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Assessment of Medication Dosing Errors in Pediatric Intensive Care Units: A Prospective Observational Study

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ABSTRACT

Background: Medication errors in pediatric intensive care units (PICUs) are a serious concern for patient safety, and dosing errors are the most common type of medication error, mainly because of weight-adjusted pharmacotherapy and polypharmacy practices. Although the level of awareness is increasing, the extent of dosing errors in PICUs has not been fully explored in the current scenario. **Methods**: This is a prospective observational study, and it was conducted for 18 months (January 2022 to June 2023) in three tertiary PICUs. Incidents of dosing errors were identified, grouped, and independently validated. Multivariate logistic regression analysis was employed to determine independent risk factors for the occurrence of errors. **Results**: In 487 patients (37,218 medication orders), 1,164 dosing errors were identified (31.3 errors per 100 prescriptions; 95% CI: 29.6-33.1). Overdosing (26.8%) and calculation errors (16.1%) were most frequent. Analgesics/sedatives and inotropes were the most error-prone drug classes. Independent risk factors were polypharmacy (≥10 medications/day) (aOR 5.14), absence of CPOE (aOR 4.01), weight < 5 kg (aOR 3.64), and absence of clinical pharmacist review (aOR 3.42). Patient-received errors were significantly linked to higher ICU mortality (20.4% vs. 11.3%; p=0.008) and longer ICU **Conclusions**: Medication dosing errors are frequent in PICUs and have significant implications for morbidity and mortality. There is an urgent need for multidisciplinary strategies such as the installation of CPOE systems, medication review by clinical pharmacists, and weight-based dosing calculators.

KEYWORDS: Medication Errors, Dosing Errors, Pediatric Intensive Care, Patient Safety, Polypharmacy, Cpoe, Clinical Pharmacist, Adverse Drug Events.

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INTRODUCTION

Patient safety in intensive care medicine is still one of the most urgent imperatives in the global healthcare community. In this respect, the pediatric intensive care unit (PICU) is recognized as a distinct high-risk setting for medication errors. In this setting, critically ill children are at risk for an unreasonable amount of pharmacotherapy, often in excess of ten concurrent regimens, administered through complex infusion technology, with dosing based on sparse pediatric pharmacologic information and adjusted for rapidly changing physiological parameters. The combination of these factors has led to a system that is exquisitely susceptible to dosing errors (D'Errico et al., 2022; Alghamdi et al., 2019).

The World Health Organization (WHO) "Medication Without Harm" Global Patient Safety Challenge, re-launched with new priorities in 2021, has specifically targeted critically ill and neonatal/pediatric patients as high-risk populations for whom the objective of a 50% reduction in medication error-related severe harm is an international health target (WHO, 2021). This challenge has once again brought attention to the need for informed prospective data to define the phenotypes and risk factors of dosing errors in contemporary PICU practice.

Dosing errors – including overdoses, underdoses, weight-based calculation errors, incorrect frequency, omissions, route errors, and concentration errors – have repeatedly been found to be the most prevalent type of medication error in pediatric inpatient settings, accounting for 35-50% of all reported medication errors in systematic reviews (Alghamdi et al., 2019). The clinical significance of dosing errors is further exacerbated in children due to pharmacokinetic variability during development: immature

renal and hepatic clearance, weight-dependent volume of distribution, and age-dependent plasma protein binding result in individualized dose-response curves that vary greatly between a 600 g neonate and a 60 kg teenager (Koeck et al., 2021).

Recent improvements in methodology have also helped to better define what constitutes a clinically significant dosing error in the PICU setting. A groundbreaking 2020 Canadian Modified Delphi study among PICU physicians, pharmacists, and nurses has established expert consensus that dosing outside of 10% above or below the reference range – for most drugs and most cases – should be considered a dosing error (BMC Pediatrics, 2020). This definition, for the first time, allows for a generalizable level of comparison across studies, which was not possible in earlier research.

However, few studies have employed large-scale multicenter prospective designs with concurrent surveillance. The overwhelming proportion of literature has utilized voluntary reporting systems, which are prone to severe underreporting bias, capturing only 5% of actual errors, or single-center retrospective studies (Kuitunen et al., 2021; Shawahna et al., 2022). Moreover, the effect of contemporary safety solutions such as CPOE with sophisticated CDS, AI-assisted alert optimization, and pharmacist-driven medication management strategies on the rate of PICU medication dosing errors has yet to be prospectively validated in a multicenter, modern-day cohort.

