Response to Medication Dosing Alerts for Pediatric Inpatients Using a Computerized Provider Order Entry System

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Keywords

ADE, adverse drug events, CDS, clinical decision support; CIS, clinical information system, CPOE, computerized provider order entry

Summary

Objective: Medication dosing errors are of particular concern in hospitalized children. Avoidance of such errors is essential to quality improvement and patient safety. Computerized provider order entry (CPOE) systems with clinical decision support (CDS) have the potential to reduce medication errors. The objective of this study was to evaluate provider response to the dosing alerts in a CPOE system with CDS for pediatric inpatients and to identify differences in provider response based on clinician specialty.

Patients and methods: We conducted a retrospective analysis of all medication dosing alerts over a 1-year period (January 1 through December 31, 2008) for all pediatric inpatients at Hospital for Special Surgery. Alerts were analyzed with respect to medication dosing, prescriber, and action taken by the prescriber after the alert was triggered (i.e., accepted suggested change, ignored recommendation/overrode, or cancelled the order).

Results: During the study period, 18,163 medication orders were placed and 1,024 dosing alerts were fired. Overdosing of medications accounted for 91% of the alerts and underdosing 9%. The pediatric-trained providers ignored more alerts and cancelled fewer orders than the non-pediatric-trained providers ($p<0.001$). Both groups changed the order similarly based on CDS recommendations.

Conclusions: Differences in response to CDS were found between pediatric-trained and non-pediatric-trained providers caring for pediatric patients; however, both groups changed orders based on CDS similarly. CPOE with built-in CDS may be of particular value when providers with different specialties and types of training are caring for pediatric patients.

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1. Introduction

Hospitalized children are vulnerable to iatrogenic harm and pose unique safety risks in our health care system. Medication errors are of particular concern for pediatric patients because of the need for accurate weight-based dosing. In addition, the physiologic reserves of children are lower, and they may be unable to verbalize adverse reactions. Medication dosing errors, which most often occur at the time of prescribing, are a common type of error in pediatric patients [1–3]. A number of studies have shown that computerized provider order entry (CPOE) systems with clinical (dosing) decision support (CDS) have the potential to reduce medication errors and improve safety for pediatric patients [4, 5]. Alerts that signal an error to the provider are important components of any CPOE system with CDS. Typical alerts include dose range checking, drug-drug interactions, allergies, and duplicate orders. It is important that they be appropriate and effective, because over alerting may lead to "alert fatigue," and cause important safety alerts to be ignored [6, 7].

At our institution, providers from a variety of specialties (including orthopedics, anesthesia, and pediatrics) are involved in the medical and surgical management of pediatric patients. Physician assistants, nurse practitioners, residents, fellows, and attendings from these various specialties care for patients. A mandatory, hospital-wide CPOE system with CDS was implemented in July of 2007.

2. Objectives

The purpose of this study was to quantify medication dosing errors in our pediatric population and to determine whether differences exist in response to medication dosing alerts based on pediatric training. Specifically we were interested in differences between pediatric trained providers such as pediatricians, pediatric anesthesiologists and pediatric rheumatologists and providers without specific pediatric training such as orthopedic surgeons and residents, surgical physician assistants and anesthesiologists. To our knowledge, this issue has not been explored. In addition, analysis of how providers use the system allows us to identify opportunities for customization and improvement. This is particularly valuable when a variety of providers from different specialties and various levels of training are caring for pediatric patients.

3. Methods

3.1. Site of Study

Hospital for Special Surgery (HSS) serves a socio-economically and culturally diverse population of children and adults with musculoskeletal disease. Pediatric patients are admitted to HSS each year for a variety of musculoskeletal disorders including trauma, sports injuries, scoliosis, limb deformities, cerebral palsy, and rheumatologic disease, among others. In 2008, there were over 1,400 pediatric admissions to HSS, approximately 6% of total hospital admissions.

