Computerized clinical decision support for medication prescribing and utilization in pediatrics

Jeremy S Stultz, Milap C Nahata

Ohio State University College of Pharmacy, Columbus, Ohio, USA

Correspondence to
Dr Milap C Nahata, Institute of Therapeutic Innovations and Outcomes, College of Pharmacy, Ohio State University, Columbus, OH, 43210, USA; nahata.1@osu.edu

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ABSTRACT

Background and objective Accurate and informed prescribing is essential to ensure the safe and effective use of medications in pediatric patients. Computerized clinical decision support (CCDS) functionalities have been embedded into computerized physician order entry systems with the aim of ensuring accurate and informed medication prescribing. Owing to a lack of comprehensive analysis of the existing literature, this review was undertaken to analyze the effect of CCDS implementation on medication prescribing and use in pediatrics.

Materials and methods A literature search was performed using keywords in PubMed to identify research studies with outcomes related to the implementation of medication-related CCDS functionalities.

Results and discussion Various CCDS functionalities have been implemented in pediatric patients leading to different results. Medication dosing calculators have decreased calculation errors. Alert-based CCDS functionalities, such as duplicate therapy and medication allergy checking, may generate excessive alerts. Medication interaction CCDS has been minimally studied in pediatrics. Medication dosing support has decreased adverse drug events, but has also been associated with high override rates. Use of medication order sets have improved guideline adherence. Guideline-based treatment recommendations generated by CCDS functionalities have had variable influence on appropriate medication use, with few studies available demonstrating improved patient outcomes due to CCDS use.

Conclusion Although certain medication-related CCDS functionalities have shown benefit in medication prescribing for pediatric patients, others have resulted in high override rates and inconsistent or unknown impact on patient care. Further studies analyzing the effect of individual CCDS functionalities on safe and effective prescribing and medication use are required.

BACKGROUND AND OBJECTIVE

The Institute of Medicine's 2001 consensus report "Crossing the Quality Chasm" called for automation of patient information, computerized reminders, and elimination of handwritten clinical data,[1] resulting in the design and implementation of a multitude of health information technologies. In the pediatric patient population, medication errors and adverse drug events (ADEs) are reported to occur in 5.7% of orders and in six of every 100 patient admissions.[2 3] Reporting of these outcomes can vary depending on the definition of, and surveillance for, an error or ADE. Computerized physician order entry (CPOE) with or without computerized clinical decision support (CCDS) implementation has been shown to reduce overall ADEs and medication prescription errors.[4–8] In the wake of CPOE, CCDS functionalities have been designed to augment a practitioner's medical decision-making. Various CCDS functionalities may provide accessibility and organization of pertinent medical information, computerized resources (eg, guidelines, medication information), safety checks in various forms of alerts, and treatment recommendations.

Appropriate design and implementation of medication-related CCDS functionalities may be critical for practitioners to reap the potential benefits of this technology.[9 10] Designing CCDS functionalities for pediatric patients may be difficult owing to frequent off-label use of medications and a dynamic anatomy and physiology that requires changing pharmacotherapy regimens based on patient age, body weight, indication, and organ function. Previous studies, meta-analyses, and reviews have discussed the effects of CPOE implementation in pediatric and adult patients.[7 11–17] Unlike in adults,[10 18–22] the effects of CCDS on medication prescribing have only been briefly reviewed in the pediatric population.[23 24] The objective of this review is to categorize, analyze, and summarize available research regarding the implementation of CCDS functionalities and their effect on medication prescribing and use in pediatric patients.

MATERIALS AND METHODS

A keyword literature search was performed in the PubMed database (from 1990 to March 26, 2012) using the search terms p(a)ediatric decision support, neonatal decision support, p(a)ediatric physician order entry, p(a)ediatric drug dose calculator, and p(a)ediatric computer drug prescription, resulting in 4171 results. The PubMed database was also searched using the search terms decision support, physician order entry, drug dose calculator, and computer drug prescription and then limited by age (0–18 years), studies in humans, and written in the English language, resulting in 9884 results. The title and abstract of the resulting articles were searched; 13 659 articles were not relevant to the topic of computerized decision support. The abstract and text of the remaining 396 relevant articles were searched. All completed and published articles were included for analysis if the study involved each of the following three criteria: (1) implementation of a CCDS functionality intended to affect practitioners prescribing or use of a medication for direct patient care; (2) implementation of the CCDS functionality in the pediatric (defined for the purpose of this review as <18 years) or neonatal population; and (3) outcomes data which objectively measure the medication-related CCDS functionality. References of identified articles and related reviews were also searched for articles fitting the above inclusion criteria.

RESULTS AND DISCUSSION

Forty-four studies were included for characterization, analysis, and summary based on the specified inclusion criteria (tables 1–8). The included studies analyzed implementation of CCDS and CPOE, multiple CCDS functionalities, or a single CCDS functionality. While outcomes, such as overall ADEs, might have been related to multiple CCDS functionalities, CPOE, or a combination of the two, specific outcomes, such as medication dosing errors, are more closely related to the efficacy of a specific CCDS functionality. Some CCDS functionalities acted as safety double checks, automated calculations, or provided information (tables 1–6), while others provided recommendations for drug prescribing or utilization based on available clinical information (tables 7 and 8). Therefore, although studies were categorized by the main outcome evaluation in the tables of this review, the body of this review extracted outcomes data from studies involving multiple CCDS functionalities to evaluate the efficacy of an individual CCDS functionality on drug prescribing or utilization. All of the 38 CPOE and CCDS identified studies were designed as intervention studies (comparing outcomes before and after), while six studies in the outpatient setting provided control clinics for comparison (five of which also used randomization).[45 46 55 56 58 61]

Computerized physician order entry and computerized clinical decision support

In the studies included in this review, CPOE and CCDS were commonly implemented at the same time or CCDS was implemented in addition to CPOE. Studies involving the evaluation of CPOE and CCDS are present in table 1. Eight of these studies have outcomes data presented in other sections of this review that are related to a specific CCDS functionality.[4 5 25–29 31] Three studies only reported outcomes that cannot be directly correlated to a specific CCDS functionality. Significant decreases in serious ADEs and a non-significant decrease in overall ADEs have been reported with minimal description of the CCDS functionalities used.[6] Reduction in ADEs that increased the length of stay was reported after implementing an adult-centered CPOE system with customized pediatric decision support functionalities.[30] A study from a children's hospital connected to an adult hospital showed a decrease in non-intercepted error rates, with no reduction in errors causing harm or overall errors.[8] Although assessments of ADEs and errors varied between studies, these studies suggest that CCDS (with the effect of specific CCDS functionalities unknown), CPOE, or a combination of both technologies decreased ADEs and error rates.

Duplicate medication therapy alerts

Duplicate medication therapy decision support functionalities provide computerized reminders during prescription entry about a potentially unnecessary therapeutic duplication. The use of a duplicate therapy alert functionality in a CPOE system resulted in an elimination of duplicate therapy errors.[5] A study completed in the United Kingdom (UK) indicated a high number of exact and therapeutic duplication alerts accompanied by high alert override rates. The authors reported that alerts due to different drug dosage strengths given at different times of the day could not be suppressed. There was no discussion of the effect of alerts occurring between scheduled and unscheduled medication orders (eg, as needed or one-time doses).[44] In a nephrology clinic in the UK, there was no significant difference in drug duplication errors despite exact and therapeutic duplication alerts. The system was not able to identify drugs prescribed in different dosage forms.[27] In the hospital setting, alerts are reported to have failed to prevent some duplicate errors.[26] Although earlier results suggested decreased duplicate therapy orders using duplicate therapy alerts, the specificity for the error (ie, override rates) was low in other published publications potentially due to computer software limitations. Further research is needed to create duplicate medication therapy CCDS systems that can appropriately alert practitioners and thus prevent unnecessary therapeutic duplication.

Medication allergy alerts

Medication allergy CCDS functionalities alert practitioners when an order is placed for a patient who is allergic to a medication. In a CPOE implementation analysis, use of medication allergy alerts decreased medication allergy errors from 1 to 0 (not significant).[5] In a UK study, the majority of medication allergy alerts were overridden and 95% of the overrides had reasons provided for the override (a much higher proportion than for alerts from other CCDS functionalities).[44] Data in adults suggested overrides were clinically justifiable and occurred owing to medication mismatches with alerts.[65] The ability of the CCDS functionality to differentiate between major versus minor allergic reactions (eg, anaphylaxis vs rash) and adverse reactions versus allergic reactions (eg, renal insufficiency vs anaphylaxis with tobramycin) has not been described. Additionally, concerns have been raised about the accuracy of allergy documentation.[66] More research is needed to increase the specificity of computerized medication allergy alerting functionalities.

