Interventions to Reduce Pediatric Medication Errors: A Systematic Review

abstract

BACKGROUND AND OBJECTIVE: Medication errors cause appreciable morbidity and mortality in children. The objective was to determine the effectiveness of interventions to reduce pediatric medication errors, identify gaps in the literature, and perform meta-analyses on comparable studies.

METHODS: Relevant studies were identified from searches of PubMed, Embase, Scopus, Web of Science, the Cochrane Library, and the Cumulative Index to Nursing Allied Health Literature and previous systematic reviews. Inclusion criteria were peer-reviewed original data in any language testing an intervention to reduce medication errors in children. Abstract and full-text article review were conducted by 2 independent authors with sequential data extraction.

RESULTS: A total of 274 full-text articles were reviewed and 63 were included. Only 1% of studies were conducted at community hospitals, 11% were conducted in ambulatory populations, 10% reported preventable adverse drug events, 10% examined administering errors, 3% examined dispensing errors, and none reported cost-effectiveness data, suggesting persistent research gaps. Variation existed in the methods, definitions, outcomes, and rate denominators for all studies; and many showed an appreciable risk of bias. Although 26 studies (41%) involved computerized provider order entry, a meta-analysis was not performed because of methodologic heterogeneity. Studies of computerized provider order entry with clinical decision support compared with studies without clinical decision support reported a 36% to 87% reduction in prescribing errors; studies of preprinted order sheets revealed a 27% to 82% reduction in prescribing errors.

CONCLUSIONS: Pediatric medication errors can be reduced, although our understanding of optimal interventions remains hampered. Research should focus on understudied areas, use standardized definitions and outcomes, and evaluate cost-effectiveness. *Pediatrics* 2014;134:338–360

AUTHORS: Michael L. Rinke, MD, PhD,[a] David G. Bundy, MD, MPH,[b] Christina A. Velasquez, MD,[c] Sandesh Rao, MD,[d] Yasmin Zerhouni, MD,[e] Katie Lobner, MLIS,[f] Jaime F. Blanck, MLIS, MPA,[f] and Marlene R. Miller, MD, MSc[g]

[a]Department of Pediatrics, Children's Hospital at Montefiore, Bronx, New York; [b]Department of Pediatrics, Medical University of South Carolina, Charleston, South Carolina; Departments of [c]Emergency Medicine, [d]Internal Medicine, and [g]Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland; [e]Department of Surgery, University of California, San Francisco East Bay, Oakland, California; and [f]Welch Medical Library, Johns Hopkins University, Baltimore, Maryland

KEY WORDS

pediatric, medication error, systematic review, intervention, computerized physician order entry

ABBREVIATIONS

ADE—adverse drug event
CDS—clinical decision support
CPOE—computerized provider order entry
CINAHL—Cumulative Index to Nursing and Allied Health Literature
ISMP—Institute for Safe Medication Practices

This statement attests that all of the above listed authors contributed significantly to the (1) conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published. All authors agree to be accountable for all aspects of the work.

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Address correspondence to Michael L. Rinke, MD, PhD, Children's Hospital at Montefiore, 3415 Bainbridge Ave, Bronx, NY 10467. E-mail: mrinke@montefiore.org

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Medication errors are common in pediatric patients; 5% to 27% of all pediatric medication orders result in a medication error.[1–3] Medication errors cause significant mortality and morbidity, including 7000 patient deaths annually from medication errors in the United States.[4,5] Pediatric inpatients may have 3 times more medication errors than adult inpatients, and these errors are frequently harmful.[2] For children, 1% of all medication errors carry significant potential for harm, with 0.24% of errors causing actual harm.[2] Children are at high risk for these errors[6] due in part to the need for weight-based dosing.[7,8]

To reduce this preventable harm, pediatric health systems, institutions, and providers must understand, implement, and augment interventions to reduce pediatric medication errors.[9] Previous systematic reviews on pediatric medication error epidemiology or specific pediatric medication error intervention subsets,[10–20] including 1 review by our group,[10] found appreciable variation in medication error definitions, populations, and outcomes, precluding true synthesis of data. All previous systematic reviews looking at interventions to reduce pediatric medication errors examined subsets of interventions only,[11–18] and all searches in epidemiologic or intervention reviews were performed before 2008,[10,11,13–18] except 1 that examined nurse staffing interventions performed in 2010.[12]

The large increase in quality improvement intervention publications in the 6 years after our previous review,[10,21] the lack of a systematic review looking at all interventions to reduce pediatric medication errors, and the hypothesis that newer publications might use consistent definitions and outcomes allowing quantitative data synthesis suggest an updated systematic review on interventions to reduce pediatric medication errors is warranted. By using rigorous systematic review methodology, we aimed to determine the effectiveness of interventions to reduce pediatric medication errors, identify persistent gaps in the pediatric medication error reduction literature, and perform meta-analysis on comparable studies.

METHODS

Search Strategy

The authors searched PubMed, Embase, Scopus, Web of Science, Cochrane Library, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) for studies investigating interventions to reduce pediatric medication errors (Supplemental Information). The search included a pediatric concept and a medication error concept. Terms were searched as controlled vocabulary in applicable databases (PubMed, Embase, CINAHL, Cochrane) and as keywords in all databases. The search was run as an update to a previous literature review,[10] with the previous search strategy broadened to ensure complete article retrieval (Supplemental Information). The date parameters were limited from 2005 to the search date to capture literature published since the first review. Performing a complete search on all dates was beyond the scope of available resources. All searches were conducted on November 22, 2011. Articles included in previous systematic reviews on pediatric medication errors[10–20] were also included in the full-text review to augment our previous review and to ensure all relevant articles published before 2005 were retrieved.

Eligibility Criteria

The study types for this review included randomized controlled trials, quasi-randomized controlled trials, controlled before and after trials, and interrupted time-series studies published in any language and in any country. An intervention was defined as anything aimed at reducing medication errors. Computerized provider order entry (CPOE) was defined broadly as any electronic system that facilitates medication prescribing.[14] Clinical decision support (CDS) for CPOE was also defined broadly as any system that prompts users on correct dosages, alerted prescribers when dosages were out of prespecified ranges, or alerted drug-drug interactions.[11,14] Preprinted order sheets were broadly defined as any structured, paper-based form that prompted or required providers to enter specific medication-ordering information. Comparator groups were broadly defined by the included articles, but studies without a clear comparator group were excluded. For example, a study reporting errors discovered by pharmacist medication reconciliation but not reporting how many errors occurred without pharmacist medication reconciliation would be excluded. Studies had to include subjects $<$19 years of age in any care setting. Inpatients were defined as admitted patients not solely in the ICU, ambulatory patients were patients not admitted and excluding emergency department patients, and emergency department patients were patients seen in the emergency department, whether or not they were eventually admitted.

To capture the broadest possible range of definitions, the outcome of interest was medication errors as defined by the National Coordinating Council for Medication Error Reporting and Prevention: "A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use."[22]

Secondary outcomes included (1) preventable adverse drug events (ADEs; preventable errors that reached a patient and resulted in harm as defined by the Institute for Safe Medication Practices [ISMP] categories 5, 6, or 7 [significant temporary harm, permanent harm, near death or death])[23] and (2) serious preventable ADEs including ISMP categories 6 or 7 only (permanent harm, near death or death).[23] Studies using voluntary error reports as their outcome (numerator or denominator) were excluded because voluntary error reports may underestimate the true incidence of medication errors; it is also difficult to interpret true denominators for these interventions.[21,24] "Orders" were defined as inpatient medication prescribing, and "prescriptions" were defined as ambulatory medication prescribing. We excluded studies conducted in simulation settings only (eg, nurses administered medications to a mannequin) because of concern that they did not represent real-world efficacy. Studies designed solely to change the volume of prescribing were also excluded.