3.2. The CPOE System

HSS implemented the inpatient clinical information system (CIS) Sunrise Clinical Manager (SCM version 4.5, Eclipsys). Initial implementation consisted of CPOE, limited documentation (to support medication order entry – such as height, weight, and allergies), basic flow sheets, and an electronic medication administration record (e-MAR).

As with many institutions, we decided to implement a CIS to improve patient safety and to enhance efficiency [8]. The system eliminated illegibility, removed unapproved abbreviations, and improved many aspects of turnaround time. CDS is a major component of CIS and in its simplest form includes dose range checking, drug-drug interactions, allergy alerts, and duplicate medication order alerts. We also developed a number of custom features designed specifically for our patient population [9].

Due to our initial concerns about "alert fatigue," we chose to activate dose range checking only for certain medications, including those on the "High Alert" list of the Institute for Safe Medication Practices [10]. Dose range checking was also activated on all medications appearing anywhere in our 50 pediatric order sets (including pediatric postoperative admission, pediatric patient-controlled analgesia, pediatric rheumatology admission and medications, food and nutrition, imaging, and rehabilitation order sets).

Dosing guidelines were obtained from the published literature, including the Harriett Lane Handbook [11] and Micromedex [12].

In our institution, all licensed medical practitioners may enter orders. This is done by choosing the patient's name from a list and clicking the "Orders" icon. When the medication name is entered, a list of formulary medications and route in a drop-down menu appears (many with standardized and defaulted doses). The medication of interest is then selected and a window appears that contains pediatric dosing recommendations and maximum daily doses if applicable. Next to the dosing box there is an icon that by double clicking opens up an additional form, on which dose, route, interval, and dose adjustments may be made. Additional guidelines are available by double clicking on the "Expert Dosing" icon for calculations related to liver disease, dialysis, body surface area (BSA), and creatinine levels. After a final review, the order is entered and if no alert is fired it is electronically transmitted to the pharmacy. The pharmacist then verifies the order and makes it available to the patient.

Medications may also be ordered from within order sets. Whenever possible, the standard doses were defaulted. In addition, all medications in pediatric order sets have dosing parameters displayed next to the name of the medication. This reminds clinicians of maximum and minimum doses, as well as weight- and age-based dosing where appropriate. Dosage recommendations are also available by clicking on a dosing icon.

3.3. The Alerts

Alerts were installed for dosing, allergies, duplicate orders, and drug-drug interactions for our pediatric patients. In this study we evaluated provider response to medication dosing alerts. Weight must be entered before any medication orders will be accepted by the system. A typical medication dosing alert would warn the provider that the dose ordered is outside acceptable dose parameters and suggest an appropriate dose. In cases of errors for total daily dosing, the alert would warn that the total daily dosing is outside acceptable parameters and suggest a range of an appropriate total daily dose. The provider can override the alert (thus ignoring the recommendation), change the dose based on the alert recommendation, change to a non-recommended dose, or cancel the order.

3.4. Collection of Data

After approval from our institutional review board, we retrospectively analyzed medication dosing alerts for patients younger than 18 years of age who were admitted to HSS during the 1-year period from January 1 through December 31 of 2008. The report included all pediatric admissions, the number of medication orders placed for each patient and if a medication dosing alert was fired on a particular order. For every alert fired, the following information was obtained: patient name, date of birth (DOB), gender, weight, diagnosis, surgical attending, alert text, final order dose, ordering physician (MD)/provider. By comparing the initial order and the corresponding alert with the final order, a determination of the action taken was made, i.e., override the alert (thus ignoring the recommendation) and proceed with the initial dose, change the dose based on the alert recommendation, change to a non-recommended dose, or cancel the order altogether. In addition, the ordering MD specialty and level of training was determined using hospital staff records.