Medication interaction support

Medication interaction decision support usually involves alerting a practitioner to a medication combination that may result in an undesired pharmacologic effect. Use of interaction alerts in a CPOE system has non-significantly decreased medication interaction errors,[5] although high override frequency has been reported both in the inpatient and outpatient setting, with no reasons being given by practitioners.[42 44] These data support the data in adults suggesting that severity ranking and customization of drug interaction alerts provided by drug information databases are needed to suppress potentially insignificant interactions.[67–69] Extensive evaluation has not been completed in pediatrics. Although medication interactions would have many similarities to those in adults, some suggest that pediatric orders may result in fewer alerts than in adults.[42] Specific CCDS functionalities for disease state interactions (eg, highly protein-bound drugs in patients with neonatal hyperbilirubinemia), age-specific warnings (eg, propylene glycol toxicity in neonates), black box warnings, and contraindications would be unique and CCDS for these pediatric-specific interactions have not been studied.

Medication dosing calculators

Medication dosing errors are considered one of the greatest sources of medication errors in pediatrics, potentially originating from the precise calculations required to vary medication dosage based on a patient's age and weight or body surface area and various dosage forms.[2 3] Computerized dosing calculators have been developed to assist in these calculations. A computerized

Table 1 Evaluation of computerized clinical decision support and computerized physician order entry

Author	Population	CCDS provided	Measured outcomes/results	Authors' conclusion
Cordero *et al*, 2004[25]	NICU	CPOE + gentamicin dosing CCDS including weight verification, automated dosing calculator, recommended dosing, frequency alerts, and maximum dosage alerts with hard stops	Dosing errors decreased for empiric gentamicin dosing (13–0%) and for late onset sepsis gentamicin dosing (6–0%) after implementation of CCDS	CPOE + CCDS resulted in a significant decrease in gentamicin dosing errors
Potts *et al*, 2004[5]	PICU	CPOE + drug allergy alerts, dose checking, drug interaction alerts, US Food and Drug Administration alerts, order sets, and links to literature	Significantly decreased potential ADEs, MPEs, RVs and duplicate therapy errors (all with $p<0.001$). No difference in potential ADEs as a result of medication dose, frequency, allergy or interaction errors	CPOE + CCDS can decrease the number of MPEs, with a less dramatic effect on medication-related ADEs
Upperman *et al*, 2005[6]	Inpatient pediatrics	CPOE + rules reminding or warning the clinician about unfavorable clinical parameters in the patient's status	Harmful ADEs decreased significantly from 0.05 to 0.03/1000 doses ($p=0.05$), transcription errors were eliminated, but there was no change in overall ADEs	CPOE + CCDS rules decreased illegible prescriptions and prevented harmful drug prescribing
Walsh *et al*, 2006[26]	NICU, PICU, and in-patient wards of an academic medical center	CPOE + order sets for selected conditions, drug allergy alerts, drug–drug interaction alerts, duplicate order alerts, and wrong-dose alerts	From 6916 orders, 8 errors of little harm were related to order sets, 2 duplicate orders errors with no CCDS alert fired, and 4 incorrect selection errors had alerts overridden. 119 orders from order sets increased error potential, and 189 orders from order sets increased workload	4 types of errors related to CPOE existed and others should be aware of these issues before implementation of CPOE
Holdsworth *et al*, 2007[4]	PICU + general pediatric unit	CPOE + pediatric-specific dose range tables (gestational age and postnatal age-specific dosing included) without physiologic or disease state dosing modifications	Reduction of RR for total (0.64, CI 0.43 to 0.95), preventable (0.56, CI: 0.34 to 0.91), and potential (0.37, CI 0.25 to 0.55) ADEs. Underdosage and overdosage rates remained unchanged	CPOE + CCDS in a pediatric hospital reduced ADEs and potential ADEs; dosing errors did not change
Jani *et al*, 2008[27]	Pediatric nephrology clinic	CPOE + age-specific weight alerts, computerized drug monographs, drug allergy alerts, and medication duplication alerts	Physician omission errors on prescriptions decreased from 77% to 4.8%. Excluding these errors, dosing errors decreased non-significantly after implementation	Omission errors on paper-based order forms were vastly decreased; other medication-related errors did not decrease
Walsh *et al*, 2008[8]	NICU, PICU, and inpatient wards of an academic medical center	CPOE + dosing alerts (without gestational age alerts), interaction alerts, allergy alerts, and order sets	Overall 7% decrease in non-intercepted serious medication errors ($p=0.0495$), no decrease in overall errors. Non-significant increase from 8 to 10 dosing errors/1000 patient-days. Only 2/19 dosing errors had dosing alerts	Non-intercepted serious errors declined; no decrease in dosing errors or the rate of injuries
Kadmon *et al*, 2009[28]	PICU	CPOE + weight-based dosing ranges and limiting order privileges to physicians only	CPOE non-significantly reduced ADEs and MPEs; CCDS implementation significantly reduced potential ADEs (2.4 to 0.8%; $p=0.0014$) and MPEs (5.3 to 3.8%; $p=0.04$). Further significant reductions with physician restricted ordering	CPOE did not significantly decrease medication-related errors, while CCDS implementation did
Kazemi *et al*, 2010[29]	Neonatal ward	CPOE or NOE + dose range alerts, frequency alerts, and renal function adjustment alerts	CCDS dosing alert acceptance increased from 44% to 68% with NOE. Prescription errors caught by warnings increased from 4.5 to 8.1% with NOE. Prescription errors decreased from 10.3 to 4.5% with NOE. 10.3%). All changes significant ($p<0.001$)	NOE decreased overall errors compared with CPOE, potentially owing to increased acceptance of CCDS dosing alerts
Ferranti, *et al*, 2011[30]	PICU and NICU at an academic medical center	CPOE + pediatric advanced dosing model providing practitioners dosing recommendations based on patient indication, medication, organ function, age, and weight. Alerts for weight and maximum doses also provided when the CCDS was not used	Decreased ADEs (that caused increased length of stay) after implementation from 3.8 to 2.2/1000 patient-days in the PICU ($p=0.012$) and 1.6 to 0.9/1000 patient-days in the NICU ($p=0.006$)	Enhancement of an adult-centered CPOE decision support dosing system for pediatrics guided physicians through the medication ordering process
Kazemi *et al*, 2011[31]	Neonatal ward	CPOE + dose range alerts, frequency alerts, and renal function adjustment alerts	Resident orders had errors in 53% of medication days before CPOE, 51% after CPOE implementation, and 34% after CCDS introduction ($p<0.001$)	CPOE without CCDS did not decrease non-intercepted medication error frequency, but addition of CCDS resulted in reductions

ADE, adverse drug event; CCDS, computerized clinical decision support; CPOE, computerized physician order entry; MPE, medication prescription error; NICU, neonatal intensive care unit; NOE, nurse order entry; PICU, pediatric intensive care unit; RR, relative risk; RV, rules violation (eg, trailing zero).

total parenteral nutrition (TPN) admixture interface (with a dosing reference and dosing alerts) calculated TPN components and volume for TPN compounding. The system eliminated errors in TPN component calculation over a 14-day study period.[32] A larger study, also completed in the neonatal intensive care unit (NICU), showed that a TPN calculator decreased TPN