Abstracts from conference presentations and full-text articles were included. All authors of abstracts included in the systematic review were contacted for additional information (*n* = 3), and 2 responded.

Data Abstraction and Study Quality Assessment

Two independent, nonblinded authors (M.L.R. and C.A.V., S.R., or Y.Z.) reviewed each title and abstract for inclusion. Full-text review was also conducted by 2 independent, nonblinded authors (M.L.R. and C.A.V., S.R., or Y.Z.) and discrepancies were resolved through author consensus discussions. Both abstract reviews and full-text reviews were piloted on sample abstracts or articles respectively, to ensure reviewer consistency in judging inclusion criteria. For non–English-language studies included in the full-text review (*n* = 13), independent reviewers with fluency in the article's language translated and abstracted data from the article. To ensure accurate translations, the primary author (M.L.R) independently translated all foreign-language articles with computer translation software, previously shown to be effective for systematic reviews.[25] As above, 2 authors made inclusion decisions for non–English-language studies based on translations.

Using identical methodology as our previous review,[10] data abstraction for included articles was conducted in sequential fashion, as the second abstractor (M.L.R.) was able to see the first reviewer's or translator's abstracted data. Data abstraction was conducted via an electronic abstraction form, which was pilot tested for consistency among reviewers (Supplemental Fig 3). When data were unclear or missing, the corresponding author was contacted via e-mail at least twice. In addition to collecting the standard systematic review data points of population, intervention, and outcomes, we also abstracted data on quality improvement markers.[26] We selected the following markers to help assess whether studies used robust quality improvement methodologies: sustainability (number of months that data were collected after beginning the intervention), cost of intervention, patient or family involvement at any point in the design, conduct or interpretation of the study, and target population acceptance of the intervention (defined as any qualitative or quantitative assessment of feedback from the participants at whom the intervention was directed).

To assess article quality, 2 independent reviewers (M.L.R. and C.A.V., S.R., or Y.Z.) used the Cochrane Effective Practice and Organization of Care Review Group guidelines.[27] Individual article potential bias from funding sources and aggregate article publication bias (the number of studies published with positive and negative findings) were also assessed. Finally, study rigor was assessed by examining if a second person verified that medication errors met error definitions stated in the manuscript. This was done because reviewer discrepancies often exist in determining whether a medication error is truly an error.[28]

Synthesis of Results and Statistical Analysis

Outcomes were expressed as the number of medication errors, defined by the articles' authors, per 100 events observed, also defined by the articles' authors. Events observed included orders, medication administration opportunities (administered doses and omitted doses), patients, patient days, admissions, prescriptions, and medication days (a prescribed medication that is continued during a day and leads to an administration). Clinical and methodologic heterogeneity was assessed by examining potential variations in primary and secondary outcomes (error definitions), interventions, study populations, and settings. A random-effects meta-analytic model was used given the heterogeneity of included studies and the nonstandardization of study medication error definitions. For CPOE studies, we hypothesized that there was sufficient homogeneity in subsets of studies (CPOE with CDS versus manual order entry, CPOE with CDS versus CPOE, CPOE with CDS versus manual order entry in PICUs, CPOE with CDS for continuous infusions versus manual order entry) to aggregate outcome statistics. The I^2 statistic was used to calculate the degree of heterogeneity for meta-analysis. As noted below, the I^2 statistic was >80% for each subset, suggesting that studies were too heterogeneous for meta-analysis.

RESULTS

Search Results

Our search identified 6246 abstracts composed of 3788 unique abstracts. A total of 3588 abstracts were excluded during abstract review. An additional 74 articles from previous systematic reviews were identified for full-text review.[10–20] A total of 274 articles were included in full-text review, and of these, 63 were deemed eligible for inclusion in the systematic review (Fig 1).[1,29–91] Ten articles (16%) were included from previous systematic reviews, and 53 (84%) were identified by the current search protocol. The most common reason for exclusion in the full-text review was articles discussing strategies to reduce medication errors without data that met inclusion criteria (n = 77). Of these 77 studies, 29 were excluded for using voluntary error reports only, 27 had no preintervention or during-intervention comparator group, 13 discussed qualitative outcomes only, and 8 were excluded for other reasons. A summary of all articles included in this study is presented in Table 1.

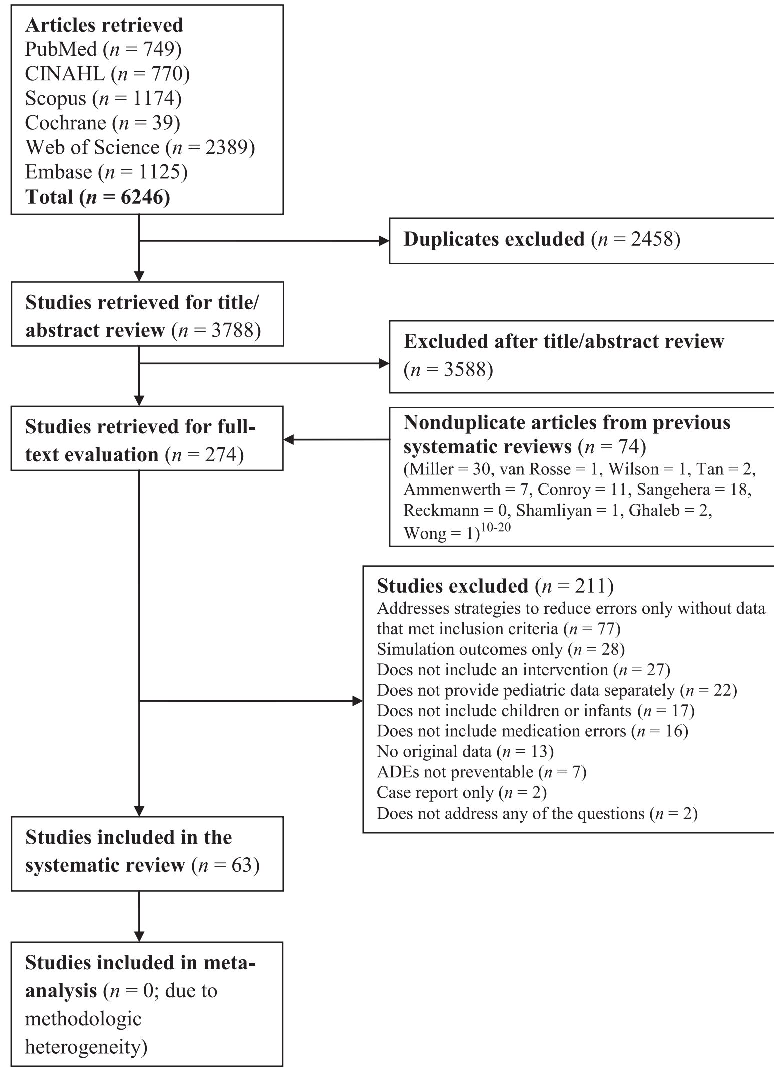

FIGURE 1
Summary of search and screening process.

Aggregate Data Synthesis

Most studies were conducted in the United States (51%) and in a single site (95%) that was academic/university-affiliated (90%). Nine studies (14%) included emergency department patients and 7 (11%) included ambulatory patients. Twenty-six studies (41%) investigated the effects of CPOE on medication errors (22 investigated CPOE and CDS and 4 investigated CPOE without CDS), 20 studies (32%) investigated the effects of education, 9 (14%) investigated the effects of preprinted order sheets, 8 (13%) investigated the effects of protocol implementation, 7 (11%) investigated the effects of publicizing/reporting error rates, and 5 (8%) investigated the effects of increased pharmacist participation in medication ordering. Additional interventions are described in Table 2. Only 6 studies (10%) investigated solely administering errors and 2 (3%) investigated solely dispensing errors. Twelve articles (19%) assessed severity of errors by using variations on "no harm, minor harm, severe harm, or death," with a wide variation in the number of severity categories from 2 to 11 (mean: 3.7). Wide variation also existed in the denominator used for outcome rates (Table 2).