3.5 Statistical Analysis

Patterns by pediatric trained versus non-pediatric trained providers for alert response types are reported with percentages reflecting corresponding numerators (frequency of alert response type) and denominators (total alerts). Relative risk values were computed as the ratios of the likelihoods (per-

centages) for pediatric trained versus non-pediatric trained providers respectively. Chi-square tests were conducted to evaluate patterns in rates for alert response types within pediatric and non-pediatric groups, resulting in eight Chi-square analyses. Each statistically significant Chi-square analysis was followed by a post-hoc Chi-square and pairwise t-test for proportions (for confirmatory purposes) to verify which specific response rates within each group were different from the others.

All significant levels for Chi-squares and t-tests were set at $p<0.05$ as a minimum alpha level, and confidence intervals were set a 95%, as shown in ▶Table 2. All analyses were conducted using SPSS v 17.0 or higher (Chicago, IL) verified with SAS (Cary, NC).

4. Results

During the study period, there were 1,413 pediatric admissions. 18,163 medication orders were placed for these patients (by 192 prescribers), and 1,024 medication dosing alerts were fired. The alerts were categorized into narcotic pain medications (35.2%), digestive system medications (31.1%), non-narcotic pain medications (17.8%), central nervous system (CNS) medications (10.7%), and antibiotics (5.3%). Overdosing accounted for 91% of the alerts and underdosing 9%.

4.1. All Providers

There were 1024 total alerts. Examination of all providers' initial responses to dosing alerts revealed that 55.3% (566) overrode the alert and did not modify the initial order, 22.6% (231) changed the order dose based on the alert recommendation, 1.6% (16) changed the order but not to the recommended dose, and 20.6% (211) cancelled the order (▶Fig. 1).

4.2. Pediatric vs. Non-Pediatric Trained

Pediatric trained providers included pediatricians, pediatric anesthesiologists, pediatric rheumatologists, pediatric nurse practitioners, and pediatric residents. Non-pediatric trained providers included anesthesiologists (attendings, residents, and fellows), orthopedic residents and fellows, and physician assistants (orthopedics and anesthesiology). Of the 1,024 medication dosing alerts, 413 (40.3%) were triggered on orders from pediatric providers and 611 (59.7%) from non-pediatric trained providers. A comparison of the alert responses of pediatric and non-pediatric trained clinicians revealed the following: 64.6% (267/413) vs. 48.9% (299/611), respectively, overrode the alert (thus ignoring the recommendation) and proceeded with the initial dose ($p<0.001$), 22.3% (92/413) vs. 22.7% (139/611) changed the order based on the alert recommended (p = n.s.), 2.4% (10/413) vs. 1.0% (6/611) changed to a non-recommended dose (p = n.s.), and 10.7% (44/413) vs. 27.3% (167/611) cancelled the order ($p<0.001$) with relative risk magnifying the degree of difference among the two groups (▶Table 1).

4.3. Selected Medications by Class

The medication dosing alerts were grouped into 5 main categories: narcotic and non-narcotic pain medications, digestive system medications, antibiotics, and CNS medications. First we analyzed the response to medication alerts within each class of medications for pediatric providers and non-pediatric providers. We looked for differences among the drug classes within each training type and within each response type. For example, we examined whether pediatric trained providers override alerts for antibiotic medications differently than alerts for narcotic medications. We found significant differences in two categories in the pediatric trained group; override rates and change to recommended dosing rates for non-narcotic pain medications (▶Table 2). We found significant differences in three categories in the non-pediatric trained group; override and cancelled rates for antibiotics, and change to recommended in non-narcotic pain medications (▶Table 2). There was no statistically significant difference for narcotics, digestive system or central nervous system medications alert response rates within either group.

