOE	3.28	1.94–5.55	<.001
ECMO referral	3.27	1.14–9.40	.028

* A stepwise logistic regression analysis that included variables whose P values were <.25 in univariate analysis was performed. Additional regression analyses demonstrated that variable interactions were not significantly associated with outcome.

† PRISM score was excluded from this regression model.

previously needed to place the same order by written form. Because the vast majority of computer terminals were linked to the hospital computer system via wireless signal, communication bandwidth was often exceeded during peak operational periods, which created additional delays between each click on the computer mouse. Sometimes the computer screen seemed "frozen."

This initial time burden seemed to change the organization of bedside care. Before CPOE implementation, physicians and nurses converged at the patient's bedside to stabilize the patient. After CPOE implementation, while 1 physician continued to direct medical management, a second physician was often needed solely to enter orders into the computer during the first 15 minutes to 1 hour if a patient

arrived in extremis. Downstream from order entry, bedside nurses were no longer allowed to grab critical medications from a satellite medication dispenser located in the ICU because as part of CPOE implementation, all medications, including vasoactive agents and antibiotics, became centrally located within the pharmacy department. The priority to fill a medication order was assigned by the pharmacy department's algorithm. Furthermore, because pharmacy could not process medication orders until they had been activated, ICU nurses also spent significant amounts of time at a separate computer terminal and away from the bedside. When the pharmacist accessed the patient CPOE to process an order, the physician and the nurse were "locked out," further delaying additional order entry.

Before CPOE implementation, the physician expressed an intended order either through direct oral communication or by writing it at the patient's bedside (often reinforced with direct oral communication), with the latter giving the nurse a visual cue that a new order had been placed. The nurse had the opportunity to provide immediate feedback, which sometimes resulted in a necessary revision of that order. In addition, these face-to-face interactions often fostered discussions that were relevant to patient care and management. After CPOE implementation, because order entry and activation occurred through a computer interface, often separated by several bed spaces or separate ICU pods, the opportunities for such face-to-face physician–nurse communication were diminished.

DISCUSSION

Can CPOE Implementation Result in Increased Mortality?

In this study of hospitalized children who were admitted via interfacility transport, we have observed an unexpected increase in mortality coincident with CPOE implementation. Although our observation complements the report by Koppel et al⁷ that highlights potential problems with CPOE resulting from “systems integration failure” and “human-machine interface flaws,” our finding does not support the overwhelming majority of studies that have reported that CPOE systems reduce potential ADEs^{2-4,9-11} and improve hospital resource utilization, resulting in decreased hospital lengths of stay and reduced medical costs.^{3,12} Of particular interest and concern, our result seems to conflict with other investigators from our own institution who recently reported in their study that examined 8619 discharges during a 9-month observation period a significant decrease in harmful ADEs from 0.05 ± 0.017 per 1000 doses before CPOE implementation to 0.03 ± 0.003 per 1000 doses after CPOE implementation.⁴ Although differences in study method and data source used by Upperman et al⁴ can partly explain our vastly divergent observations, we are reminded by Berger and Kichak that “although the literature suggests [CPOE] systems have the potential to improve patient outcomes through decreased adverse drug events, actual improvements in medical outcomes have not been documented.”⁵ In other words, no study has actually reported a direct association between CPOE and reduced mortality, and this salutary relationship has been inferred from CPOE's ability to reduce potential ADEs because ADEs can contribute to poor outcome¹³ as well as increased lengths of stay and hospital costs.^{13,14} Certainly, in the absence of our current investigation, we might also have inferred improved patient outcomes at our hospital from the reduction in harmful ADEs, yet through independent inquiry, we now report a direct association between CPOE and increased mortality among patients who are admitted through interfacility transport. Our unexpected finding might suggest that surrogate outcome measurements such as “medication error rate” or “ADEs” alone may not be suf-

ficient to determine CPOE efficacy. Indeed, these narrowly defined outcome markers may not readily measure the broader issues of “systems integration” and “human-machine interface” that Koppel et al⁷ recently described as potentially relevant factors in assessing CPOE's global impact on patient care. We explore these concepts in the context of our study with the following discussion.

Can CPOE Implementation Affect Bedside Care and Delivery of Time-Sensitive Therapies?

We have described a few examples of the changes that occurred after CPOE implementation in the manner by which critically ill children who were admitted through our transport system were resuscitated and stabilized. Although order delays related to the inability to “preregister” patients into the system have been resolved through CPOE programming modifications, other matters remain more problematic to address. It has been shown that additional time is needed to enter orders through CPOE as compared with written form, although some of this “lost time” may be recovered later through improved overall efficiency.^{15,16} We also observed the need to spend additional time upfront to enter orders through CPOE as compared with written form. In general medical-surgical wards, this “upfront time cost” may have little consequence. However, in the transport/ICU setting, where multiple, rapid-fire interventions are regularly performed, this upfront time cost might have significant patient care consequences. For some critical conditions, including shock, patient survival has been shown to be time-sensitive and dependent on successful, early resuscitation.^{17,18} The ongoing development of preprogrammed order sets has helped to reduce some of the upfront time cost of order entry, but it still has not eliminated the need for a second physician to be devoted solely to enter orders on the arrival of a critically ill child. Slightly downstream from order entry, nurses must continue to spend significant amounts of time at the computer terminal and away from the bedside, effectively reducing staff-to-patient ratios during this critical period. Adult and pediatric studies have consistently reported that reduced staff-to-patient ratios can have an adverse impact on outcome, particularly in patients with shock.¹⁹

We noted several changes to health care team dynamics and the manner by which bedside care was delivered to our patients after CPOE implementation. The interactions between ICU team members have remained fundamentally altered. Delays in the administration of critical medication resulting from complete centralization of pharmacy services as a consequence of CPOE implementation also remain. Before CPOE implementation, antibiotics and vasoactive drugs were administered according to national guideline-recommended timelines^{20,21}; however, after CPOE implementation, we have found that fewer than half of the patients received critical antibiotics and vasoactive infusions within these timelines. In this regard, we continue to investigate alternative methods to reduce the time from order

entry to initiation of antibiotic and vasoactive infusion therapy.