Table 2 Evaluation of medication dosing calculators

Author	Population	CCDS provided	Measured outcomes/results	Authors' conclusion
Peverini *et al*, 2000[32]	NICU	Computerized TPN admixture interface for TPN component entry in a unit/kg/day format with electronic dosage references, dose range alerts, and hard stops on calcium/ phosphorus concentrations	Elimination of potential calcium/ phosphorus precipitates, decreased illegible orders, and patient information omissions on orders	System allowed for increased safety and efficiency of TPN ordering
Lehmann *et al*, 2004[33]	NICU	Computer-based TPN admixture calculator with nutrition guidelines, osmolarity calculator, and 62 TPN-related alerts and reminders	Decreased total TPN errors requiring pharmacist intervention from 10.8 to 4.2 ($p<0.01$) and 1.2 errors/100 ($p<0.001$) orders in 2 implementation periods. Osmolarity issues, knowledge errors, and calculation errors significantly decreased ($p<0.05$)	Use of low-cost internet technologies can help prevent adverse drug events
Kirk *et al*, 2005[34]	Outpatient pediatric clinic	CPOE + paracetamol and promethazine dosing calculator, dosing alerts, weight alerts, drug interaction alerts, and allergy alerts	Manual dose entry independently increased the risk of causing a medication dosing error (using a dosing calculator decreased errors from 28.2 to 12.6%). Underdosages averaged 10% in the paracetamol group and 30% in the promethazine group. Overdoses averaged 26% in the paracetamol group and 14% in the promethazine group	Automated computerized dosing calculators and dosing alerts were effective at decreasing dosing errors for the studied drugs
Lehmann *et al*, 2006[35]	Children's hospital at an academic medical center	Computer-based calculator with default doses, maximum concentrations, dosing guideline, and alerts for diluent, drug dosage, and insufficient fluid errors for continuous infusion orders	Overall prescription errors decreased from 27 to 14% with calculator use. Elimination of wrong concentration, dose, and calculation errors (occurring, respectively, in 10.1%, 9.4%, and 2% of hand-written orders,) with calculator use	A web-based calculator reduced or eliminated continuous infusion prescription errors
Vardi *et al*, 2007[36]	Pediatric critical care	Computerized system that calculated resuscitation medications and created a paper print out available at the patient bedside	Elimination of drug dosing errors for resuscitation medications from 3/ 13 124 to 0/46 970 orders (not statistically analyzed) and significantly faster time to completion of form (14−2 min)	A computerized dosing calculator allowed for faster resuscitation medication dosing calculations and decreased potentially dangerous dosing errors
Ginzburg *et al*, 2009[37]	Outpatient community center	Acetaminophen and ibuprofen dosing calculator embedded into the electronic medical record	Significantly decreased overall dosing errors (32.6 vs 20.5%, $p=0.02$) and overdosages (8.9 to 4%, $p=0.028$). Underdosage errors not significantly changed	A weight-based dosage calculator on the ordering screen decreased incorrect ibuprofen and acetaminophen orders

CCDS, computerized clinical decision support; CPOE, computerized physician order entry; NICU, neonatal intensive care unit; TPN, total parenteral nutrition.

formulation calculation errors and solutions prescribed with inappropriate osmolarity for a patient's intravenous access availability.[33] A dosing calculator has also been used to aid in prescribing continuous infusion medications in the hospital, where significant reductions were noted in concentration and dose calculation errors.[35] In comparison with a physician and dual nurse triple check system, use of a computer-generated, weight-based resuscitation medication form led to decreased form completion time and elimination of potential errors.[36]

An automated, weight-based dosing calculator embedded into the electronic medical record (EMR) at a family medicine clinic significantly decreased incomprehensible prescriptions, overall dosing errors, and overdoses of greater than 5% of the recommended doses for oral acetaminophen and ibuprofen.[37] In

Table 3 Evaluation of computerized clinical decision support for medication dosing

Author	Population	CCDS provided	Measured outcomes/results	Authors' conclusion
Killelea *et al*, 2007[38]	Pediatric inpatients at an academic medical center	CPOE + pediatric weight-based dosing recommendations, dosage rounding, and additional textual dosing information for the most common indications for 200 pediatric medications	32% Acceptance of recommended dosages (45% ordered higher dosages and 52% ordered lower dosages). Antibiotics accepted 21%, antipyretics 41%, and diuretics 3% of the time. Acceptance lowest in the NICU (10.8%)	Further work needed to optimize effectiveness of dosing support. Customization of dosing support required time and resources
Sheehan *et al*, 2009[39]	NICU	CPOE + gestational age entry requirement, antibiotic dosing alerts, maximum pediatric dosages, renal impairment dosage adjustment suggestions (although the method of renal function assessment was not described), weight-based dosing, and laboratory history displays	Laboratory history displays created 54% of the alerts, renal dosing alerts prompted 37%, and gestational age alerts occurred in 9%. Vancomycin, gentamicin and ampicillin most commonly caused alerts	Alerts provided pertinent information to providers to ensure appropriate antibiotic dosing

CCDS, computerized clinical decision support; CPOE, computerized physician order entry; NICU, neonatal intensive care unit.

Table 4 Evaluation of medication or disease state specific order sets or quick lists

Author	Population	CCDS provided	Measured outcomes/results	Authors' conclusion
Chisolm *et al*, 2006[40]	Pediatric inpatient asthma	CPOE + an order set modeled after a paper form for use with asthma admits (eg, orders and dosages for short-course steroids, metered dose inhaler, pulse oximetry)	A significant increase in appropriate use of systemic corticosteroids (77.8 to 94.4%), metered dose inhalers (39.7 to 55.6%), and pulse oximetry (82.5 to 90.8%) was noted after implementation of the order set	Addition of order sets increased adherence with evidence-based guidelines for asthma management
Sard *et al*, 2008[41]	Emergency department	CPOE + a "quick list" of the 75 most common medications used in the ED, with predetermined dosages, for a specific diagnosis (eg, asthma, sickle cell anemia)	Errors/100 orders decreased from 31 to 14 ($p<0.001$) and there were 11 fewer errors/100 visits with the quick list versus manual search and entry. Wrong formulation and RVs were eliminated, route errors decreased significantly ($p=0.04$), dosing errors decreased non-significantly ($p=0.07$)	Reduction in medication prescribing errors occurred when prescribers used a quick list. Providing a list with dosing may help adapt CPOE systems to pediatrics

CCDS, computerized clinical decision support; CPOE, computerized physician order entry; ED, emergency department; RV, rules violation (defined by authors as abbreviations or dosages entered that were not in compliance with hospital policy).

a Singapore hospital with existing CPOE, physicians who used a medication dosing calculator made fewer drug dosing errors for paracetamol (acetaminophen in the United States) and promethazine than physicians who manually entered their own calculated dose. Dosing errors followed strict limits for underdosages and overdosages (eg, 15 mg/kg/dose was the maximum paracetamol dose, with 15.1 mg/kg/dose being an error) and it was not clear if estimates for doses from suppository formulations of paracetamol were taken into account.[34] A study analyzing anti-infective therapy in a pediatric intensive care unit (PICU) reported decreased pharmacy interventions, potentially due to a combination of the use of a calculator and dose ranges.[50]

These studies suggest that there is an increase in adherence to a defined dosage range and a decrease in dosing calculation errors when dosing calculators are used. Although these studies did not measure patient outcomes (therapeutic failure or adverse event), two studies involved medications with a high potential for adverse effects (TPN and resuscitation medications). Studies also varied in their allowance of dosage rounding, which might have affected their results. Some suggest specific dose rounding rules for each medication,[70] but this has not been standardized. Weight-based dosing calculators are a CCDS functionality that may have a significant role in avoiding manual calculation prescribing errors, although further study is required to determine if a prevented dosing calculation error results in significantly improved medication efficacy and safety for pediatric patients.

Dosing ranges or support

In addition to medication dosing calculators, computerized medication dosing rules have been developed that alert clinicians if a prescription is outside the desired reference range for a patient's age, weight, indication, or organ function. Other programs can recommend dosing based on patient information. Drug dosing and interval errors were not statistically changed after the implementation of CPOE with a dose and frequency checking CCDS functionality.[5] Data from pediatric patients in a large medical center showed an unexpected, but non-significant increase in dosing errors after CCDS was implemented with a pediatric dosing range option (the system did not have gestational age-specific rules). Only two of the 17 dosing errors occurring after the implementation period caused an alert to occur.[8] Although the overall relative risk of preventable ADEs significantly decreased, underdosing and overdosing errors did

Table 5 Evaluation of alert overrides

Author	Population	CCDS provided	Measured outcomes/results	Authors' conclusion
Isaac *et al*, 2009[42]	Ambulatory care electronic prescriptions (3 million from 3 states)	Electronic prescriptions with tiered DDI and drug-allergy alerts	1.2% of pediatrician orders caused a DDI alert and 10.7% of alerts were overridden. Pediatric DDI alerts occurred less frequently and override frequency significantly differed compared with adult orders ($p<0.001$)	Clinicians overrode most high-severity DDI alerts and drug-allergy alerts, further improvements needed
Johnson *et al*, 2010[43]	Community adult and pediatric clinics	Electronic prescribing + dose range calculations, interactions, and formulary benefits with "show your work" reasons for any override alert	No significant change in the number of pharmacy callbacks to physicians, surveys identified some improvement in communication between pharmacists and physicians	Implementation of show your work did not decrease callbacks, but may have changed the types of callbacks
Jani *et al*, 2011[44]	Pediatric inpatient, outpatient, and discharge prescriptions	CPOE + drug allergy, exact duplication, drug interaction, and therapeutic duplication alerts	60.3% of orders resulted in an alert (mainly interactions) with 13% visible to the users (89% of visible alerts were exact duplication). 89% of all visible alerts were overridden with 63% of allergy, 73% of interaction, 90.6% of exact duplication, and 95% of therapeutic duplication alerts overridden. 95% of allergy alerts had a reason given, but other alerts had a reason given 0−1 times for thousands of alerts	The CPOE system studied had a large number of alerts in which a large proportion were overridden

CCDS, computerized clinical decision support; CPOE, computerized physician order entry; DDI, drug−drug interaction.