With regard to our secondary outcomes, 6 studies (10%) reported preventable ADEs and no studies reported serious preventable ADEs. Of the studies reporting preventable ADEs,[1,40,45,62,66,73] 2 studies[1,45] reported statistically significant decreases in ADEs after an intervention: a 77% reduction in preventable ADE prescribing errors using multiple error reduction strategies (n = 16 of 12 026 pre versus 3 of 9187 post) and a 43% reduction in all types of preventable ADE errors using CPOE with CDS (n = 46 of 1197 pre versus 26 of 1210 post), respectively. Two of the other studies[40,66] reported only 1 preventable ADE during their respective pre- and postintervention periods, and a third study[62] reported 2 preventable ADEs, 1 during the pre- and 1 during the postintervention periods.

TABLE 1 Summary of Article Characteristics and Results by Primary Intervention

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
CPOE interventions										
Abboud et al[29] (2006)	ITS	Inpatient (entire hospital)	CPOE with CDS	Monitoring patient for effect errors	Aminoglycoside peak level and trough not obtained appropriately	Medication orders, computerized	4	31/177 (18)	31/159 (20)	NS
Boling et al[84] (2005)	ITS	Inpatient (entire hospital)	CPOE with CDS	Prescribing errors	Antidotes prescribed for opioids, benzodiazepines, and potassium	Medication administrations	7	1/7256 (0.01)	8/13 997 (0.06)	$P = .17$
Brown et al[33] (2007)	ITS	NICU (1 unit)	CPOE	Prescribing errors	Parenteral nutrition volume, electrolyte solubility, and osmolarity errors	Medication orders, computerized and manual	6	12/177 (7)	44/303 (15)	$P = .016$
Cordero et al[38] (2004)	ITS	NICU (1 unit)	CPOE with CDS	Prescribing errors	Gentamicin dose >10% deviation from recommended dose	Medication orders, computerized and manual	6	0/117 (0)	16/136 (12)	N/D
Dinning et al[77] (2005)	CBA	Inpatient (2 units)	CPOE and preprinted order sheet	Prescribing errors	Chemotherapy order set changes	Medication orders, computerized and manual	Not reported	19/101 (19)	290/598 (48)	$P < .0001$
Di Pentima et al[41] (2010)	ITS	Inpatient (entire hospital)	CPOE with CDS and infectious disease physician real-time feedback	Prescribing errors	Vancomycin order inappropriate by clinical indications, microbiology data, or dosing standards	Patient days	36	1.4[c] per 1000 patient days	1.8[c] per 1000 patient days	$P < .05$
Farrar et al[90] (2003)	ITS	Not specified	CPOE with CDS[d]	Prescribing errors	Not specified	Medication orders, computerized	Not reported	7/114 (6)	46/103 (45)	N/D
Fontan et al[79] (2003)	CBA	Nephrology inpatient (1 unit)	CPOE and unit dose drug distribution system	Prescribing and administering errors	Error in drugs name, form, dosage, route, prescriber's name, or lack of knowing drug interaction, or deviation from prescribed and administered	Medication orders, computerized and manual, and medication administrations	Not reported	Prescribing: 419/3943 (11) Administering: 888/3943 (23)	Prescribing: 518/589 (88) Administering: 189/646 (29)	Prescribing: $P < .0001$ Administering: $P < .001$

TABLE 1 Continued

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
Ginzburg et al[43] (2009)	ITS	Ambulatory (multiple clinic sites)	CPOE with CDS[d]	Prescribing errors	Acetaminophen or ibuprofen overdosage or underdosage of strength or regimen, or incomprehensible dosing directions	Prescriptions, computerized	5	46/224 (21)	103/316 (33)	$P = .002$
Hilmas et al[80] (2010)	ITS	PICU and NICU (2 units)	CPOE with CDS, standardized concentrations, infusion pumps, education	Prescribing errors	Continuous infusion medication calculation errors, exceeding maximum concentration error, incomplete and illegible orders	Medication orders, computerized and manual	Not reported	0/200 (0)	98/200 (49)	N/D
Holdsworth et al[45] (2007)	ITS	Inpatient (entire hospital)	CPOE with CDS	All types of errors	ADE: an injury from a medicine or lack of an intended medicine	Admissions	6	37/1210 (3)	76/1197 (6)	RR: 0.64 (95% CI: 0.43–0.95)
Jani et al[46] (2010)	ITS	Inpatient and ambulatory (entire hospital and clinics)	CPOE with CDS	Prescribing errors	Unintentional significant reduction in the probability of treatment being timely and effective or increase in the risk of harm in renal patients	Medication orders, computerized and manual and prescriptions, computerized and manual	5	57/4784 (1)	88/3939 (2)	$P = .001$
Kadmon et al[47] (2009)	ITS	PICU (1 unit)	CPOE with CDS	Prescribing errors	Incorrect order that could cause harm if executed, incomplete or illegible order, and order not compliant with institutional regulation	Medication orders, computerized and manual	37	18/1250 (1)	103/1250 (8)	$P < .001$

TABLE 1 Continued

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
Kazemi et al[51] (2011)	ITS	Inpatient (1 unit)	CPOE with CDS (CPOE without CDS data not listed)	Prescribing and transcribing errors	Antibiotic and anticonvulsant nonintercepted errors in dose and frequency	Medication days	3	Prescribing: 442/1331 (33) Transcribing: 15/331 (1)	Prescribing: 876/1668 (52) Transcribing: 15/1688 (1)	Prescribing: $P < .001$ Transcribing: $P = .5$
Kim et al[53] (2006)	ITS	Inpatient (1 unit)	CPOE with CDS	Prescribing errors	Incorrect chemotherapy order format or calculation, order and treatment plan do not match, cumulative dose not on treatment plan, and nursing checklist not included	Medication orders, computerized and manual	12	163/5918 (3)	157/4978 (3)	N/D
Kirk et al[54] (2005)	CBA	Inpatient, ED, ambulatory (3 units)	CPOE with CDS[d]	Prescribing errors	Acetaminophen or promethazine underdose, overdose, no frequency, no dose given or excessive total daily dose	Prescriptions, computerized	6	299/2381 (13)	534/1893 (28)	ARR: 0.44 (95% CI 0.34–0.52)
Lehmann et al[58] (2004)	ITS	NICU (1 unit)	CPOE with CDS	Prescribing errors	TPN order error	Medication orders, computerized and manual	24	8/656 (1)	60/557 (11)	$P < .001$
Lehmann et al[59] (2006)	ITS	Inpatient (entire hospital)	CPOE with CDS	Prescribing errors	Continuous intravenous medication order error	Medication orders, computerized and manual	5	8/142 (6)	35/129 (27)	N/D
Mullett et al[62] (2001)	ITS	PICU (1 unit)	CPOE with CDS	Prescribing errors	Antiinfective dosage was subtherapeutic or supratherapeutic	Patient days	6	364/3381 (11)	458/2898 (16)	$P < .001$
Potts et al[67] (2004)	ITS	PICU (1 unit)	CPOE with CDS	Prescribing errors	Order incomplete, incorrect, or inappropriate excluded fluids, dialysate, TPN, chemotherapy	Medication orders, computerized and manual	2	110/7025 (2)	2662/6803 (39)	$P < .001$
Sard et al[69] (2008)	ITS	ED (1 unit)	CPOE with CDS[d]	Prescribing Errors	Order incomplete, incorrect, or inappropriate	Medication orders, computerized	12	55/398 (14)	101/326 (31)	$P < .001$