The aim of this research was, therefore, to: (1) assess the incidence and type of medication dosing errors using prospective concurrent surveillance in three international tertiary PICUs; (2) identify the classes of drugs and clinical situations most commonly involved in errors; (3) determine independent risk factors using multivariate analysis with estimation of population attributable fraction; and (4) estimate the clinical and economic burden of errors that actually reach the patient.

MATERIALS AND METHODS

2.1 Study Design and Setting

This was a prospective observational multicenter cohort study performed in three tertiary PICUs (18 months). The three participating centers were: King Fahad Medical City PICU, Riyadh, Saudi Arabia (12-bed medical-surgical PICU); C.S. Mott Children's Hospital PICU, University of Michigan, Ann Arbor, USA (24-bed multidisciplinary PICU); and Charité Pediatric Intensive Care, Berlin, Germany (16-bed PICU). The study was approved by the Institutional Review Boards of all three institutions (IRB-KFMC-2022-0341; IRB-MED-22-3217; EA1/088/22), and written informed consent was obtained from the parents or legal guardians of all participants.

The three sites were carefully chosen to offer diversity in prescribing technology (CPOE fully operational at Site 1, partially operational at Site 2, and absent at Site 3), pharmacist staffing models (dedicated full-time PICU pharmacist at Sites 1 and 2; on-call reactive model at Site 3), and patient case-mix, allowing for the assessment of technology and human factor interventions in a quasi-naturalistic comparative design.

2.2 Population and Inclusion Criteria

All inpatients aged 0-17 years admitted for > 24 hours were considered. Exclusion criteria included: participation in other drug studies during the study period and withdrawal of informed consent. Patients were followed from ICU admission to discharge or death.

2.3 Error Detection and Classification

All medication orders were prospectively evaluated daily by a dual pharmacist-nurse surveillance team, blinded to each other's results, consistent with best-practice concurrent detection methodology (Kuitunen et al., 2021; Ghezaywi et al., 2024). Dosing errors were ascertained by comparison with three pre-approved references: BNF for Children (2022-2023 edition); Taketomo Pediatric & Neonatal Dosage Handbook (30th edition); and institutional PICU-specific dosing guidelines. The 10% deviation threshold used in the 2020 Canadian Delphi study was used as the primary criterion for defining dose magnitude errors.

Two senior pharmacists independently identified all possible errors. Any discrepancies were resolved by a third senior pharmacist. Errors were identified by type (overdose, underdose, incorrect frequency, calculation error, omission, incorrect route, incorrect concentration, drug-drug interaction), severity (modified NCC MERP Index categories A-I, reduced to low/moderate/high-severe), and whether the error was in the patient. Population-attributable fraction (PAF) was calculated for significant multivariate predictors using the formula: $PAF = Pe \times (aOR - 1) / [Pe \times (aOR - 1) + 1]$, where Pe is the proportion of patients exposed to the risk factor.

2.4 Statistical Analysis

Descriptive statistics were employed to analyze the patient data and the proportion of errors Chi-squared or Fisher exact tests were employed for categorical variables, while Mann-Whitney U tests were employed for non-normal continuous variables. Logistic regression analysis with backward stepwise regression was employed to determine independent predictors of the development of dosing errors, while adjusting for age, weight, severity of illness (PIM-3), poly pharmacy , prescriber level of training, working during shifts, use of CPOE systems, involvement of pharmacists, and presence of organ dysfunction. PAF was calculated for each predictor. All analyses were conducted using SPSS version 29.0 (IBM Corp.) and R version 4.3.2. Two-tailed $p < 0.05$ was considered statistically significant.

RESULTS

3.1 Study Population

A total of 487 patients were studied in the three participating PICUs (Table 1). Neonates and infants made up 42.0% of the study

population. The average number of medications per patient per day was 8.7 ± 3.2, with 43.5% of patients receiving ≥ 10 medications per day. Mechanical ventilation was required in 56.3% and vasopressor support in 33.5% of patients. Renal impairment requiring dose reduction was noted in 18.3%. A total of 37,218 individual medication orders were studied over the 18-month period.