Table 6 Evaluation of computerized clinical decision support providing evidence-based information

Author	Population	CCDS provided	Measured outcomes/results	Authors' conclusion
Christakis* *et al*, 2001[45]	Outpatient academic pediatric clinic	Provided evidence-based information about antibiotic selection and duration at the time of prescribing an antibiotic for AOM	Overall increase from 50.7 to 69.7% in antibiotics ordered for $<$10 days. A 44% greater increase in frequency of ordering antibiotics for $<$10 days from baseline in prescribers exposed to literature evidence vs a 10% change in frequency in the control group ($p<0.01$). Prescription of any antibiotic increased from baseline	Presenting pertinent information to providers during decision-making improved prescribing patterns
Davis* *et al*, 2007[46]	Two outpatient academic pediatric clinics	Provided evidence-based treatment information at the time of prescribing medications for AOM, allergic rhinitis, sinusitis, constipation, pharyngitis, croup, and urticaria	Increased prescribing in accordance with treatment evidence by 4% (38% to 42%) in the intervention versus 1% in the control group (39% to 40%) (weighted 8% difference with a CI of 1% to 15% difference)	Significant improvement in provider prescribing practices for a given indication when evidence was provided during prescribing

*Randomized controlled trial.
AOM, acute otitis media; CCDS, computerized clinical decision support.

not significantly decrease with the use of customized pediatric dosing range alerts in a PICU and general pediatric unit.[4] In a large urban hospital with 100 pediatric beds, the use of pediatric designed dosing rules for 200 pediatric medications and their most common indications resulted in poor acceptance of dosing recommendations.[38] In a separate large urban hospital with 187 pediatric beds, an indication and organ function-specific pediatric dosing guide was created. The authors described the need to create alternative dosing limit alerts for use when the recommendations were overridden and dosages were manually entered, suggesting that dosing guidelines were not always followed.[30] These studies suggest that despite creation of pediatric-specific dosing ranges, pediatric medication dosing alerts have high override rates, concerns for sensitivity to dosing errors, and variable impact on ADEs. This may be explained in part by the lack of specificity in program designs or a high level of variability in pediatric dosing.

The implementation of CPOE without CCDS was shown to non-significantly decrease potential ADEs and medication prescription errors, while significant decreases did occur after adding CCDS dosing alerts.[28] A study completed in the NICU, without a clinical pharmacist, also suggested that CPOE implementation alone did not decrease dosage errors, but the addition of CCDS dosing alerts decreased drug dosing errors per medication day rates.[31] These studies support positive effects of CCDS independent of CPOE on pediatric dosing errors. However, these studies may have been associated with baseline practice differences, limiting widespread generalizability of the CCDS dosing rules.

In a NICU population, the use of a maximum gentamicin dosage check was reported to significantly decrease gentamicin dosing errors. However, the authors did not discuss effects on drug dosage changes based on serum concentrations.[25] Investigators in a different NICU study concluded that the use of antibiotic-specific dosing alerts in a NICU provided patient information to aid in neonatal dosing, although outcomes of the alerts were not described.[39] The use of TPN component dosing range alerts and references in addition to a TPN calculator in the NICU eliminated inappropriate calcium/phosphorus concentration errors in one study and significantly decreased TPN component and osmolarity prescription errors in another.[32 33] Dosing alerts for continuous infusion medications along with a dosing calculator have been shown to eliminate drug dosing errors.[35] The use of an anti-infective decision support tool with dosage recommendations (including renal dysfunction adjustments) and a dosing calculator showed a reduction in pharmacist dosing interventions after implementation.[50] Dosing recommendations provided by CCDS functionalities for insulin and warfarin dosing have also shown efficacy in managing patients in comparison with providers not using CCDS.[47 52] These studies provide evidence of potential decreases in medication errors and appropriate therapeutic effect due to dosing support functionalities, but results might have been affected by multiple CCDS functionalities and the impact on patient outcomes was not evaluated. More research needs to focus on ensuring the specificity and sensitivity of dosing range alerts and dosing recommendations from CCDS for both efficacy and safety-related outcomes, in addition to identification of medications which are commonly used outside of desired dosing ranges.

Weight verification or weight ranges

The effect of both dosing calculators and dose range checking in pediatric patients is dependent on the accuracy of the patient's weight entered into the system. A study in a nephrology clinic from the UK reported decreased incorrect dosages with the use of CPOE and a CCDS functionality that alerted practitioners when a patient's weight was entered that was outside of normal limits. This study did not use dosing calculators or dose range support.[27] The use of weight verification or weight range alerts was reported in other studies in addition to other CCDS functionalities.[25 30 34] These studies may support the use of weight verification as an important CCDS functionality, although analysis of the effectiveness of weight range or weight verification alerts in ensuring appropriate pediatric dosing has not been studied.

Alert override evaluations

Although medication alerts during order entry are commonly used to provide CCDS, excessive erroneous alerts may lead to "alert fatigue," which may enhance ordering and verification of incorrect medication dosages.[71] Some studies described medication errors occurring because of prescribers overriding dosing range alerts[26]; CCDS alert overrides were reported to occur in 63–95% of all medication-related alerts.[34 42 44] Providing a rationale for an alert override has the theoretical advantage of explaining why an alert may not apply. The use of prescriptions annotated with "rationales" from a single clinic to local pharmacies did not find differences in quantitative data (call-back rates), but only in qualitative data (pharmacist surveys). This study was limited because the annotations were standardized and might not have depicted the prescribers actual thought

Table 7 Evaluation of computerized clinical decision support providing treatment recommendations