TABLE 1 Continued

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
Skouroliakou et al[70] (2005)	CBA	NICU (1 unit)	CPOE with CDS	Prescribing Errors	TPN mistake in fluid volume, composition, or flow rate	Medication orders, computerized and manual	6	0/941 (0)	28/941 (3)	$P < .0001$
Taylor et al[72] (2008)	ITS	NICU (1 unit)	CPOE with CDS	Administering errors	Administration variance: omitted, >60 min from scheduled, incorrect dose, wrong route, administered without an order	Medication administrations	8	31/268 (12)	50/253 (20)	RR: 0.53 (95% CI: 0.3–0.8)
Trotter and Maier[88] (2009)	ITS	Inpatient (entire hospital)	CPOE with CDS	Prescribing errors	Illegible, wrong dosage or solvent, incorrect dilution, regulation forgotten, and lack of dose information	Medication orders, computerized and manual	10	3/5480 (0.1)	484/4118 (12)	N/D
Walsh et al[73] (2008)	ITS	Inpatient (entire hospital)	CPOE with CDS	All types of errors	Error in drug ordering, transcribing, dispensing, administering, or monitoring	Patient days	8	94/1848 (5)	62/1386 (4)	IRR: 1.14 (95% CI: 0.8–1.5)
Warrick et al[74] (2011)	ITS	PICU (1 unit)	CPOE	Prescribing and administering errors	Dosing error, incomplete order, insufficient information, illegible, errors in the prescribing decision, dose omission	Medication orders, computerized and manual and medication administrations	6	Prescribing: 12/257 (5) Administering: 4/278 (1)	Prescribing: 14/159 (9) Administering: 43/528 (8)	Prescribing: NS Administering: $P < .05$
Education interventions										
Alemanni et al[76] (2010)	ITS	Inpatient (non-ICU), PICU, NICU (3 units)	Education, publicizing error rates, protocols	Administering errors	Unintentional omission or performance of a drug-related act, which may present a risk or cause an adverse event for the patient	Medication administrations	Not reported	Inpatient (non-ICU)[c] (17) PICU (6) NICU (14)	Inpatient (non-ICU)[c] (36) PICU (21) NICU (26)	N/D

TABLE 1 Continued

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
Bertsche et al[31] (2010)	ITS	Neurology inpatient (1 unit)	Education program for nurses and parents	Administering errors	Errors in oral or gastric tube medication tablet dissolution, splitting or storage, inappropriate medication combinations, inappropriate liquid handling	Medication administrations	1	38/489 (8)	289/675 (43)	$P < .001$
Burkhart et al[34] (2005)	ITS	Ambulatory (multiple pediatric practices and public recruitment)	In-person education on inhaler technique	Administering errors	Metered-dose inhalers for asthma incorrect administration	Patients who completed education	1	7/36 (19)	39/42 (93)	$P < .001$
Campino et al[37] (2009)	ITS	NICU (1 unit)	Education, standardizing processes, and updating protocols	Prescribing errors	Dosage, units, route, or administration interval were illegible, incorrect, or not specifically written	Medication orders, manual	10	47/1512 (3)	868/4182[e] (21)	$P < .001$
Davey et al[40] (2008)	ITS	Inpatient (1 unit)	Education and bedside prescribing guideline	Prescribing errors	Dose >10% deviation or good prescribing practices not followed	Medication orders, manual	1	Education: 44/266 (17) Prescribing guideline: 56/330 (17)	Education: 76/249 (31) Prescribing guideline: 59/320 (18)	Education: $P = .023$ Prescribing guideline: $P = .73$
Eisenhut et al[78] (2011)	ITS	Inpatient (multiple inpatient units)	Education	Prescribing errors	Nonadherence to guidance given in the British National Formulary for children	Admissions	2	120/588 (21)	188/421 (45)	N/D
Kozer et al[56] (2006)	CBA	ED (1 unit)	Education	Prescribing errors	Dose >20% deviation, >2 h deviation from interval between doses, wrong units or route	Medication orders, manual	1	66/533 (12)	46/363 (13)	OR: 1.07 (95% CI: 0.66–1.7)
Leonard et al[60] (2006)	ITS	Inpatient (entire hospital)	Education, zero tolerance policy, prescriber feedback, publicizing of error rates	Prescribing errors	Any medication order with missing or incorrect information	Medication orders, manual	13	400/996 (40)	606/777 (78)	$P = .001$

TABLE 1 Continued

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
Pallás et al[65] (2008)	ITS	NICU (1 unit)	Education and PDA dose calculation software	Prescribing errors	Illegible, incorrect dose, unapproved abbreviations, missing route, interval, units	Medication orders, manual	14	171/1435 (12)	2498/6320 (40)	OR: 0.30 (95% CI 0.26–0.34)
Raja Lope et al[82] (2009)	ITS	NICU (1 unit)	Education	Administering errors	Omission error, extra dose, incorrect preparation, dose, drug, rate, route, or time or deteriorated drug	Medication administrations	3	522/169 (309)	849/188 (452)	N/D
Sagy[85] (2009)	ITS	Inpatient (entire hospital)	Education	Prescribing errors	Missing allergies, demographics, mg/kg dose, signature, license number or total dose, illegible, inaccurate calculation, unapproved order writing style	Medication orders, manual	12	38/140 (27)	533/256 (208)	$P < .05$
Sullivan et al[71] (2010)	ITS	Inpatient (entire hospital)	Education	Administering errors	Insulin administration deviated or omitted from written order	Medication administrations	6	19/1119 (2)	131/882 (15)	$P < .001$
Yamanaka et al[75] (2007)	ITS	Inpatient (3 units)	Education and protocol development	Dispensing and administering errors	Dose omission, failure to document dose, incorrect documentation, lack of medication in the pharmacy, wrong time, wrong medication, medication not checked, lack of access, delivery route not specified, incorrect route	Medication administrations	Not reported	1498/8550 (18)	1717/8152 (21)	$P < .001$
Zukowski et al[87] (2011)	ITS	ED (1 unit)	Education and computer dose calculation tool	Prescribing errors	Incomplete directions, dosing, quantity, and formulation errors	Prescriptions, manual	2	57/264 (22)	50/170 (29)	$P = .069$

TABLE 1 Continued

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
Preprinted order sheet interventions										
Alagha et al[30] (2011)	ITS	PICU (1 unit)	Preprinted order sheets, education, performance feedback	Prescribing errors	Wrong drug, dose, frequency, concentration, missed dose, incomplete orders	Medication orders, manual	5	391/1097 (36)	1107/1417 (78)	$P < .001$
Broussard et al[32] (2009)	ITS	Inpatient (entire hospital)	Preprinted order sheets	Prescribing errors	Sedation medications dose $\pm$10% of recommended dose, mg/kg written, reversal agents ordered	Sedation events (patients)	12	7/42 (17)	39/42 (93)	$P < .05$
Burmester et al[35] (2008)	ITS	PICU (1 unit)	Preprinted order sheets, physician education, publicizing error rates	Prescribing errors	Incomplete or incorrect medication orders	Medication orders, manual	36	200/4182 (4)	613/3648 (17)	$P < .001$
Cimino et al[1] (2004)	ITS	PICU (9 units in different hospitals)	Each of 9 PICUs did something different, including preprinted order sheets, real-time feedback on errors, increased pharmacist staffing, education	Prescribing errors	Dosage, units, route, and administration interval were incorrect	Medication orders, manual	3	698/9187 (8)	1335/12 026 (11)	$P < .001$
Cunningham et al[39] (2008)	RCT	Inpatient and ED (multiple inpatient units and 1 ED)	Preprinted order sheets and integrated care pathway	Prescribing errors	Good prescribing practice for dosing, administration, clarity, legal issues, or other not followed	Patients	6	1614/157 (1028)	1943/130 (1495)	$P = .002$
Kozer et al[55] (2005)	RCT	ED (1 unit)	Preprinted order sheets	Prescribing errors	Dose >20% deviation, >2 h deviation from interval between doses, wrong units or route	Medication orders, manual	1	37/376 (10)	68/411 (17)	OR: 0.55 (95% CI: 0.34–0.90)