4.4. Cancelled Orders

We reviewed all the cancelled orders to see whether subsequent orders had been placed by the same provider and whether the subsequent response differed from the original response. Of the initial 44 orders that were cancelled by pediatric providers, 14 were reordered with no change, 14 were reordered with a change based on CDS and 16 remained cancelled. Of the 211 orders that were cancelled by non-pediatric trained providers, 16 were reordered with no change, 39 were reordered with a change based on CDS and 112 remained cancelled. A comparison of pediatric vs. non-pediatric trained providers revealed that 31.1% vs. 9.6% reordered the cancelled medication with no change ($p<0.001$) and therefore ultimately overrode the alert; 31.1% vs. 23.5% reordered the medication based on CDS ($p<0.01$), and 37.8% vs. 66.9% let the cancellation stand ($p<0.001$) (▶Fig. 2). We combined the initial response to medication alerts with this subsequent data on the cancelled orders and the cumulative results are as follows: for pediatric vs. non-pediatric providers, respectively: 68.1% vs. 51.7% overrode the alert ($p<0.001$), 25.4% vs. 29.5% changed the order based on CDS (ns), 2.4% vs. 0.6% (ns) changed to a non-recommended dose, and 4.1% vs. 18.2% cancelled the order ($p<0.001$) (▶Fig. 3).

5. Discussion

Although medication errors may occur during ordering, transcribing, dispensing, administering, and monitoring, most errors occur at the ordering stage [1]. Computerization of ordering for children has been seen as an especially powerful tool for error prevention because alerts are displayed directly to the prescriber before entry. CPOE with CDS has been recommended by numerous groups, including the Institute of Medicine (IOM) [16], the Institute for Healthcare Improvement (IHI) [13], and the American Academy of Pediatrics [14]. Numerous studies have shown that CPOE, especially with CDS, can reduce the number of all types of medication errors [4, 5, 8, 15, 16]. The number of certain common ordering errors, such as those due to illegibility or incompleteness, is reduced. The decision rules provide further safeguards: errors are less frequent when providers are given the appropriate dose, frequency, and route [17].

Research is emerging to help identify the utility of CPOE systems in the pediatric population; however, this field is still evolving. Kirk et al looked at prescribing practices in an outpatient setting for two common pediatric medications. They found the medication error rate among pediatricians was lower than non-pediatricians using both computer based and traditional ordering systems [18]. Van der Sijs et al found that surgery residents differed from internal medicine residents in their appropriateness of alert handling in a small simulation study [19]. Most of the literature evaluates CPOE systems within specific patient populations, providers, and medical settings, with little crossover. At our institution, all patients under 18 years of age are managed and followed by the pediatric service (including pediatric residents and attendings). However, orders are written by a variety of providers with and without specific pediatric training. Since most errors occur at the ordering stage, CDS and alerts have the potential to prevent errors in all medical settings and may be particularly valuable when providers do not have specific pediatric training.

In our institution at the time of this study, not every medication order was eligible for an alert. Our institution is currently implementing medication dosing alerts for all medications so that a true alert rate can be determined. In addition, our report did not include provider information on all orders so we are unable to compare the overall alert rate between pediatric and non-pediatric providers. In this study, a majority of the medication dosing alerts were for overdosing. Underdosing of analgesia, a common problem in pediatrics [4] was not a frequent cause of alerts in our population. As most of the pediatric patients at HSS have surgery, pain management is a primary focus of care. Providers at HSS are experienced in pain control and the use of various narcotics in pediatric patients, which may explain why underdosing of analgesia is less frequent.

The override rate of medication dosing alerts for all providers was high (55%) consistent with previous studies. In a review of 17 studies, van der Sijs et al [7] found that 49–96% of medication safety alerts were overridden. Three of the studies explored the reasons. The main reason was alert fatigue occurring because the alert was irrelevant, was shown many times, or was not serious. Other

reasons were physicians' confidence in their own judgment, patient resistance to a change, wrong information, or lack of time. Overriding of an alert does not necessarily present a safety issue. There are appropriate reasons for a provider to deviate from a decision rule, including a legitimate difference of opinion or an underlying medical condition requiring a different dose/frequency. In 3 studies with override rates of 57% [6], 90% [20], and 80% [21], the rates of adverse events were 2.3%, 2.5%, and 6%, respectively [7].