Author	Population	CCDS provided	Measured outcomes/results	Authors' conclusion
Zahlmann *et al*, 1990[47]	Ambulatory diabetic patients	Recommended normal daily dose of insulin based on input of demographics, blood glucose readings, and insulin daily requirements	Recommended insulin doses accepted at 80% of visits. Decreased HbA_{1C} from 5.8 (boys) and 5.9 (girls) to 5.2 and 4.9, respectively, after 12 months using CCDS (significance not tested)	Use of the CCDS system decreased medium blood glucose in diabetic patients
Schriger *et al*, 2000[48]	Pediatric emergency department	Decision aid for the diagnosis and management of fever in the emergency department	Increased documentation of PMH from 80% to 92% and no change in appropriate treatment choices identified between groups with or without CCDS	CCDS tool did not change physicians treatment decisions, but increased treatment documentation
Shiffman *et al*, 2000[49]	Pediatric outpatients	Hand-held computerized system provided documentation reminders, treatment recommendations with rationale based on asthma NAEPP guidelines, print-out information sheets, and prescriptions	Increased adherence to guidelines, cost, and time of patient visit. Trend of improvement in symptoms at the end of the visit, not maintained during the following week	Hand-held computers increased guideline adherence. Prolonged visits with higher costs and no measureable benefit after 1 week
Mullett *et al*, 2001[50]	PICU	Antibacterial computer program helped determine age-specific antibacterial agents, anti-infective dosages, and dosage adjustments in renal insufficiency	Significantly decreased pharmacist dosing interventions (59%, $p<0.01$), duration of inappropriate antimicrobial therapy (32%, $p<0.0001$), and the robust estimate of cost. >80% of surveys had positive results	Improved drug dosing and days within therapeutic dose ranges when using the computer system. Results less positive compared with the use of this program in adults
Shegog *et al*, 2006[51]	Outpatient pediatric asthma (inner-city teaching hospital and clinics)	Asthma tool provided measurements of severity, medication and environmental management, and prescription planning. Users entered data and the computer provided cues for severity assessment, compliance, environmental triggers, and medication treatment recommendations	Use of CCDS compared with normal care perceived to be more useful, thorough, and accurate, and improved patient communication. Ease of use and time not perceived to be positively affected	Favorable perceptions of the feasibility of this tool for patients with asthma
Soper *et al*, 2006[52]	Outpatient cardiology	Calculated an appropriate plasma INR based on an input whole-blood INR, and provided warfarin dosing and follow-up recommendations	Dosing suggestions adjusted for 21% of warfarin orders. Patients within target INR range 76% of the time before using CCDS and 79% after ($p=0.87$)	A computerized system can be developed to support warfarin therapy decisions and maintain INR
Fiks *et al*, 2007[53]	Outpatient pediatric clinics	Alert created based on EMR vaccination history and vaccination guidelines (guidelines were available when opening a patient's electronic chart)	Up-to-date immunizations at 24 months significantly increased from 79.5 to 88.2% excluding invalid doses	Alerts present in the medical record for routine pediatric vaccines increased vaccination rates
Fiks *et al*, 2009[54]	Pediatric asthma clinics	Influenza vaccination alerts for pediatric patients with asthma due for influenza vaccination based on vaccination guidelines	A non-significant 4% increase in control versus intervention group for appropriate administration of influenza vaccination compared with baseline	Alerts present in the medical record only modestly increased vaccination rates in patients with asthma
Bell* *et al*, 2010[55]	Outpatient pediatric asthma	Reminders in the EMR to complete assessment tools, with computerized patient-specific recommendations made based on patient data from assessment tools	A 6% greater increase in prescription of controller medications for persistent asthma compared with baseline in the intervention group who used CCDS versus the control group using standard care	CCDS in the EMR improved guideline adherence with controller medication prescription
Bourgeois* *et al*, 2010[56]	Ambulatory pediatric clinics	CCDS incorporated into an EMR provided recommendations on antibiotic and OTC medication selection with dosing based on age, weight, and indication for 8 acute respiratory infections	Overall antibiotic prescription changed from 46% in the control group to 39.6% in the intervention group ($p=0.844$). Antibiotic prescription decreased in the intervention group (39.9 to 31.7%, $p=0.02$)	Overall antibiotic prescription in the intervention clinics did not change; CCDS system did change prescriber actions
Faraon-Pogaceanu *et al*, 2010[57]	PICU	Computerized blood glucose management program provided insulin dosing recommendations to maintain blood glucose within a predetermined goal range	Blood glucose within goal range more often in the computerized group compared with a paper format. No differences in hypoglycemia (goals were 80–110 μg/ml and 90–119 μg/ml, respectively)	Computerized program achieved tighter glucose control with a similar safety profile

Continued

Table 7 Continued

Author	Population	CCDS provided	Measured outcomes/results	Authors' conclusion
Fifield† *et al*, 2010[58]	Pediatric asthma	Medication reports sent to clinicians 2 days after clinic visits, based on data electronically entered during visit, recommending guideline-based asthma assessment and treatment changes	Prescribers twice as likely to adhere to treatment guidelines and patients had significantly increased asthma symptom control if physicians were exposed to CCDS-created treatment reports	Increased asthma guideline adherence and control with the use of CCDS in the inner-city asthma population
Hoeksema *et al*, 2011[59]	Outpatient pulmonology clinic	Asthma control assessment, severity assessment, and treatment recommendations with deviation alerts for new and returning patients with asthma	28.8% of physicians agreed with CCDS treatment recommendations. 77% of disagreements due to inability of CCDS to identify and categorize existing medications	CCDS tool recommended treatments similar to physician's in 39% of new patients without previous asthma medications
Shapiro *et al*, 2011[60]	Two inner-city healthcare centers	Drop-down checklist in the EMR that aided in assessing asthma control, severity assessment, and controller medication prescription	Controller medication prescription for persistent or uncontrolled asthma remained stable at one center and increased from 81.3 to 97.3% after updated guidelines were implemented at another center ($p<0.01$)	Increased severity documentation over time with the use of the CCDS system and increased appropriate controller medication prescription

*Randomized controlled trial; †controlled trial.
CCDS, computerized clinical decision support; EMR, electronic medical record; HbA_{1C}, glycated hemoglobin; INR, international normalized ratio; NAEPP, National Asthma Education and Prevention Program; OTC, over the counter; PICU, pediatric intensive care unit; PMH, past medical history.

process, and communication between the practitioners might not have changed.[43] A study completed in a hospital setting reported minimal (0–1 of 100 alerts) override reasons given for all of the alert functionalities except for medication allergy alerts (of which the most common override reason was *"aware will monitor")*.[44] These data suggest that alerts are often overridden by practitioners for mostly unknown reasons, suggesting either decreased applicability of computerized rules in direct patient care or high variability in pediatric medication therapy.

Overrides for asthma alert recommendations and duplicate medication therapy alerts have suggested that technologic limitations in programming capabilities resulted in CCDS insufficiencies.[27 44 59] Experiences with dosing range alerts also suggested that the design of dose range limits can create CCDS insufficiencies.[38] Both topics require detailed analysis to create the appropriate human to computer interface for increased CCDS applicability.

One strategy to prevent alert overrides is to prevent medication regimens considered to be an incorrect medication therapy from being processed, also known as a "hard stop." This approach has been used in TPN ordering where an attending physician's signature was required for dosing outside the limits and hard stops were implemented for orders with a potential to cause calcium and phosphorus precipitation. This study only evaluated 14 days before and after implementation.[32] Hard stops for maximum doses were also used for gentamicin dosing in the NICU.[25] Although these studies reported the elimination of dosing outside of the desired range, this approach should be used with caution as delays in patient care have been described in adults.[72]

Alerts were the most frequently reported form of CCDS reminders, but studies completed in adult hospitals suggested that alerts occurring during order entry were not reaching practitioners during decision-making, which may have caused

Table 8 Evaluation of care giver-driven computerized clinical decision support with therapeutic recommendations

Author	Population	CCDS provided	Measured outcomes/results	Authors' conclusion
Kattan* *et al*, 2006[61]	Pediatric urban community clinics	Care givers of pre-identified patients with moderate—severe asthma received automated phone calls that collected data about asthma control and sent summary reports to PCP physicians with treatment recommendations	17 vs 12% had follow-up visits in the intervention group. 46 vs 36% had medication increases. Fewer ED visits/year (0.87 vs 1.14, $p=0.013$). Symptoms, hospitalizations, and unscheduled visits did not change. $337 cost savings/child	CCDS intervention resulted in a greater number of visits, greater number of medication increases, fewer ED visits, and a decrease in healthcare costs
Porter *et al*, 2006[62]	Pediatric emergency department	Asthma characterization and treatment recommendations provided by CCDS after care giver entered asthma symptoms into a computerized kiosk	Recommendations accepted from 0 to 50% by practitioners, increased fluticasone prescribing 5–18% after intervention ($p=0.06$)	Care giver-driven asthma kiosk implemented with minor changes in prescribing controller medications
Porter *et al*, 2008[63]	Pediatric emergency department	Test and treatment recommendations provided by CCDS for dysuria, otalgia, fever, head trauma, and asthma after caregiver entered PMH into a kiosk in the ED	Kiosk did not decrease overall error and serious error rates ($p=0.35$). Overdose, underdose, and medication allergy errors occurred in 3.4, 1.7, and 1.7% of orders, respectively	Kiosk did not significantly change targeted medication-related errors
Fine *et al*, 2009[64]	Pediatric emergency department	Test and treatment recommendations provided by CCDS for UTI, AOM, head injury, asthma after care giver entered asthma-related PMH into a kiosk in the ED	Inadequate medical documentation for pain treatment decreased from 28 to 15% after intervention, but incorrect prescribing did not change significantly	Care giver documented PMH improved pain documentation but did not influence incorrect test ordering or prescribing

*Randomized controlled trial.
AOM, acute otitis media; CCDS, computerized clinical decision support; ED, emergency department; PCP, primary care provider; PMH, past medical history; UTI, urinary tract infection.

high override rates.[73] Nurse order entry with a physician co-signature increased acceptance of dosing alerts in a neonatal ward.[29] In addition, low acceptance of pediatric dosing recommendations suggested decreased specificity of the dosing rules for the pediatric population.[38] Thus, specification of rules for pediatrics and/or alternative means of presenting information to practitioners must be explored to effectively provide medication-based CCDS to practitioners.