TABLE 1 Continued

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
Larose et al[57] (2008)	ITS	ED (1 unit)	Preprinted order sheets	Prescribing and administering errors	Resuscitation room patient with incorrect/missing order date, time, signature, dose, route, interval, generic name or as needed reason, or illegible	Medication orders, manual	5	Prescribing: 8/347 (2) Administering: 12/347 (3)	Prescribing: 32/372 (9) Administering: 23/372 (6)	Prescribing: change: 6% (95% CI: 3–10%) Administering: change: 3% (95% CI: 1–6%)
Robinson et al[68] (2006)	ITS	Inpatient (entire hospital)	Preprinted order sheets, education, policy creation, chemotherapy certification	Prescribing errors	Chemotherapy error in writing orders: modification, clarification or omission	Patients	24	31/221 (14)	77/331 (23)	N/D
Increased pharmacist participation in drug therapy interventions										
Gibson et al[42] (1975)	ITS	Inpatient (entire hospital)	Increased pharmacist involvement in drug therapy	Prescribing errors	No evidence for use of drug or drug contraindicated in patient, excluded radiologic, IV vehicle solutions, fluid replacement, diagnostic, surgical and sedation drugs and drugs not listed in PDR	Medication orders, manual	9	46/441 (10)	53/439 (12)	N/D
Kaushal et al[50] (2008)	CBA	Inpatient and PICU (3 units)	Increased pharmacist involvement in drug therapy	All types of errors	Serious (preventable and nonintercepted near miss) errors in drug ordering, transcribing, dispensing, administering, or monitoring	Patient days	3	25/3107[f] (0.8)	45/3331[f] (1)	N/D

TABLE 1 Continued

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
Olsen et al[89] (1997)	ITS	Inpatient (1 unit)	Satellite pharmacy, unit dose drug distribution system, simplified ordering process	Administering errors	IV mixtures wrong time, dose, preparation or interval, or omitted dose	Medication administrations	2	280/540 (52)	389/856 (45)	N/D
Otero et al[64] (2008)	ITS	Inpatient (entire hospital)	Increased pharmacist participation in ordering, education, reduction in interruptions	Prescribing and administering errors	American Society of Health System pharmacists definition of medication errors	Medication orders, manual, and medication administrations	24	Prescribing: 105/1144 (9) Administering: 99/1588 (6)	Prescribing: 102/590 (17) Administering: 150/1174 (13)	Prescribing: $P < .05$ Administering: $P < .05$
Other interventions										
Campino et al[36] (2008)	ITS	NICU (1 unit)	Reviewing data and registering error rates	Prescribing and transcribing errors	Dosage, units, route, or administration interval were illegible, incorrect, or not specifically written	Medication orders, manual and transcriptions	6	Prescribing: 803/4182 (19) Transcribing: 665/4182 (16)	Prescribing: 40/122 (33) Transcribing: 25/122 (21)	Prescribing: $P < .001$ Transcribing: $P = .173$
Ozel et al[44] (2010)	RCT	Ambulatory (multiple practices from different institutions)	Premeasured bags of glucose compared with scoops or weighing for metabolic disorder emergency feedings	Dispensing errors	Glucose polymer–based feedings >10% correct amount of carbohydrate administration in 1 L of water	Patients	2	33/53 (62)	81/106 (76)	$P = .03$
Kaji et al[48] (2006)	ITS	Ambulatory (1 county's emergency medical service)	Color-coded tape for weight-based drug dosing	Administering errors	Epinephrine incorrect exact first dose for prehospital patients	Patients	36	16/37 (43)	75/104 (72)	OR: 3.0 (95% CI: 1.4–6.6)
Kalina et al[49] (2009)	ITS	Inpatient and ED (entire hospital)	Multidisciplinary team to care for pediatric trauma patients	Prescribing and administering errors	Inappropriate dose or drug prescribed, inappropriate medication, route or rate administered	Patients	12	Prescribing: 15/134 (11) Administering: 9/134 (7)	Prescribing: 25/125 (20) Administering: 19/125 (15)	Prescribing: $P = .05$ Administering: $P = .05$

TABLE 1 Continued

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
Kazemi et al[52] (2010)	ITS	Inpatient (1 unit)	Nurse transcription of order into computer with CDS after physician handwrites order, and physician verification afterward[g]	Prescribing and transcribing errors	Antibiotic and anticonvulsant overdoses, underdoses, or curtailed or prolonged intervals	Medication orders, computerized	3	372/2297 (16)	419/2357 (18)	RR: 0.91 (95% CI: 0.8–1.03)
MacDonald et al[81] (2006)	CBA	Ambulatory (multiple practices from different institutions)	Home delivery of dietary products for inherited metabolic disorders	Dispensing errors	Incorrect protein substitute delivered	Patients	12	0/28 (0)	12/32 (38)	$P < .05$
Morriss et al[61] (2009)	ITS	NICU (1 unit)	Barcodes for medication administration	All types of errors	Error in ordering, transcribing, dispensing, administering, or monitoring a medication	Medication administrations	4	3690/46 308 (8)	3204/46 090 (7)	$P < .001$
O'Brodovich and Rappaportl[63] (1991)	ITS	Inpatient (2 units)	Unit dose drug distribution system	Administering errors	Omitted, wrong, extra, unordered or expired dose, wrong route, doses > or <30 min from scheduled, allergy	Medication administrations	3	51/241 (21)	105/282 (37)	N/D
Porter et al[66] (2008)	CBA	ED (2 units)	Parent computer-entered data given to provider with treatment recommendations	All types of errors	Error in drug ordering, transcribing, dispensing, administering, or monitoring	Patients	12	653/575 (113)	1102/836 (132)	$P = .42$
Sturgess et al (2011)[91]	ITS	PICU (1 unit)	Environmental changes, policies, publicizing error rates, feedback to providers	Prescribing errors	Unintentional significant reduction in either the probability of treatment being timely and effective or increase in the risk of harm	Patient days	25	796/1781 (45)	969/1111 (87)	$P < .001$

TABLE 1 Continued

Study (Year)	Study Design	Setting (Number of Units[a])	Intervention	Main Type of Errors Collected	Medication Error Definition[b]	Type(s) of Denominator	Months of Observation After Start of Intervention	Intervention Group Error Data (%)	Comparison Group Error Data (%)	Statistical Tests
Thomas et al[86] (2011)	ITS	NICU (1 unit)	Standardizing processes and updating protocols	Administering and monitoring patient for effect errors	Gentamicin dose given >60 min from scheduled, inappropriate action taken after gentamicin level result	Patients	Not reported	Administering: 10/56 (18) Monitoring: 13/56 (23)	Administering: 14/53 (26) Monitoring: 21/53 (40)	Administering: $P = .02$ Monitoring: $P = .04$

ADE, adverse drug event; Ambulatory, excludes ED patients; ARR, adjusted relative risk; CBA, controlled before and after design; CI, confidence interval; CPOE with CDS, computerized provider order entry with clinical decision support; ED, emergency department; Inpatient, study used admitted patients not solely in the ICU; IRR, incidence rate ratio; ITS, interrupted time series; IV, intravenous; orders, written and administered in a health care setting; N/D, not done (article did not list statistical tests for this outcome); NS, article did not list *P* value but noted it was not significant; OR, odds ratio; PDA, personal digital assistant; PDR, Physician's Desk Reference; prescriptions, given to a patient to be filled and administered outside of a health care setting; PICU, pediatric intensive care unit; RCT, randomized controlled trial; RR, relative risk; TPN, total parenteral nutrition.