Pediatric providers had a higher override rate (68%) than non-pediatric providers (51%). We speculate that clinical experience and confidence of pediatric providers accounts for these differences. Non-pediatric trained providers adhered to the alert by either cancelling, or changing the order based on CDS more often than the pediatric trained providers overall (51% vs. 36.4%). We suspect this difference is from a greater willingness to adhere to alerts as they have had no formal pediatric training. It would be interesting in the future to assess whether non-pediatric trained providers have different response patterns to medication safety alerts when prescribing for adults compared to pediatric patients.

Although the override rate of 51% by non-pediatric providers was significantly less than pediatric providers, we were surprised at the magnitude. How useful are the pediatric medication alerts if more than half are ignored by providers without specific pediatric training? A universal challenge of CPOE systems is minimizing false-positive alerts that may overwhelm providers and finding the appropriate threshold to identify real risk. Continuous override monitoring has been suggested to ensure an appropriate number of alerts and maintain responsiveness and trust [22].

The other significant difference between the two groups was that non-pediatric trained providers tend to cancel more orders after an alert has been triggered (2.57 greater probability). Because we speculated that in some cases the order was cancelled with the intent to reorder immediately, we performed a review of the cancelled orders. This was in fact the case for the pediatric trained providers: they often reordered the medication unchanged after "canceling" it (meaning the alert was overridden). Non-pediatric trained providers, however, left the order cancelled. The alert did its job in that a change was made when a medication was ordered incorrectly, the change being that the order was cancelled. However, the system is designed to provide decision support for correct ordering, and yet non-pediatric providers cancelled rather than reordered the medication correctly. This implies a difference in the actual application and use of the CPOE system between providers. Further study is needed to elucidate this difference. We suspect that the medication may have been reordered by a different provider after another source was accessed such as a more senior level provider, a pediatric provider, or literature consultation by another provider.

In addition to comparing the pediatric and non-pediatric providers, we examined the response to alerts within medication classes. We suspected that within medication classes a different pattern of response to alerts would emerge, specifically, that CDS recommendations would be followed for medications that are seemingly more "high risk," such as narcotics or CNS medications. However, within the pediatric group the significant difference found in response rates was a lower override rate for non-narcotic pain medications as well as a higher rate of change based on CDS compared to the other medication categories. In the non-pediatric group, the differences were a higher override rate for antibiotics, a higher change rate for non-narcotic pain medications, and a lower cancel rate for antibiotics. In both groups there were no differences for seemingly "high risk" medications such as narcotics or CNS medications. As noted, our institution is unique in the amount of post-operative pain management our providers experience but this result suggests providers response to alerts are not influenced by medication type.

Our results show that while there are differences between providers regarding overriding and canceling orders, both pediatric and non-pediatric trained providers change orders based on CDS similarly, close to 25% of the time. Other studies have attempted to quantify responses to computer-generated dosing suggestions. In an adult community-based medical setting, Taylor and Tamblyn [23] found that the change rate in response to a variety of alerts was 14%. The highest revision rate in response to an alert was 23% when the alert was related to a medication dosing error (similar to our findings). Killelea et al. [24] studied acceptance or rejection of CDS medication rules in a pediatric service and found that approximately one-third accepted the rule exactly, and two-thirds changed it. However, their study looked at acceptance of decision support at the initial time of ordering and not the subsequent response to alerts. We are unaware of any published analysis comparing acceptance

or rejection of CPOE-generated alerts in pediatrics that compares responses based on specialty. Interestingly, both pediatric and non-pediatric trained providers changed the order based on CDS similarly, approximately one-fourth of the time, suggesting that CPOE with CDS may have equal utility across specialties.

Some limitations of our study are that we did not measure the effect of CPOE on medication errors or adverse drug events, and so are unable to say whether the system reduced errors or harm, the ultimate goal of computer-based ordering systems. Determining and removing justifiable overrides along with understanding why and when alerts are overridden or followed is necessary to build and improve CPOE systems. McCoy et al has recently described a framework for evaluating alert systems with two helpful alert related measurements; 'alert appropriateness' requiring expert review and 'provider response appropriateness' which is based on the appropriateness of an alert to begin with and the real time clinical situation [25]. This study did not focus on alert appropriateness or provider response appropriateness but rather differences in alert response based on specialty. However, this framework should be applied to further evaluate and ultimately improve our system. Another limitation of this study is that the study site is unique with a majority of patients having musculoskeletal disease.