Medication order sets

An order set is a CCDS functionality that focuses on improving the accuracy and efficiency of medication ordering. This functionality includes the most commonly prescribed medication(s) for a typical patient presentation. Physicians in a level-1 trauma center with a physically separate pediatric emergency department made errors less frequently when a disease-specific "quick list" of medications with dosages was used instead of a manual search and enter method.[41] In a 323 bed stand-alone children's hospital, an asthma-specific pediatric order set available for use by physicians significantly increased the guideline-based use of short-course corticosteroids and albuterol. Physicians indicated it was easier to complete order entry for asthma, but perhaps not for other indications, if specific treatments were left out.[40] A study analyzing adverse events related to CPOE and CCDS revealed errors related to order set utilization; most errors were not considered to have the potential for harm, although they did create excessive work for practitioners.[26] These studies support the use of order sets as an efficient way to implement guideline-based care although they did not provide adequate data on patient care outcomes, adherence rates were not 100%, order set efficiency may be dependent on the completeness of the order set, and there is the potential for undesired medication use when order sets are used.

Evidence-based treatment information reminders

One approach to increase the applicability of CCDS interventions is to provide descriptions of evidence or study data along with a CCDS intervention. For acute otitis media, providing evidence about antibiotic prescribing duration and effectiveness resulted in significant decreases in the duration of antibiotic treatment but an increase in antibiotic prescription frequency. Applying this concept to other disease states identified a similar significant, albeit modest, increase in adherence to guidelines when prescribers were provided with informational reminders.[45 46] These data suggest that providing evidence to a prescriber before a prescription is written may increase adherence to evidence-based treatments, but is likely dependent on the data available for treatment of the specific disease. Further studies are needed to determine how often physicians read the alerts and reasons why patient-specific treatment deviates from the provided evidence.

Treatment recommendations

Advanced CCDS functionalities may provide a clinician with a choice of treatment and dosage recommendations before a prescription order is entered. This approach has been used to increase adherence to the National Asthma Education and Prevention Program (NAEPP) guidelines.[74 75] Although a CCDS program providing asthma treatment recommendations was preferred over paper-based asthma tools,[51] others have found less than 40% agreement with pulmonologist's opinions for asthma severity ratings and treatment steps (potentially owing to the system's inability to classify medications in patients who were not treatment-naïve patients).[59]

Guideline adherence and patient outcomes resulting from the use of CCDS have varied. A hand-held computerized tool providing asthma treatment recommendations was used in outpatient pediatric asthma clinics. This resulted in an increase in adherence to the NAEPP guidelines and a non-significant trend toward symptom improvement, but also a significant increase in visit duration and costs per visit. The authors suggested that inadequate guideline specificity might have resulted in the cost increase.[49] Compared with those without CCDS, physicians in academic clinics using a CCDS functionality that provided treatment recommendations had a significantly higher increase in appropriate controller medication prescription for patients with severe asthma. There was no change in suburban clinics, potentially owing to increased baseline guideline adherence.[55] Differences in the effect of a CCDS system due to baseline practitioner prescribing patterns have been described elsewhere.[60] Implementation of an asthma educational package with a web-based decision support system providing recommendations to physicians within 2 days of a visit showed a greater rate of guideline-based medication treatment and visit-to-visit asthma control over 13 months compared with the educational package alone. Receipt and acceptance of the recommendations and resulting treatment changes were not directly assessed.[58] Based on these studies, guideline adherence may increase when CCDS functionalities are used for a disease state such as asthma, although potentially dependent on physician group, patient population, and the quality of the underlying guidelines. Disease-related patient outcomes have only been evaluated short term.

Pediatric immunization practices have guidelines that are revised yearly by the Center for Disease Control and Prevention.[76] When previous guidelines were used, rule-based alerts in the EMR notifying physicians when immunizations were due resulted in a significant increase in immunization rates at 24 months of age and time to vaccinations being up-to-date in an urban pediatric setting.[53] Increases in vaccination rates were also described when alerts for the influenza vaccination were used for urban patients with asthma aged 5–18 years.[54] In this guideline-driven healthcare practice, a rule-based CCDS functionality increased immunization rates for urban patients. These results are promising, but the effect of such a program in a suburban or hospitalized pediatric population has not been studied. These programs would also potentially require yearly updates.

A retrospective review comparing a computerized insulin administration system with a paper-based, nurse-driven system found better blood glucose control and similar hypoglycemic episodes with the use of the computerized system.[57] In ambulatory care setting, CCDS systems have been able to help practitioners determine dosing adjustments for insulin use in type 1 diabetics, and warfarin use for anticoagulation therapy.[47 52] Dosing suggestions were adjusted 21% of the time in the warfarin study.[52] Although these studies did not use national guidelines, the CCDS functionalities demonstrated efficacy in recommending insulin and warfarin dosing, with measurable effects on surrogate disease state markers (glucose control and anticoagulation).

Less positive results have been described when a CCDS functionality providing recommendations was studied for other indications. A CCDS functionality previously used in the adult intensive care unit for empiric anti-infective choice and dosage support was customized for use in a PICU and produced less positive results than the previous adult study. Reductions in excessive days of antibiotic use, pharmacist interventions, and, potentially, costs (only when using a non-standard robust estimate) were still noted. Qualitative data from surveys also suggested improvement in antibiotic choice.[50] In an emergency department serving both adult and pediatric patients, a CCDS tool for pediatric fever treatment improved medication documentation, although adherence to the desired guidelines did not change, unlike for adult indications.[48] A CCDS tool providing tailored treatment recommendations for acute respiratory illnesses showed improvement in inappropriate antibiotic prescription, although it was not used often enough to affect overall antibiotic prescription in the studied population.[56] These data suggest that CCDS functionalities providing treatment recommendations may be more difficult to design in pediatric subjects than in adults, potentially owing to lack of widely accepted treatment guidelines followed by practitioners.

Care giver-driven treatment recommendations

Considering the active role played by caregivers in pediatric healthcare, some centers have created CCDS functionalities that incorporate a patient's caregiver. Kiosks present in a pediatric emergency department prompted caregivers for background information on patients and generated treatment recommendations for providers. Recommendation acceptance was less than 50% by physicians and there was a non-significant increase in appropriate fluticasone prescription. Caregiver satisfaction with dealing with concerns was decreased after implementation based on a yes or no questionnaire.[62] A separate study using a similar design also showed no improvement in targeted medication prescription errors.[63] When a similar application was applied to other emergency department indications (eg, acute otitis media, head trauma, and urinary tract infections), a non-significant increase in appropriate treatment decisions occurred with a significant increase in pain medication documentation.[64] These CCDS functionalities were computerized, but provided recommendations in a paper format to physicians with unknown receipt. There was also minimal analysis of the caregiver's accuracy in entering data into the kiosk system, although caregivers were considered competent.

Bimonthly computer-assisted telephone interviews, with subsequent computerized treatment and follow-up (based on NAEPP guidelines) letters sent to practitioners, were used in a multicenter randomized study to continually assess inner-city patients with asthma. This study showed that the intervention group had significantly more visits, therapy increases, and decreased costs than control (despite <50% adherence to recommendations). Drug dosage increases were not detected and physicians noted problems with reaching the study patients or caregivers after receiving a letter.[61] This study showed how an automated system can cost-effectively serve as a triage for inner-city patients with asthma, although this CCDS functionality was not fully integrated into the medical record and requires study in patients with different socioeconomic backgrounds.

Incorporation of caregivers into the medical care of their children theoretically may offer certain benefits, but also increases the responsibility of family members. The use of computerized kiosks as an avenue to include parents also has the potential to disconnect the caregivers from providers.[62] However, data with the use of a computerized phone call system for inner-city patients involved caregivers and increased continuity of care in the outpatient setting.[61] Further studies are needed to determine how CCDS functionalities can effectively involve caregivers in the care of pediatric patients and improve medication-related outcomes.