[a] Unless specified, units are all in the same institution or hospital. If the word "multiple" is used, the authors did not specify the number of units but it was >1.

[b] Unless specified via underlining, the article looked at all types of medications.

[c] Raw data not given for this article.

[d] Comparison group was CPOE without CDS.

[e] Comparison group was intervention group for Campino et al,[36] although slightly different error rates were reported between the 2 studies.

[f] Data present control and intervention group for postintervention period; data were comparable before the intervention.

[g] Comparison group was CPOE with CDS.

With regard to the robustness of quality improvement methodology, only 10 studies (16%) reported whether their intervention was accepted by the target population and 5 studies (8%) involved patients or families at any point in the design, conduct, or interpretation of the study. Sixteen studies (25%) collected data for ≤3 months after implementing the intervention.

There was an appreciable risk of bias in most studies (Fig 2), with, for example, 67% of the 52 interrupted time-series studies not protecting against secular changes. Sixty studies (95%) reported positive results for their intervention, suggesting possible publication bias. Thirty-four of those studies reported statistically significant positive results, 7 reported non–statistically significant results ($P > .05$), and 19 did not report statistical inferences for the outcome of interest. Of the 3 studies included that did not report positive results for their intervention, 2 reported non–statistically significant results. Thirty-seven studies (59%) did not report funding sources for their research, and four of those who did (6%) had a potential conflict of interest. In 27 studies (43%), no one verified that the errors collected were truly errors, and in 9 additional studies (14%) it was unclear if someone verified errors.

Data Synthesis for Specific Interventions

Of the 63 studies included, 52 (83%) were able to be included in qualitative data synthesis for a specific intervention: 26 for CPOE, 14 for education, 9 for preprinted order sheets, and 5 for increased pharmacist participation in drug therapy. One study[1] evaluated both preprinted order sheets and increased pharmacist preparation, and 1 study[77] evaluated both CPOE and preprinted order sheets. Although summary ranges are presented below, appreciable heterogeneity still exists between many studies using the same intervention. All other intervention subsets (protocol implementation, publicizing/reporting error rates, double checking, environmental changes, unit drug dose distribution system, non-CPOE technology for medication administration) were too heterogeneous for synthesis (Table 3).

Of the 26 CPOE interventions, 4 investigated the effects of CPOE without CDS compared with manual order entry[33,74,77,79] and reported a 44% to 88% reduction in prescribing errors. Five studies examined the effect of CPOE with CDS for multiple medications on inpatients[45,46,51,73,88] and found a 14% increase in errors to a 99% decrease in all types of errors. The study reporting a 14% increase in all types medication errors[73] noted that this change was non–statistically significant ($P > .05$) and also reported a statistically significant 7% decrease in nonintercepted, serious medication errors. Ginzburg et al[43] and Kirk et al[54] looked at ambulatory prescribing errors for acetaminophen or ibuprofen and reported a 36% reduction (n = 103 of 316 pre vs 46 of 224 post) and an adjusted risk of 56% (n = 534 of 1893 pre vs 299 of 2381 post) in these types of prescribing errors, respectively. When applying meta-analytic models, I^2 statistics for each CPOE subset were >80%. On the basis of criteria in the *Cochrane Handbook for Systematic Reviews of Interventions*,[92] this finding suggests large heterogeneity and therefore meta-analysis results are not presented.

Although 20 studies reported provider education as part of their intervention to reduce pediatric medication errors, 14 studies[31,34,37,40,56,60,65,71,75,76,78,82,85,87] used education as their main intervention to reduce pediatric medication errors. Seven of these 14 studies collected data for ≤3 months after implementing the intervention and 2 did not report on the months of

TABLE 2 Aggregate Data Synthesis for 63 Included Studies

Characteristic	Number of Studies (%)
Population	
Location of study	
United States	32 (51)
Other North America	5 (8)
Europe	18 (29)
Africa	1 (1)
Asia	5 (8)
Australia	0
South America	2 (3)
Study conducted at 1 site	60 (95)
Type of institution	
Academic/university-affiliated site	57 (90)
Community/private practice site	1 (1)
Mix, Army medical center or prehospital emergency care services	3 (5)
Not reported	2 (3)
Patient locations[a]	
Inpatients	31 (49)
PICU patients	16 (25)
NICU patients	19 (30)
Emergency department patients	9 (24)
Ambulatory patients	7 (11)
Not reported	2 (3)
Patient ages	
All pediatric ages	44 (70)
Infants only (0–1 y)	13 (21)
Children only (2–11 y)	1 (1)
Adolescents only (12–18 y)	0
Mix but not all	5 (8)
Intervention	
Type of study	
Interrupted time series	52 (82)
Controlled before and after design	8 (13)
Randomized controlled trials	3 (5)
Type of intervention[a]	
CPOE ± CDS	26 (41)
Education and training	20 (32)
Preprinted order sheet	9 (14)
Protocol implementation	8 (13)
Publicizing/reporting error rates	7 (11)
Increased pharmacist participation in medication ordering	5 (8)
Double checking	4 (6)
Environmental changes	4 (6)
Unit drug dose distribution system	3 (5)
Non-CPOE technology for medication administration	2 (3)
Other	10 (16)
Outcomes	
Types of medication errors collected	
All types	5 (8)
Prescribing only	38 (60)
Administering only	6 (10)
Dispensing only	2 (3)
Transcribing only	1 (1)
Monitoring patient for effect only	1 (1)
Mix but not all	10 (16)
Error severity	
Assessed severity of errors in any way	15 (24)
Reported preventable ADEs	6 (10)
Reported serious preventable ADEs	0
No verification of errors	27 (43)
Types of denominators used	
Manual medication orders	31 (49)

TABLE 2 Continued

Characteristic	Number of Studies (%)
Computerized medication orders	20 (32)
Patients/admissions	14 (22)
Patient days	10 (16)
Computerized prescriptions	3 (5)
Manual prescriptions	2 (3)
Medication days	2 (3)
Other	3 (5)
Quality improvement markers	
Reported acceptance of intervention by target population	10 (16)
Involved patients or families at any point in the design, conduct, or interpretation of the study	5 (8)
Median months data were collected after intervention (interquartile range)	6 (3–12)
Reported the cost of the intervention	0

[a] Some studies included mixes of locations, interventions, and/or denominators so these *n* values are >63.

observation after implementation. The 5 studies that collected data for >3 months after implementing the intervention[37,60,65,71,85] reported a 49% to 87% reduction in any type of medication error.

The 9 studies that investigated the effectiveness of preprinted order sheets in reducing pediatric medication errors[1,30,32,35,39,55,57,68,77] reported a 27% to 82% reduction in prescribing errors. Of the 5 studies investigating increased pharmacist participation in drug therapy[1,42,50,64,89], 4 reported a 17% to 50% decrease in medication errors. The fifth article[89] reported a 16% increase (n = 389 of 856 pre versus 280 of 540 post) in administering errors after the intervention but investigated the impact of opening a satellite pharmacy; although we assume that closer proximity of pharmacists led to increased involvement in the prescribing/administering process, it was unclear whether this was the case and therefore this article may not be comparable to the others.