6. Conclusions

Our study found that pediatric and non-pediatric trained providers differed in some areas of alert response including override rates and cancellation of orders, but that both groups changed medications using CDS similarly. This finding suggests that CPOE systems can be equally helpful to both pediatric and non-pediatric trained providers caring for children but may need to be tailored based on provider specialty. Future studies need to focus on the reasons for overriding an alert or changing a dose, and should capture these data in real time. Ongoing analysis is particularly useful and necessary in medical settings with a variety of providers such as physician extenders and specialty crossover.

Clinical Relevance Statement

A variety of providers take care of pediatric patients, both with and without specific pediatric training and computerized provider order entry (CPOE) systems have the potential to reduce medication errors using built in clinical decision support (CDS) tools.
To date, there is no study addressing the provider response to clinical decision support based on specialty training in the pediatric literature. The most effective CPOE systems need tailoring and customization based on provider specialty and patient population.

Conflicts Of Interest

Steve Shaha is currently an employee of the EMR vendor which provided our institution's system. However, Steve Shaha has no financial interest in the system's success or any employment or income related benefits associated with this study or manuscript, nor are these findings or data intended for any marketing-related uses. All other authors have no conflicts of interest to disclose.

Protection Of Human And Animal Subjects

The study was performed in compliance with the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, and was reviewed by Hospital for Special Surgery Institutional Review Board.

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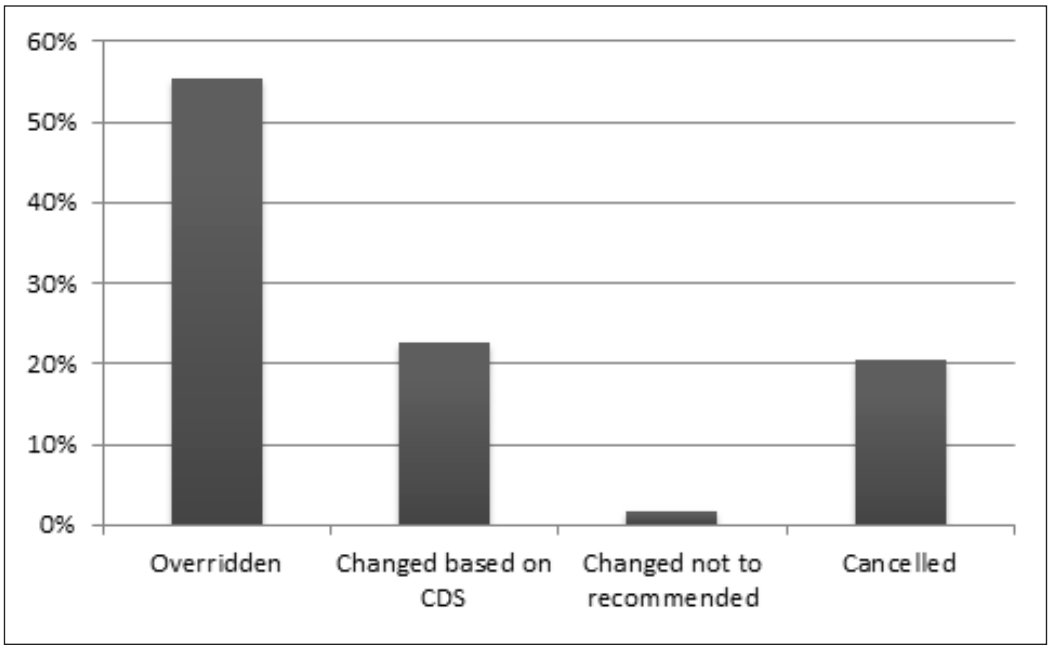