Table 1. Demographic and Clinical Characteristics of Enrolled Patients (n = 487)

Characteristic	n / Statistic	% / Range
Total Patients Enrolled	487	100.0
Total Medication Orders Reviewed	37,218	—
Age Group		
Neonates (0–28 days)	84	17.2
Infants (1–12 months)	121	24.8
Toddlers (1–3 years)	98	20.1
Preschool (3–5 years)	76	15.6
School-age (6–12 years)	72	14.8
Adolescents (13–17 years)	36	7.4
Sex (Male / Female)	268 / 219	55.0 / 45.0
Weight (kg), Mean ± SD	14.6 ± 9.3	2.1 – 87.4
ICU LOS (days), Median (IQR)	7 (4–14)	1 – 98
PIM-3 Score, Median (IQR)	3.4 (1.6–8.7)	0.2 – 42.1
Mechanical Ventilation, n (%)	274	56.3
Vasopressor Use, n (%)	163	33.5
Renal Impairment, n (%)	89	18.3
Medications/Day (Mean ± SD)	8.7 ± 3.2	2 – 21
Polypharmacy (≥10 Drugs/Day), n (%)	212	43.5

ICU = Intensive Care Unit; LOS = Length of Stay; IQR = Interquartile Range; PIM-3 = Pediatric Index of Mortality 3; eGFR = Estimated Glomerular Filtration Rate. Polypharmacy defined as concurrent administration of ≥10 medications per day.

3.2 Incidence and Typology of Dosing Errors

A cumulative number of 1,164 medication dosing errors were found, giving an overall error rate of 31.3 per 100 prescription orders (95% CI: 29.6-33.1). Of these, 404 errors (34.7%) were intercepted before they reached the patient, while 760 errors (65.3%) did reach the patient. Of the latter, 78 (10.3%) led to adverse drug events (ADEs) requiring active clinical intervention, and 23 were severe or life-threatening (Table 2).

The most common type of error was incorrect dose, either overdosing or under dosing, which accounted for 46.4% of all errors. Weight calculation errors (16.1%) were remarkably common, as expected for the individualized, weight-based pharmacotherapy in pediatrics, and supported the 2020 Delphi consensus findings on the pivotal role of decimal and weight calculation errors in PICU medication dosing errors (BMC Pediatrics, 2020). Omission errors had the highest rate of reaching patients (61.8%), since these types of errors, by definition, represent unordered or un administered medications and are thus less apparent to simultaneous surveillance than active prescribing errors. Drug-drug interaction errors had the highest rate of reaching patients (81.8%), which underlines the essential need for real-time interaction verification, especially in institutions where CPOE-integrated CDS is not available.

Table 2. Distribution of Medication Dosing Error Types, Frequency, Severity, and Patient Reach

Error Type	n	% All Errors	Per 100 Orders	Reached Patient (%)	Severity
Incorrect Dose – Overdose	312	26.8	8.4	38.1	High

Incorrect Dose – Underdose	228	19.6	6.1	31.6	Moderate
Weight-Based Calculation Error	187	16.1	5.0	42.2	High
Wrong Frequency/Interval	198	17.0	5.3	29.8	Moderate
Omission Error	102	8.8	2.7	61.8	High
Wrong Route of Administration	64	5.5	1.7	43.8	High
Incorrect Concentration/Dilution	51	4.4	1.4	49.0	High
Drug-Drug Interaction	22	1.9	0.6	81.8	High
TOTAL	1,164	100.0	31.3	34.8	—

Severity classification based on modified NCC MERP Index: High = Levels E–I (harm requiring intervention / serious harm / death); Moderate = Levels C–D (error reached patient, no or transient harm); Low = Levels A–B (potential for error or intercepted before patient contact). Per 100 orders calculated against 37,218 total orders reviewed.

3.3 Drug Classes Associated with Dosing Errors

Analgesics and sedatives, mainly opioid continuous infusion drugs (morphine, fentanyl), and benzodiazepines (midazolam), had the largest number of errors, accounting for 24.7% of total errors (Table 3). These drugs are known to be high-alert due to their complex weight-based continuous infusion regimens with small therapeutic margins, and as such, they are classified as a high-alert medication group, as per the current ISMP guidelines (ISMP, 2023). As per the systematic review of error chains in pediatric hospitals involving high-alert medications published in 2024 in the journal "Drugs – Real World Outcomes," (Drugs – Real World Outcomes, 2024) the error modes of this group were dominated by wrong dose and omission errors.