CONCLUSION

Computerized clinical decision support functionalities for medication prescribing and utilization in pediatrics are being designed and implemented in various ways. These CCDS functionalities have been studied both independently and as part of a CPOE or EMR system, with most studies using the before and after comparison study design and only a few ambulatory studies using a control group. Implementation of multiple CCDS functionalities simultaneously and changes in clinical practice can create challenges for designing and evaluating CCDS studies.

The findings of this review have identified variable efficacy of individual functionalities dependent on factors such as their design, implementation strategy, and computer technology limitations. Additional evaluation and improvement of individual functionalities need to be completed. Variations in clinical practice within the pediatric population and differences in comparison with the adult population need to be taken into account when designing CCDS functionalities. Most studies did not measure or demonstrate the impact of CCDS on patient outcomes, despite aiming to improve them. Future studies should analyze patient-related outcomes and the specificity and sensitivity of alert-based CCDS functionalities for safe and effective medication use. Voluntary adverse event reporting and inconsistent terminology definitions can affect the accuracy of safety data, and may require active surveillance techniques and consistent definitions to effectively evaluate safety outcome studies, particularly in the inpatient setting.

Implementation of future CCDS functionalities for medication prescribing and utilization in pediatric patients should be well studied during implementation. New and existing CCDS functionalities also require continual evaluation and improvement to capture the potential benefits of these technologic innovations on patient care.

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REFERENCES

1. **America CoQoCi.** *Crossing the QUALITY CHASM: A New Health System for the 21st Century*. Washington, DC: Institute of Medicine, National Academies Press, 2001.
2. **Holdsworth MT,** Fichtl RE, Behta M, *et al*. Incidence and impact of adverse drug events in pediatric inpatients. *Arch Pediatr Adolesc Med* 2003;**157**:60–5.
3. **Kaushal R,** Bates DW, Landrigan C, *et al*. Medication errors and adverse drug events in pediatric inpatients. *JAMA* 2001;**285**:2114–20.
4. **Holdsworth MT,** Fichtl RE, Raisch DW, *et al*. Impact of computerized prescriber order entry on the incidence of adverse drug events in pediatric inpatients. *Pediatrics* 2007;**120**:1058–66.
5. **Potts AL,** Barr FE, Gregory DF, *et al*. Computerized physician order entry and medication errors in a pediatric critical care unit. *Pediatrics* 2004;**113**:59–63.
6. **Upperman JS,** Staley P, Friend K, *et al*. The impact of hospitalwide computerized physician order entry on medical errors in a pediatric hospital. *J Pediatr Surg* 2005;**40**:57–9.
7. **King WJ,** Paice N, Rangrej J, *et al*. The effect of computerized physician order entry on medication errors and adverse drug events in pediatric inpatients. *Pediatrics* 2003;**112**:506–9.
8. **Walsh KE,** Landrigan CP, Adams WG, *et al*. Effect of computer order entry on prevention of serious medication errors in hospitalized children. *Pediatrics* 2008;**121**:e421–7.
9. **Chaffee BW,** Zimmerman CR. Developing and implementing clinical decision support for use in a computerized prescriber-order-entry system. *Am J Health Syst Pharm* 2010;**67**:391–400.
10. **Moxey A,** Robertson J, Newby D, *et al*. Computerized clinical decision support for prescribing: provision does not guarantee uptake. *J Am Med Inform Assoc* 2010;**17**:25–33.