DISCUSSION

In this systematic review of all types of interventions to reduce pediatric medication errors, multiple interventions revealed statistically significant effects. Unfortunately, appreciable gaps in the pediatric medication error literature were identified: no studies that met inclusion criteria investigated the effects of medication reconciliation, only 1% of studies were conducted at community hospitals, 11% of studies were conducted in ambulatory populations, 10% of studies reported preventable ADEs, 10% of studies examined administering errors, 3% of studies examined dispensing errors, and appreciable variation existed in the methods, definitions, outcomes, and rate denominators. No study reported outcomes using a standard definition of serious preventable ADEs. Although 41% of studies involved some version of CPOE, a meta-analysis could not be performed because of methodologic heterogeneity. Despite a large increase in the number of published studies aiming to reduce pediatric medication errors since 2005,[10] our knowledge of interventions to prevent pediatric medication errors remains hampered by nonuniform definitions, nonuniform data collection methodology, and nonuniform outcome reporting. The heterogeneity in current pediatric medication error intervention studies prevents wide generalizability of results and yields unclear guidance to hospitals on which interventions are best to adopt.

Interestingly, studies implementing CPOE and those implementing preprinted order sheets reported similar reductions in medication errors despite vastly different cost levels.[93] CPOE with CDS studies[43,51,54,69,90] reported a 36% to 87% reduction in prescribing errors when compared with CPOE without CDS. Preprinted order sheet studies reported a 27% to 82% reduction in prescribing errors,[1,30,32,35,39,55,57,68,77] when compared with manual order entry, a condition comparable to CPOE with versus without CDS. Of CPOE studies that looked at the broadest range of patients and outcomes, Holdsworth et al[45] and Trotter and Maier[88] reported reductions in error rates, whereas Walsh et al[73] reported a non–statistically significant increase in all-cause medication errors. Kadmon et al[47] and Potts et al[67] looked at CPOE with CDS for all medications in PICU settings and reported significant reductions in prescribing errors (88% and 95%, respectively), whereas Algaha et al[30] and Burmester et al[35] also reported significant reductions in errors for all medications using preprinted order sheets in PICU settings (53% and 76%, respectively). Comparable outcomes between CPOE and preprinted order sheets could imply that resource-constrained settings may wisely focus on implementing integrated care pathways and preprinted order sheets if CPOE with CDS is deemed too expensive despite national efforts to incentivize its implementation.[94] These conclusions are limited by the heterogeneous nature of outcomes and definitions in these studies, which likely contributes to the wide range of outcomes. The authors would recommend investigating each relevant study (Table 1) to clearly understand its applicability and context before drawing policy-level conclusions.

In 2001, the ISMP published guidelines for preventing medication errors in pediatrics[9] that recommended CPOE, barcoding technology, unit dose-dispensing systems, and educational systems for all providers. More than a decade later, we are unable to find bias-free, robust, and rigorous evidence in the literature to support these recommendations for children. Clearly, not all interventions require randomized controlled trials before implementation, but it is integral in current resource-constrained environments to identify interventions with maximum return on investment both in terms of dollars and, more importantly, patient lives. Future research should focus on determining the reduction in medication errors compared with the investment in resources and time required for an intervention's implementation, because institutions are faced with multiple potential interventions to reduce medication errors. Applicability and efficacy of interventions in non–university-affiliated and/or developing countries are also prime areas for future study because 90% of studies were conducted at academic/university-affiliated medical centers and 88% of studies were conducted in North America or Europe.

One of the first steps in remedying the gaps identified in this study is the standardization of definitions and research methodologies for medication error studies. Universal adoption of the National Coordinating Council for

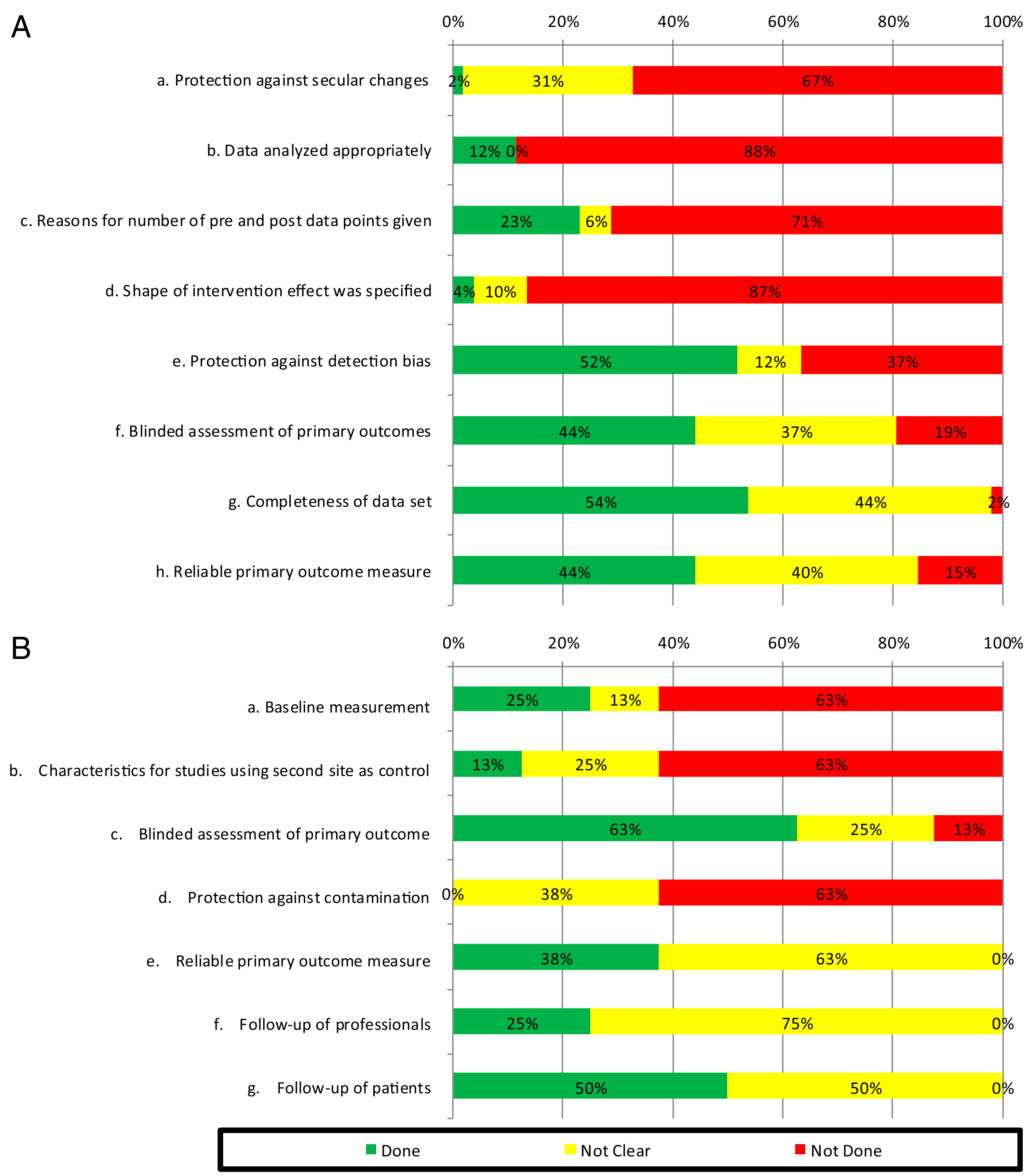

FIGURE 2

Risk of bias of studies by type of trial. A, Interrupted time-series studies (52 studies). B, Controlled before/after studies (8 studies). C, Randomized controlled trials (3 studies). Article quality was assessed with the Cochrane Effective Practice and Organization of Care Review Group guidelines,[27] and sample definitions of criteria above can be found on their Web site or on the data collection sheets in Supplemental Fig 3.