Fig. 1 All providers: Response to medication dosing alerts

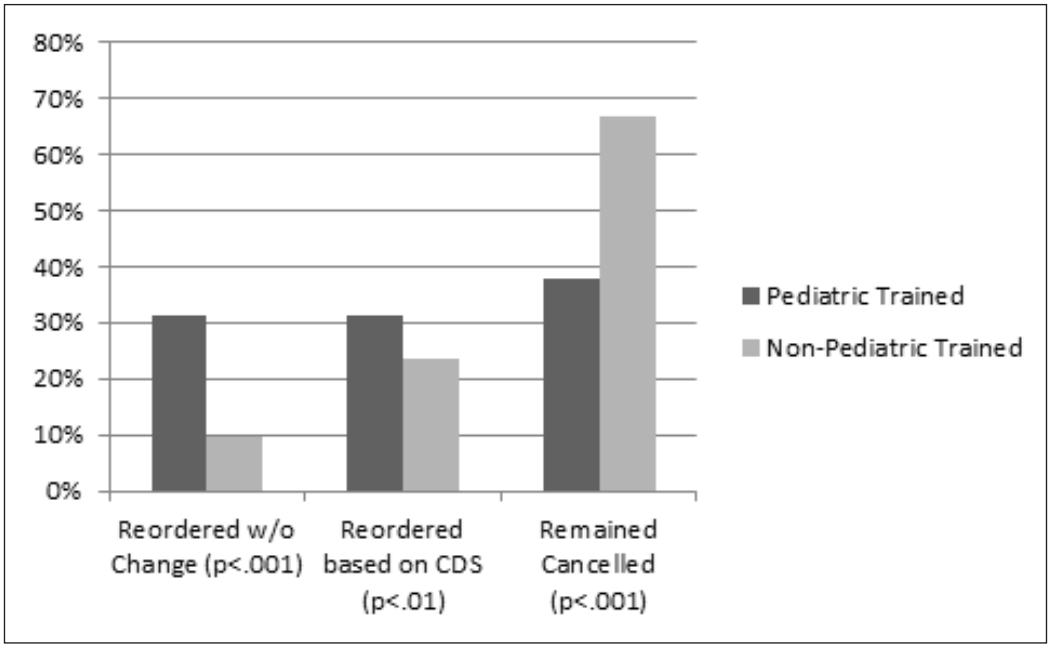

Fig. 2 Outcome of cancelled orders: pediatric vs. non-pediatric trained providers. "Reordered w/o Change" refers to providers who simply reordered the same medication, ignoring the CDS recommendation.