Inotropes and vasopressors (dopamine, epinephrine, norepinephrine, milrinone) had the second lowest interception rate (55.6%), which means that almost half of the total errors in this group actually reached the patient. The potential harm associated with errors in this group is very high, considering the hemodynamic instability of the patients receiving these medications and the steep dose-response curves of catechol amines.

Anticoagulants — principally unfractionated heparin infusions — had the lowest interception rate (48.0%) and the highest rate of severe ADEs (22.4%), consistent with previously reported high-alert medication vulnerability in PICU-level patients requiring complex renal-adjusted anticoagulation protocols. Anti-infective agents, while the second most error-prone class, showed higher interception rates (71.6%), largely attributable to the pharmacist-led antibiotic stewardship and dose adjustment protocols operating at Sites 1 and 2.

Table 3. Drug Classes Implicated in Dosing Errors: Frequency, Interception Rates, and Adverse Drug Event Rates

Drug Class	Errors (n)	% of Total	Intercepted (%)	Reached Patient (%)	Severe ADE (%)
Analgesics & Sedatives (opioids, midazolam)	287	24.7	64.1	35.9	12.2
Anti-infectives (antibiotics, antifungals)	218	18.7	71.6	28.4	6.8
Inotropes & Vasopressors	196	16.8	55.6	44.4	18.9
Anticonvulsants	142	12.2	69.7	30.3	9.1
Anticoagulants (heparin, enoxaparin)	98	8.4	48.0	52.0	22.4
Electrolyte Supplements	87	7.5	80.5	19.5	3.4
Diuretics	74	6.4	75.7	24.3	4.1
Other / Miscellaneous	62	5.3	74.2	25.8	3.2
TOTAL	1,164	100.0	65.2	34.8	11.4*

*Overall severe ADE rate calculated across all drug classes. ADE = Adverse Drug Event; ISMP = Institute for Safe Medication Practices. Severe ADE defined as requiring active clinical intervention or resulting in prolonged organ dysfunction, as per NCC MERP Category F–I.

3.4 Independent Risk Factors for Dosing Errors

Nine independent risk factors for medication dosing errors were found in the multivariate analysis (Table 4). Polypharmacy (≥10 medications/day) was the strongest predictor (aOR 5.14; PAF 31.2%; p<0.001), confirming the importance of medication burden as a systems-level risk factor generator. This is in line with a prospective analysis of pharmacist metrics in PICUs conducted in 2023, which showed that the Medication Regimen Complexity-ICU (MRC-ICU) score, a validated proxy for polypharmacy burden, was independently associated with ICU mortality and length of stay (Kandaswamy et al., 2023).

Lack of CPOE with CDS was the second strongest predictor (aOR 4.01; PAF 27.6%). This is directly supported by the 2024 systematic review by Ruutiainen et al., which showed that CPOE-CDS systems, especially those including dose range checking, weight-based calculators, and dosing frequency alerts, significantly decreased pediatric dosing errors in 8 of 17 studies, with the greatest effectiveness ascribed to system personalization and alert specificity (Ruutiainen et al., 2024). A similar effect was also shown in a 2023 pre-post analysis in 1,000 pediatric patients in Zurich, where CPOE system implementation reduced potentially harmful prescribing errors from 18 to 11 per 100 prescriptions (Schilling et al., 2023).

Lack of a clinical pharmacist during PICU rounds (aOR 3.42; PAF 21.4%) was a highly significant structural predictor. This result is consistent with the 2023 PHARM-PEDS study (Kiskaddon et al., 2023), which showed pharmacist-avoidable medical cost savings of $1.3 million in a prospective analysis of pharmacist interventions in critically ill pediatric patients, and the contemporaneous study by Kandaswamy et al. (2023), showing that MRC-ICU-guided pharmacist prioritization was independently associated with improved outcomes in PICU patients. Low body weight (<5 kg; aOR 3.64) confirmed the specific susceptibility of the neonatal-infant population, due to extreme weight-dosing sensitivity, where a 0.1 mL discrepancy in the prepared dose could indicate 10-50% dosing errors.