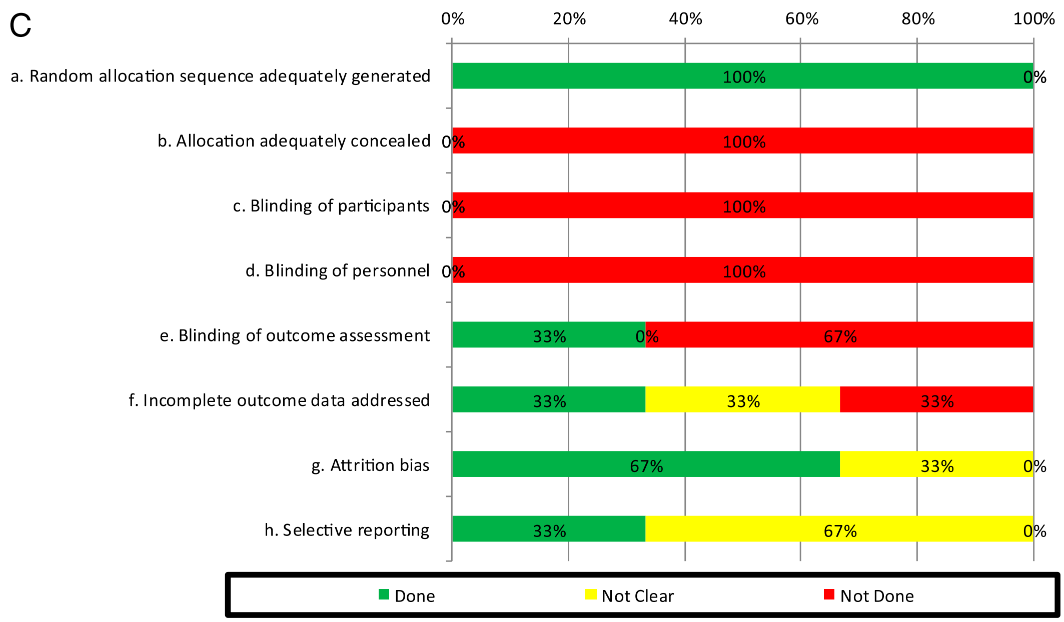

FIGURE 2
Continued.

TABLE 3 Qualitative Synthesis for Selected Intervention Subsets

Intervention	First Authors and References	Outcomes
CPOE[a] (N = 26)		
CPOE without CDS to reduce prescribing errors	Brown,[33] Dinning,[77] Fontan,[79] and Warrick[74]	44% to 88% reduction in prescribing errors
CPOE without CDS to reduce administering errors	Fontan[79] and Warrick[74]	21% to 88% reduction in administering errors
CPOE with CDS for medications on inpatients	Holdsworth,[45] Jani,[46] Kazemi 2011,[51] Trotter,[88] and Walsh[73]	14% increase in errors; 99% reduction in all types of errors
CPOE with CDS for PICU patients	Kadmon[47] and Potts[67]	88% to 95% reduction in prescribing errors
CPOE with CDS for continuous infusions	Lehmann 2006[59] and Hilmas[80]	78% to 100% reduction in prescribing errors
CPOE with CDS for total parenteral nutrition	Lehmann 2004[58] and Skourolaikou[70]	91% to 100% reduction in prescribing errors
CPOE with CDS for antiinfective medications	Abboud,[29] Cordero,[38] Di Pentima,[41] and Mullet[62]	10% to 100% reduction in prescribing and/or monitoring patient for effect errors
CPOE with CDS compared with CPOE without CDS	Farrar,[90] Ginzburg,[43] Kazemi 2011,[51] Kirk,[54] and Sard[69]	36% to 87% reduction in all prescribing errors; 36% to 59% reduction in ambulatory prescribing errors for acetaminophen or ibuprofen
Education (N = 14)[b]		
Reduce prescribing errors	Campino 2009,[37] Davey,[40] Eisenhut,[78] Kozer 2006,[56] Leonard,[60] Pallás,[65] Sagy,[85] and Zukowski[87]	8% to 87% reduction in prescribing errors
Reduce administering and/or dispensing errors	Alemanni,[76] Bertsche,[31] Burkhart,[34] Raja Lope,[82] Sullivan,[71] and Yamanaka[75]	14% to 81% reduction in administering and dispensing errors
Reduce all error types and collect data for >3 months	Campino 2009,[37] Leonard,[60] Pallás,[65] Sagy,[85] and Sullivan[71]	49% to 87% reduction in any type of medication error
Preprinted order sheets (N = 9)		
Reduce prescribing errors for all patients	Alagha,[30] Broussard,[32] Burmester,[35] Cimino,[1] Cunningham,[39] Dinning,[77] Kozer 2005,[55] Larose,[57] and Robinson[68]	27% to 82% reduction in prescribing errors
Reduce prescribing errors for ICU patients	Alagha,[30] Burmester,[35] and Cimino[1]	27% to 76% reduction in prescribing errors
Reduce prescribing errors for inpatient chemotherapy	Dinning[77] and Robinson[68]	39% to 60% reduction in prescribing errors
Reduce prescribing errors for emergency department patients	Kozer 2005[55] and Larose[57]	41% to 78% reduction in prescribing errors
Pharmacist participation in drug therapy (N = 5)		
Pharmacists on units	Cimino,[1] Gibson,[42] Kaushal,[50] and Otero[64]	17% to 50% reduction in all types of medication errors.
Satellite pharmacy	Olsen[89]	16% increase in administering errors

Although summary ranges are presented above, appreciable heterogeneity still exists between many studies using the same intervention, likely accounting for the large outcome ranges.
a Unless specified, CPOE interventions were compared with manual order entry.
b Twenty studies used education as part of their intervention; 14 studies used education as their main intervention.

Medication Error Reporting and Prevention guidelines[22] for grading medication errors would permit providers to know if an intervention prevents not only medication errors but also harmful medication errors. Additionally, consistent denominators for medication error rates that reflect the total opportunities for error in each category would allow for better comparisons across studies and sites: prescribing errors per 1000 orders or prescriptions, administering errors per 1000 opportunities for medication administration, and dispensing errors per 1000 medications dispensed.[93] Although patient days and patients are often easier denominators to collect, they prevent comparisons between studies because it is unclear if patients in tertiary care centers are sicker, have more medications ordered, and therefore are at greater risk for a medication error. The universal use of the SQUIRE (Standards for QUality Improvement Reporting Excellence) guidelines for quality improvement reporting,[26] although challenging to implement in its entirety, would allow readers to understand the complete quality improvement process for each intervention and increase the spread of effective studies. Finally, inclusion of cost analysis and return on investment figures in intervention studies, which is difficult in locally funded quality improvement projects, could allow policy makers and medical leaders to weigh the costs and benefits of possible interventions before choosing which of the many potential medication error interventions to implement.

Implementing these suggestions in pediatric medication error research remains challenging. We appreciate that not all quality improvement research projects can meet every metric regarding high-quality, bias-free studies as laid out by the Cochrane Effective Practice and Organization of Care Review Group guidelines.[27] Recognizing these challenges, front-line quality improvement experts would benefit from training in both quality improvement and scientific methodology to produce more impactful research. Furthermore, increased collaboration between front-line clinicians looking to improve practices and trained clinical researchers would aid in the quality and quantity of medication error research, and protect patients from these harmful errors. Finally, given the small sample size problem frequently encountered when researching pediatric patients, medication error reduction collaboratives, with larger groups of pediatric patients to study and more pediatric centers sharing resources, could make a larger impact on both medication error science and harm prevention.

CONCLUSIONS

Pediatric medication errors can be reduced through multiple interventions aimed at improving the medication process. More research is needed in the areas of ambulatory patients, nondeveloped countries, administering and dispensing errors, and community hospitals and should use standardized definitions for medication errors and outcomes. Additional cost-effectiveness data on interventions to reduce pediatric medication errors would benefit policy makers and medical leaders as they choose between multiple possible interventions. Reducing medication errors presents an important opportunity for improving the quality and diversity of current research.

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