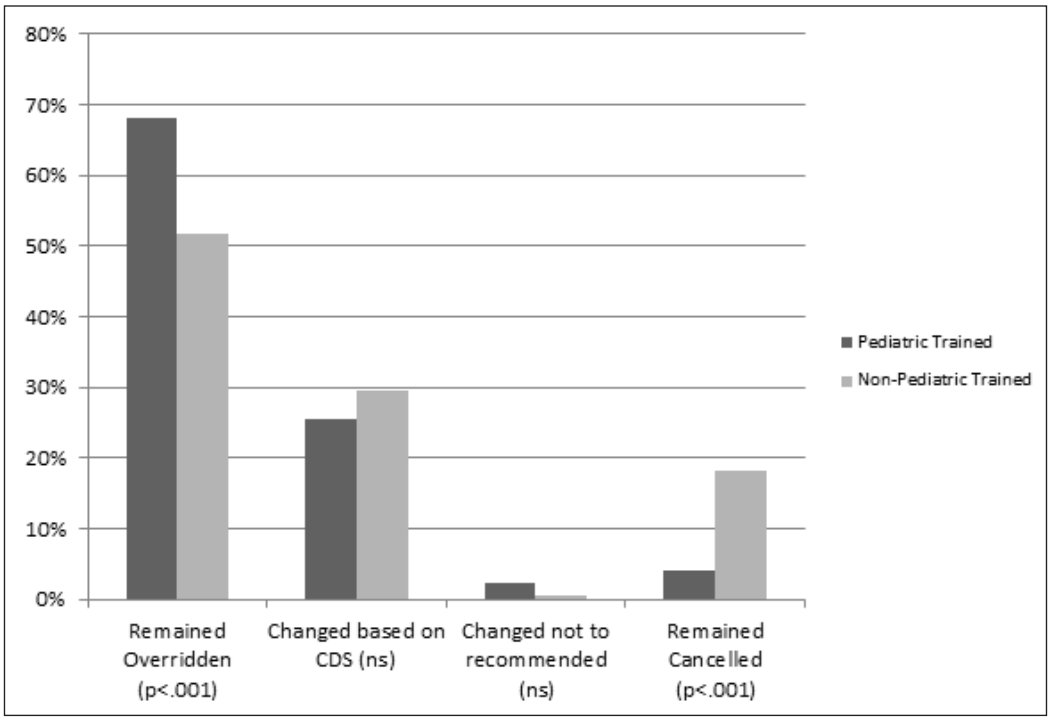

Fig. 3 Cumulative response including actions taken after original cancellation of an alert: pediatric vs. non-pediatric trained providers.

Table 1 Initial response to medication dosing alerts: Comparison of pediatric versus non-pediatric trained providers

	Alerts Overridden			Alerts Changed Based on CDS			Alerts Changed not to Recommended			Alerts Cancelled			Total Alerts	
	N	%	Relative Risk	N	%	Relative Risk	N	%	Relative Risk	N	%	Relative Risk	N	%
Total alerts	566			231			16			211			1024	
Pediatric trained	267	64.6	1.32	92	22.3	0.98	10	2.4	2.47	44	10.7	0.39	413	100
Non-pediatric trained	299	48.9	0.76	139	22.7	1.02	6	1.0	0.41	167	27.3	2.57	611	100
P-value	<.001			ns			ns			<.001				

Table 2 Initial response to medication dosing alerts by medication category: Comparing responses within medication classes for pediatric and non-pediatric trained providers

Medication Category	Alerts Overridden		Alerts Changed based on CDS		Alerts Changed not to recommended		Alerts Cancelled	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Pediatric trained								
Non-narcotic pain	49.0	0.35 – 0.63*	40.8	0.27 – 0.55*	2.0	-0.02 – 0.06	8.2	0.00 – 0.16
Narcotic pain	68.2	0.61 – 0.76	19.6	0.13 – 0.26	3.4	0.00 – 0.06	8.8	0.04 – 0.13
Digestive system	64.9	0.58 – 0.72	21.3	0.15 – 0.27	0.6	-0.01 – 0.02	13.2	0.08 – 0.18
Antibiotics	71.4	0.38 – 1.05	14.3	-0.12 – 0.40	0.0	0.01 – 0.04	14.3	-0.12 – 0.18
CNS	68.6	0.53 – 0.84	14.3	0.03 – 0.26	8.6	-0.01 – 0.18	8.6	-0.01 – 0.18
Non-pediatric trained								
Non-narcotic pain	36.1	0.28 – 0.44	39.1	0.31 – 0.47*	0.0	-0.05 – 0.05	24.8	0.17 – 0.32
Narcotic pain	53.3	0.47 – 0.60	17.0	0.12 – 0.22	0.9	0.00 – 0.02	28.8	0.23 – 0.35
Digestive system	49.3	0.41 – 0.57	20.8	0.14 – 0.27	0.0	-0.05 – 0.05	29.9	0.22 – 0.37
Antibiotics	89.4	0.81 – 0.98*	10.6	0.02 – 0.19	0.0	-0.05 – 0.05	0.0	-0.11 – 0.11*
CNS	33.3	0.23 – 0.44	21.3	0.12 – 0.31	5.3	0.00 – 0.10	40.0	0.29 – 0.51

*p<0.5

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