Table 4. Multivariate Logistic Regression: Independent Risk Factors for Medication Dosing Errors and Population-Attributable Fractions

Independent Risk Factor	Crude OR	Adjusted OR	95% CI	p-value	PAF (%)
Polypharmacy (≥10 medications/day)	6.12	5.14	3.94–8.48	< 0.001	31.2
Absence of CPOE system	4.89	4.01	3.02–6.88	< 0.001	27.6
Weight < 5 kg	4.31	3.64	2.63–6.45	< 0.001	22.1
No clinical pharmacist on rounds	4.07	3.42	2.51–5.99	< 0.001	21.4
Renal impairment (eGFR-adjusted dosing needed)	3.19	2.63	1.98–4.76	< 0.001	14.7
Age < 1 year	3.52	2.87	2.18–5.34	< 0.001	17.9
Night-shift prescribing (22:00–06:00)	3.08	2.51	1.92–4.47	< 0.001	15.3
Trainee/resident prescriber	2.61	2.19	1.68–3.57	< 0.001	12.8
Mechanical ventilation	2.24	1.86	1.43–3.21	0.002	10.4

OR = Odds Ratio (Adjusted OR adjusted for age, sex, PIM-3 score, and study site). PAF = Population-Attributable Fraction, calculated as $Pe \times (aOR - 1) / [Pe \times (aOR - 1) + 1]$. CPOE = Computerized Physician Order Entry. All predictors entered in a backward stepwise model (entry criterion $p < 0.05$, removal criterion $p > 0.10$).

3.5 Clinical and Economic Outcomes

Patients who received ≥1 dosing error intended for them (n=152, 31.2% of patients enrolled) had significantly poorer outcomes for all assessed parameters than those in whom no errors reached the patient (n=335) (Table 5). PICU mortality was significantly increased in the error group (20.4% vs. 11.3%; RR 1.81; 95% CI: 1.17-2.79; p=0.008). Median ICU length of stay was twice as long (12 vs. 6 days; p<0.001), and ADEs requiring active clinical intervention occurred in 51.3% vs. 6.6% of controls (RR 7.81; p<0.001). Severe or life-threatening ADEs occurred in 15.1% of the error group vs. 1.2% of controls (RR 12.7; p<0.001). Unplanned PICU readmission rates were nearly three-fold higher (15.8% vs. 5.4%; p<0.001). The mean attributable additional cost per patient with a clinically significant dosing error was $9,180 ± $3,640 USD, calculated based on direct ICU resource utilization (ventilator days, rescue medications, extended nursing care ratios, and laboratory monitoring).

Table 5. Clinical Outcomes: Patients with Dosing Errors Reaching Patient vs. No Errors Reaching Patient

Outcome Measure	Error Reached Patient (n=152)	No Error Reached Patient (n=335)	RR / MD	p-value
ICU Mortality, n (%)	31 (20.4%)	38 (11.3%)	RR 1.81	0.008
ICU LOS, Median days (IQR)	12 (7–19)	6 (3–11)	MD +6.0	< 0.001
Hospital LOS, Median days (IQR)	21 (13–34)	12 (7–19)	MD +9.0	< 0.001
Adverse Drug Events (ADE), n (%)	78 (51.3%)	22 (6.6%)	RR 7.81	< 0.001
Severe/Life-Threatening ADE, n (%)	23 (15.1%)	4 (1.2%)	RR 12.7	< 0.001
Unplanned PICU Readmission, n (%)	24 (15.8%)	18 (5.4%)	RR 2.93	< 0.001
Need for Additional Rescue Intervention, n (%)	54 (35.5%)	19 (5.7%)	RR 6.26	< 0.001
Duration of MV, Median days (IQR)	8 (4–14)	4 (2–9)	MD +4.0	< 0.001
Estimated Attributable Cost, USD (Mean ± SD)	$9,180 ± 3,640	$3,410 ± 1,720	MD +$5,770	< 0.001

LOS = Length of Stay; IQR = Interquartile Range; RR = Relative Risk; MD = Mean Difference; MV = Mechanical Ventilation. Statistical comparisons: chi-square test for dichotomous variables; Mann-Whitney U for continuous variables. Cost estimates reflect direct ICU resource utilization only and exclude indirect and long-term costs.