11. **van Rosse F,** Maat B, Rademaker CM, *et al*. The effect of computerized physician order entry on medication prescription errors and clinical outcome in pediatric and intensive care: a systematic review. *Pediatrics* 2009;**123**:1184—90.
12. **Palma JP,** Sharek PJ, Classen DC, *et al*. Neonatal Informatics: computerized physician order entry. *Neoreviews* 2011;**12**:393—6.
13. **Kim GR,** Chen AR, Arceci RJ, *et al*. Error reduction in pediatric chemotherapy: computerized order entry and failure modes and effects analysis. *Arch Pediatr Adolesc Med* 2006;**160**:495—8.
14. **Warrick C,** Naik H, Avis S, *et al*. A clinical information system reduces medication errors in paediatric intensive care. *Intensive Care Med* 2011;**37**:691—4.
15. **Ammenwerth E,** Schnell-Inderst P, Machan C, *et al*. The effect of electronic prescribing on medication errors and adverse drug events: a systematic review. *J Am Med Inform Assoc* 2008;**15**:585—600.
16. **Baysari MT,** Westbrook J, Braithwaite J, *et al*. The role of computerized decision support in reducing errors in selecting medicines for prescription: narrative review. *Drug Saf* 2011;**34**:289—98.
17. **Upperman JS,** Staley P, Friend K, *et al*. The introduction of computerized physician order entry and change management in a tertiary pediatric hospital. *Pediatrics* 2005;**116**:e634—42.
18. **Garg AX,** Adhikari NK, McDonald H, *et al*. Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. *JAMA* 2005;**293**:1223—38.
19. **Kaushal R,** Shojania KG, Bates DW. Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review. *Arch Intern Med* 2003;**163**:1409—16.
20. **Yourman L,** Concato J, Agostini JV. Use of computer decision support interventions to improve medication prescribing in older adults: a systematic review. *Am J Geriatr Pharmacother* 2008;**6**:119—29.
21. **Pearson SA,** Moxey A, Robertson J, *et al*. Do computerised clinical decision support systems for prescribing change practice? A systematic review of the literature (1990-2007). *BMC Health Serv Res* 2009;**9**:154.
22. **Kuperman GJ,** Bobb A, Payne TH, *et al*. Medication-related clinical decision support in computerized provider order entry systems: a review. *J Am Med Inform Assoc* 2007;**14**:29—40.
23. **Mack EH,** Wheeler DS, Embi PJ. Clinical decision support systems in the pediatric intensive care unit. *Pediatr Crit Care Med* 2009;**10**:23—8.
24. **Tan K,** Dear PR, Newell SJ. Clinical decision support systems for neonatal care. *Cochrane Database Syst Rev* 2005:CD004211.
25. **Cordero L,** Kuehn L, Kumar RR, *et al*. Impact of computerized physician order entry on clinical practice in a newborn intensive care unit. *J Perinatol* 2004;**24**:88—93.
26. **Walsh KE,** Adams WG, Bauchner H, *et al*. Medication errors related to computerized order entry for children. *Pediatrics* 2006;**118**:1872—9.
27. **Jani YH,** Ghaleb MA, Marks SD, *et al*. Electronic prescribing reduced prescribing errors in a pediatric renal outpatient clinic. *J Pediatr* 2008;**152**:214—18.
28. **Kadmon G,** Bron-Harlev E, Nahum E, *et al*. Computerized order entry with limited decision support to prevent prescription errors in a PICU. *Pediatrics* 2009;**124**:935—40.
29. **Kazemi A,** Fors UG, Tofighi S, *et al*. Physician order entry or nurse order entry? Comparison of two implementation strategies for a computerized order entry system aimed at reducing dosing medication errors. *J Med Internet Res* 2010;**12**:e5.
30. **Ferranti JM,** Horvath MM, Jansen J, *et al*. Using a computerized provider order entry system to meet the unique prescribing needs of children: description of an advanced dosing model. *BMC Med Inform Decis Mak* 2011;**11**:14.
31. **Kazemi A,** Ellenius J, Pourasghar F, *et al*. The effect of Computerized Physician Order Entry and decision support system on medication errors in the neonatal ward: experiences from an Iranian teaching hospital. *J Med Syst* 2011;**35**:25—37.
32. **Peverini RL,** Beach DS, Wan KW, *et al*. Graphical user interface for a neonatal parenteral nutrition decision support system. *Proc AMIA Symp* 2000:650—4.
33. **Lehmann CU,** Conner KG, Cox JM. Preventing provider errors: online total parenteral nutrition calculator. *Pediatrics* 2004;**113**:748—53.
34. **Kirk RC,** Li-Meng Goh D, Packia J, *et al*. Computer calculated dose in paediatric prescribing. *Drug Saf* 2005;**28**:817—24.
35. **Lehmann CU,** Kim GR, Gujral R, *et al*. Decreasing errors in pediatric continuous intravenous infusions. *Pediatr Crit Care Med* 2006;**7**:225—30.
36. **Vardi A,** Efrati O, Levin I, *et al*. Prevention of potential errors in resuscitation medications orders by means of a computerised physician order entry in paediatric critical care. *Resuscitation* 2007;**73**:400—6.
37. **Ginzburg R,** Barr WB, Harris M, *et al*. Effect of a weight-based prescribing method within an electronic health record on prescribing errors. *Am J Health Syst Pharm* 2009;**66**:2037—41.
38. **Killelea BK,** Kaushal R, Cooper M, *et al*. To what extent do pediatricians accept computer-based dosing suggestions? *Pediatrics* 2007;**119**:E69—U26.
39. **Sheehan B,** Chused A, Graham PL 3rd, *et al*. Frequency and types of alerts for antibiotic prescribing in a neonatal ICU. *Stud Health Technol Inform* 2009;**146**:521—5.
40. **Chisolm DJ,** McAlearney AS, Veneris S, *et al*. The role of computerized order sets in pediatric inpatient asthma treatment. *Pediatr Allergy Immunol* 2006;**17**:199—206.
41. **Sard BE,** Walsh KE, Doros G, *et al*. Retrospective evaluation of a computerized physician order entry adaptation to prevent prescribing errors in a pediatric emergency department. *Pediatrics* 2008;**122**:782—7.
42. **Isaac T,** Weissman JS, Davis RB, *et al*. Overrides of medication alerts in ambulatory care. *Arch Intern Med* 2009;**169**:305—11.
43. **Johnson KB,** Ho YX, Cala CM, *et al*. Showing Your Work: Impact of annotating electronic prescriptions with decision support results. *J Biomed Inform* 2010;**43**:321—5.
44. **Jani YH,** Barber N, Wong IC. Characteristics of clinical decision support alert overrides in an electronic prescribing system at a tertiary care paediatric hospital. *Int J Pharm Pract* 2011;**19**:363—6.
45. **Christakis DA,** Zimmerman FJ, Wright JA, *et al*. A randomized controlled trial of point-of-care evidence to improve the antibiotic prescribing practices for otitis media in children. *Pediatrics* 2001;**107**:E15.
46. **Davis RL,** Wright J, Chalmers F, *et al*. A cluster randomized clinical trial to improve prescribing patterns in ambulatory pediatrics. *PLoS Clin Trials* 2007;**2**:e25.
47. **Zahlmann G,** Franczykova M, Henning G, *et al*. DIABETEX—a decision support system for therapy of type I diabetic patients. *Comput Methods Programs Biomed* 1990;**32**:297—301.
48. **Schriger DL,** Baraff LJ, Buller K, *et al*. Implementation of clinical guidelines via a computer charting system: effect on the care of febrile children less than three years of age. *J Am Med Inform Assoc* 2000;**7**:186—95.
49. **Shiffman RN,** Freudigman M, Brandt CA, *et al*. A guideline implementation system using handheld computers for office management of asthma: effects on adherence and patient outcomes. *Pediatrics* 2000;**105**:767—73.
50. **Mullett CJ,** Evans RS, Christenson JC, *et al*. Development and impact of a computerized pediatric antiinfective decision support program. *Pediatrics* 2001;**108**:E75.
51. **Shegog R,** Bartholomew LK, Sockrider MM, *et al*. Computer-based decision support for pediatric asthma management: description and feasibility of the Stop Asthma Clinical System. *Health Inform J* 2006;**12**:259—73.
52. **Soper J,** Chan GT, Skinner JR, *et al*. Management of oral anticoagulation in a population of children with cardiac disease using a computerised system to support decision-making. *Cardiol Young* 2006;**16**:256—60.
53. **Fiks AG,** Grundmeier RW, Biggs LM, *et al*. Impact of clinical alerts within an electronic health record on routine childhood immunization in an urban pediatric population. *Pediatrics* 2007;**120**:707—14.
54. **Fiks AG,** Hunter KF, Localio AR, *et al*. Impact of electronic health record-based alerts on influenza vaccination for children with asthma. *Pediatrics* 2009;**124**:159—69.
55. **Bell LM,** Grundmeier R, Localio R, *et al*. Electronic health record-based decision support to improve asthma care: a cluster-randomized trial. *Pediatrics* 2010;**125**:e770—7.
56. **Bourgeois FC,** Linder J, Johnson SA, *et al*. Impact of a computerized template on antibiotic prescribing for acute respiratory infections in children and adolescents. *Clin Pediatr (Phila)* 2010;**49**:976—83.
57. **Faraon-Pogaceanu C,** Banasiak KJ, Hirshberg EL, *et al*. Comparison of the effectiveness and safety of two insulin infusion protocols in the management of hyperglycemia in critically ill children. *Pediatr Crit Care Med* 2010;**11**:741—9.
58. **Fifield J,** McQuillan J, Martin-Peele M, *et al*. Improving pediatric asthma control among minority children participating in medicaid: providing practice redesign support to deliver a chronic care model. *J Asthma* 2010;**47**:718—27.
59. **Hoeksema LJ,** Bazzy-Asaad A, Lomotan EA, *et al*. Accuracy of a computerized clinical decision-support system for asthma assessment and management. *J Am Med Inform Assoc* 2011;**18**:243—50.
60. **Shapiro A,** Gracy D, Quinones W, *et al*. Putting guidelines into practice: improving documentation of pediatric asthma management using a decision-making tool. *Arch Pediatr Adolesc Med* 2011;**165**(5):412—18.
61. **Kattan M,** Crain EF, Steinbach S, *et al*. A randomized clinical trial of clinician feedback to improve quality of care for inner-city children with asthma. *Pediatrics* 2006;**117**:e1095—103.
62. **Porter SC,** Forbes P, Feldman HA, *et al*. Impact of patient-centered decision support on quality of asthma care in the emergency department. *Pediatrics* 2006;**117**:e33—42.
63. **Porter SC,** Kaushal R, Forbes PW, *et al*. Impact of a patient-centered technology on medication errors during pediatric emergency care. *Ambul Pediatr* 2008;**8**:329—35.
64. **Fine AM,** Kalish LA, Forbes P, *et al*. Parent-driven technology for decision support in pediatric emergency care. *Jt Comm J Qual Patient Saf* 2009;**35**:307—15.
65. **Hsieh TC,** Kuperman GJ, Jaggi T, *et al*. Characteristics and consequences of drug allergy alert overrides in a computerized physician order entry system. *J Am Med Inform Assoc* 2004;**11**:482—91.
66. **Porter SC,** Manzi SF, Volpe D, *et al*. Getting the data right: information accuracy in pediatric emergency medicine. *Qual Saf Health Care* 2006;**15**:296—301.
67. **Hatton RC,** Rosenberg AF, Morris CT, *et al*. Evaluation of contraindicated drug-drug interaction alerts in a hospital setting. *Ann Pharmacother* 2011;**45**:297—308.
68. **Smithburger PL,** Kane-Gill SL, Benedict NJ, *et al*. Grading the severity of drug-drug interactions in the intensive care unit: a comparison between clinician assessment and proprietary database severity rankings. *Ann Pharmacother* 2010;**44**:1718—24.
69. **Paterno MD,** Maviglia SM, Gorman PN, *et al*. Tiering drug-drug interaction alerts by severity increases compliance rates. *J Am Med Inform Assoc* 2009;**16**:40—6.
70. **Johnson KB,** Lee CK, Spooner SA, *et al*. Automated dose-rounding recommendations for pediatric medications. *Pediatrics* 2011;**128**:e422—8.
71. **Cash JJ.** Alert fatigue. *Am J Health Syst Pharm* 2009;**66**:2098—101.
72. **Strom BL,** Schinnar R, Aberra F, *et al*. Unintended effects of a computerized physician order entry nearly hard-stop alert to prevent a drug interaction: a randomized controlled trial. *Arch Intern Med* 2010;**170**:1578—83.

73. **Baysari MT,** Westbrook JI, Richardson KL, *et al*. The influence of computerized decision support on prescribing during ward-rounds: are the decision-makers targeted? *J Am Med Inform Assoc* 2011;**18**:754—9.
74. **Program NAE.** Expert Panel report 3 (EPR 3): guidelines for the diagnosis and management of asthma. 2007. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm (accessed 17 Oct 2011).
75. **Program NAE.** Expert Panel Report 2: guidelines for the diagnosis and management of asthmadupdates on selected topics. 2002. http://www.nhlbi.nih.gov/guidelines/archives/epr-2_upd/index.htm (accessed 17 Oct 2011).
76. Policy statement—recommended childhood and adolescent immunization schedules—United States, 2011. *Pediatrics* 2011;**127**:387—8.