Can “Unintended Consequences” Manifest During Systems Integration?

In recent papers by Ash et al⁶ and Aarts et al,²² the authors advanced the concept that “unintended consequences”⁶ or “unpredictable outcomes”²² are inherently possible with any emergent change. Implementation of information systems, such as CPOE, is “typified by contingencies and proceed in a far from linear manner. They are part and parcel of organizational dynamics that, as a result of the complexity of the organizations of which we speak, cannot be foreseen, let alone be predicted.”²² In this regard, unpredicted things did happen. For example, it was discovered that with antibiotic administration, subsequent dosing schedules were not timed according to the time of initial dose administration but rather at predetermined default times. Hence, children sometimes received the first 2 doses of an antibiotic in an unacceptably brief time interval. At the back end of antibiotic administration, default “stop order” mechanisms sometimes terminated standing antibiotic orders without physician notification or knowledge.

In a review that addressed the benefits, costs, and issues regarding CPOE, Kuperman and Gibson cautioned,²³ “Computerized physician order entry is a complex undertaking and should not be the first computerized clinical system attempted by an organization. A CPOE application is more likely to be accepted if the existing clinical systems are well received.” The implementation of CPOE in our hospital occurred concurrently with the implementation of its clinical applications platform. Given this simultaneous implementation, it is possible that our unanticipated finding may not have been a result of CPOE but rather the clinical application platform on which it operates. This general, medical-surgical clinical application platform was used throughout the entire hospital, including the ICUs. It is possible that the association between ICU admission and increased mortality that we observed might have been related to using a general program in an ICU environment. We note that Cerner recently developed a Critical Care Solutions application module, suggesting that industry has recognized the possibility that a general, medical-surgical clinical application program alone may be suboptimal for the ICU. It is also possible that utilization of an adult-based clinical application platform in a children’s hospital may be suboptimal. A pediatric-specific application module remains to be developed.

Study Limitations

Several limitations of our study should be considered. First and foremost, inherent limitations of study design preclude any statements regarding cause and effect, and appropriate caution should be taken regarding the conclusions drawn from this retrospective study. In a single institution, it is difficult to assess the causality of increased mortality when a new intervention is given, especially when

the intervention affects the administration of every drug given to every patient. This dilemma has been addressed carefully with new single-drug and single-device interventions by the Food and Drug Administration regulatory agency. Presently there is no regulatory body that evaluates the safety of computer technology in administrative medicine. Without an organized systems approach to this problem, simple-minded physician investigators can provide only conjecture. We have noted delays in administration of time-sensitive medication, increased need for physicians and nurses to be taken away from the bedside and placed at the computer terminal, and specific problems with antibiotic administration. However, accurate evaluation of CPOE will require systems-based troubleshooting with well-funded, well-designed, multicenter studies that can adequately address these questions. Second, because we have examined a unique patient population admitted through interfacility transport, our findings may not be generalizable to the hospital experience as a whole. Indeed, as we alluded to earlier, our conflicting results with that of Upperman et al⁴ may stem from the different patient populations studied. Still, we propose that much like drug intervention studies, the identification of subpopulations of patients who may not benefit or may even experience negative consequences from an intervention is an informative finding. Third, our observation period after CPOE implementation was brief and may simply reflect the adjustment period that commonly follows any major, sweeping change. It is possible that had we extended our study another quarter, we might have observed a return to better-than-expected outcomes. However, changes to resident and fellow coverage of the ICUs had been initiated during the second quarter of 2003 in preparation to meet the recent Residency Review Committee restrictions of resident work time. Because it was uncertain what effects the policy restricting the resident/fellow work week to <80 hours might have on patient care and outcome, the study was closed to minimize the influence of this potential confounder. We additionally note, however, that our post-CPOE observation period actually corresponds to the post-CPOE observation period by Upperman et al⁴ that is marked by immediate reductions in harmful ADEs. Fourth, in a related consideration, the relative imbalance between our pre- and post-CPOE observation periods raises potential confounding from seasonal variability of illness often seen in children. Although we cannot exclude this possibility, we observe that overall patient characteristics and the distribution of diagnostic categories were similar during the 2 observation periods. In addition, we note that a comparison of unadjusted mortality rates for matching 5-month periods (October 29–March 31) before and after CPOE implementation reveals that mortality increased from 2.58% (16 of 621) to 6.57% (36 of 548; $P = .002$, χ^2) between these 2 matching periods. Fifth, we again consider the possibility that our finding may reflect a clinical applications program implementation and systems integration issue rather than a CPOE issue per se. Sixth, although we have attempted to control for many

important mortality covariables, it remains possible that our observation that CPOE implementation is associated with increased mortality may have resulted from an unidentified confounding factor. A “regression to the mean” phenomenon cannot be discounted.

CONCLUSION

CPOE is an important medical information technology that holds great promise as a tool to reduce human error during health care delivery. In this current study, however, we observed an unexpected increase in mortality coincident with CPOE implementation. Our unanticipated finding suggests that when implementing CPOE systems, institutions should continue to evaluate mortality effects, in addition to medication error rates, for children who are dependent on time-sensitive therapies. CPOE technology is still evolving and requires ongoing assessment of “systems integration” and “human-machine interface” effects, both predictable and unpredictable, on patient care and clinical outcomes.

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Unexpected Increased Mortality After Implementation of a Commercially Sold Computerized Physician Order Entry System

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