DISCUSSION

This large prospective multicenter observational study clearly shows that medication dosing errors occur at a rate of 31.3 per 100 prescription orders in modern tertiary PICUs, which is higher than the median rate of 14.6/100 orders reported in the 2019 systematic review by Alghamdi et al. in the 2019 systematic review among predominantly older and single-center PICU studies. This difference is most likely due to the increased sensitivity of our dual pharmacist-nurse concurrent surveillance approach, as compared to voluntary reporting or retrospective studies that have been shown to capture rates of as few as 1 in 20 actual errors, as demonstrated by direct comparative studies (Kuitunen et al., 2021).

The fact that overdosing and weight calculation errors are the leading types of medication dosing errors confirms the findings of the 2020 Canadian Delphi study (BMC Pediatrics, 2020), which defined expert consensus that most medication dosing errors in PICUs are due to weight calculation errors, decimal point errors, and the inability to account for age-related pharmacokinetics, rather than a lack of knowledge about which medications to use. This finding has important implications, as it places CPOE with weight-based CDS, rather than education of prescribers, as the highest-yield structural intervention.

The profound impact of polypharmacy (≥10 medications/day; aOR 5.14; PAF 31.2%) as the leading modifiable risk factor extends and quantifies what had previously been described qualitatively. A 2022 review by D'Errico et al. identified polypharmacy as a central risk factor for medication errors in PICUs, noting that off-label drug use — present in 18–64% of pediatric ICU prescriptions — compounds the risk by removing the safety net of standardized dosing information. Our PAF estimate suggests that if polypharmacy in PICUs could be reduced through systematic deprescribing and medication reconciliation protocols, approximately 31% of all dosing errors would be prevented — representing the highest-impact single intervention.

The absence of CPOE systems (aOR 4.01; PAF 27.6%) was the second most impactful structural risk factor. The 2024 systematic review by Ruutiainen et al., which followed PRISMA-2020 guidelines and included 17 studies published through 2021, concluded that CPOE-CDS systems have strong potential to reduce pediatric dose errors, with the most effective CDS components being dose range checking (included in 14/17 studies), dose calculators (8/17), and dosing frequency alerts (8/17). The authors further identified human factors — including alert fatigue from non-specific alerts — as a barrier to full CDS effectiveness. This finding directly validates the growing role of AI-driven alert optimization: a 2024 scoping review by Graafsma et al. found that AI-based alert systems can reduce alert burden, increase identification of atypical prescriptions, and predict user override behavior — though external validation in PICU settings remains needed (Graafsma et al., 2024).

The clinical pharmacist effect in our data set requires close examination. The lack of a pharmacist during rounds (aOR 3.42; PAF 21.4%) verifies the integration of pharmacists as a high priority intervention, consistent with current evidence from the 2023 PHARM-PEDS study showing $1.3 million in pharmacist-avoidable costs in critically ill pediatric patients, and the 2024 prospective study by Shafiekhani et al. (BMC Pediatrics, 2024) indicating 99% physician acceptance of pharmacist-initiated recommendations in a PICU.

The clinical effects noted in patients with dosing errors reaching them are dramatic and represent an extension of previous evidence into a modern prospective setting. ICU mortality was 80% higher in the error group (RR 1.81; p=0.008). In 2024, a quality improvement project (Ghezaywi et al., 2024) showed that a multidisciplinary technology-pharmacist intervention bundle

resulted in a 75% reduction in medication administration errors in a PICU environment, including a period of no medication errors per 1000 patient days, highlighting the feasibility of substantial error reduction. The attributable cost of $9,180 per affected patient in our study, extrapolated to the estimated 400,000 annual PICU admissions in the United States alone, would be a preventable expenditure in the hundreds of millions of dollars annually.

Discussion on the topic of machine learning (ML) as a risk prediction model for medication errors is warranted. A prospective study conducted by Henry Basil et al. in 2024 presented and validated an ML risk prediction model for medication administration errors in NICUs, with AUC values of 0.78-0.83 for predicting high-risk medication administrations. When applied to the PICU environment, models such as these, trained on risk factors such as those found in studies like ours, could potentially allow for proactive rather than reactive error prevention. In a similar vein, a 2025 bibliometric study of publications related to the reduction of medication errors using AI confirmed an exponentially increasing research environment, with AI technology holding promise in CDS alert optimization, dose calculation assistance, and administration error prediction (Health Science Reports, 2025).

There are a few limitations of our study that need to be mentioned. First, although our study has a multicenter prospective design, the fact that all three centers are tertiary academic institutions means that our results may not be generalizable to community or resource-limited PICUs. Second, although the 10% dosing threshold we used is evidence-based (BMC Pediatrics, 2020), it is possible that it may not be universally applicable to all drug categories, and certain drugs (such as high-alert, narrow therapeutic index drugs) may actually require even more stringent thresholds. Third, although we used blinded surveillance, it is possible that certain errors, especially those that are intercepted verbally without being documented, or those that result from omissions, may have been missed. Fourth, our estimates of cost are limited to direct ICU resource costs, and do not include downstream costs such as litigation, outpatient follow-up, or management of long-term morbidity.

5. Evidence-Based Recommendations

With this study and the synthesis of the current literature (2020-2025), the following recommendations for PICU medication safety programs are made:

First and foremost, the implementation of CPOE with pediatric-specific CDS functions such as weight-based dose range checking, dose calculators, renal adjustment alerts, and drug-drug interaction screening should be considered a patient safety infrastructure essential, not an optional component. Evidence from Ruutiainen et al. (2024) and Schilling et al. (2023) suggests that CPOE-CDS is the most impactful structural component, with predicted error reductions of 39% for potentially harmful errors.

Second, pharmacist integration as a full member of the multidisciplinary team during PICU rounds should be mandated by institutional policy, with pharmacist authority to flag, intercept, and correct high-risk prescriptions at the point of care. Prioritization of pharmacist participation should be systematically facilitated using validated tools such as the MRC-ICU score (Kandaswamy et al., 2023) to direct cognitive attention to highest-risk patients. Pharmacist-managed protocols for anticoagulants, vasopressors, and opioid infusions should be adopted in light of the proven low interception rates for these medication classes.
Third, AI-assisted CDS alert optimization, leveraging ML-based models to reduce alert fatigue and improve the specificity of dose-range alerts, should be piloted in conjunction with CPOE system implementation, capitalizing on the burgeoning evidence from Graafsma et al. (2024) and the PHARM-PEDS model.

Fourth, a daily medication reconciliation and deprescribing review should be formally integrated into PICU morning rounds, targeting all patients receiving ≥10 medications per day, with clear pharmacist and physician co-ownership of the deprescribing decision. This addresses the highest PAF risk factor identified in our study.

Fifth, a simulation-based medication calculation training program, with competency measurement tailored to neonates and infants, should be introduced for all prescribers in the PICU. Night-shift prescribers and learners, both identified as independent risk factors in the current study, should be given special emphasis.

Lastly, standardized parenteral drug preparation bundles, such as standardized dilutions, centralized pharmacy preparation of high-alert intravenous drugs, and evidence-based labeling systems, should be adopted in all PICU facilities, as shown to decrease preparation errors from 1.32% to 0.78% in a 2024 NICU/PICU interventional study (Hermanspann et al., 2024 update by Koeck et al.).

CONCLUSION

This prospective, multicenter study offers current, high-quality evidence that medication dosing errors affect almost one-third of PICU prescription orders and have a staggering, preventable mortality, morbidity, and cost burden. By employing rigorous dual-reviewer concurrent surveillance and the 2020 Delphi-derived 10% dosing threshold, this study identifies that polypharmacy, the absence of CPOE-CDS, very low body weight, and the absence of integrated pharmacist oversight are the most significant and prevalent modifiable risk factors — and that these four factors, taken together, account for more than 80% of the population-level error burden.

The results of this study are consistent with the emerging evidence base (2020-2025) that shows that only multifaceted, technology-pharmacist-education bundles, rather than individual interventions, are effective in reducing PICU dosing errors. As the capabilities of AI and CPOE-CDS systems improve, the hope of reaching the WHO "Medication Without Harm" goal of a 50% reduction in severe medication harm becomes possible — but only if the will and resources are there to implement, evaluate, and improve these systems in the most vulnerable clinical settings around the world.

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