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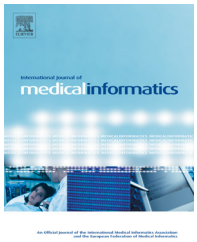

# Prescription order risk factors for pediatric dosing alerts

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ABSTRACT

*Objectives:* To determine dosing alert rates based on prescription order characteristics and identify prescription order risk factors for the occurrence of dosing alerts.
*Methods:* A retrospective analysis of inpatient medication orders and dosing alerts occurring during October 2011 and January, April, and July 2012 at a pediatric institution. Prescription orders and alerts were categorized by: medication class, patient age, route of administration, and month of the year.
*Results:* There were 228,259 orders during the studied period, with 11,072 alerted orders (4.9%). The most frequently alerted medication class was the non-analgesic central nervous system agent class (14% of alerts). Age, route, medication class, and month all independently affected dosing alert rates. The alert rate was highest for immunosuppressive agents (54%), neonates (6.7%), and orders for rectal administration (9.5%). The alert rate was higher in adult patients receiving their care at a pediatric institution (5.7%) compared to children (4.7%), but after multivariate analysis, pediatric orders had higher odds for an alert (OR 1.1, 95% CI 1.05–1.16). Mercaptopurine had the highest alert rate when categorized by active ingredient (73.9%). Albuterol 2.5 mg/mL continuous aerosol and heparin 1000 units in 0.9% sodium chloride injection solution were the unique medications with the highest alert rates (100.0% and 97.7%, respectively).
*Conclusions:* Certain types of prescription orders have a higher risk for causing dosing alerts than others. Patient age, medication class, route of administration, and the month of year can affect dosing alert rates. Design and customization efforts should focus on these medications and prescription order characteristics that increase the risk for dosing alerts.


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## 1. Introduction

Implementation of computerized provider order entry (CPOE) and computerized clinical decision support (CDS) has increased in pediatric institutions over the past 15 years [1], with reports of decreased medication related errors and adverse drug events [2–5]. However, CDS functionality efficacy has varied [6], with some continuing errors potentially related to CPOE and/or CDS [7].

Dosing errors are the most frequently reported medication errors in the pediatric population [8,9]. Dosing alerts have been designed and implemented to prevent dosing errors [4,10,11]. The Agency for Healthcare Research and Quality designated age and weight specific single dose range checking as a core criterion for a pediatric electronic health record [12]. While some studies suggest dosing alert CDS has decreased dosing errors independent of CPOE [13,14], others report no changes in dosing errors [2,11]. Dosing alerts have also been associated with high override rates, excessive inappropriate alerts and inaccuracies compared to reference ranges [10,11,15–17]. Excessive inappropriate alerts may increase the risk for alert fatigue [18,19], but appropriate dosing alerts are likely still helping prevent some dosing errors from reaching patients [19]. Increasing the appropriateness of dosing alerts is an important, yet challenging task that requires continual refinement.

To aid with dose range customization efforts, it is important for pediatric institutions to know what types of orders are at high risk for causing alerts. Identification of frequently alerted medication orders is important for two reasons: (1) To identify medication orders that could case alert fatigue, and (2) to identify medication orders that are frequently improperly prescribed. Minimal data has been published identifying medication order characteristics that affect pediatric dosing alert rates.

The aims of this study were to determine the dosing alert rate at our institution based on prescription order specific characteristics, to identify prescription order specific risk factors for dosing alerts, and to identify the most frequently alerted medication orders in a manner that can be replicated at other institutions.

## 2. Methods

Nationwide Children's Hospital (NCH) is a stand-alone pediatric referral center, with over 350 beds, including neonatal, pediatric, and cardiothoracic intensive care units, an emergency department, and other specialized inpatient units. As described in our previous studies [10,19], NCH utilizes the Epic electronic health record and CPOE system (Epic Systems Corporation, Verona, WI, USA) with a combination of non-customized dose ranges provided by First DataBank (First DataBank, South San Fransisco, CA, USA) and ranges customized by NCH practitioners.

### 2.1. Data collection

Reports were generated that included all medication orders and all dosing alerts occurring during the months of October 2011 and January, April, and July of 2012. Data collection during four separate months allowed for assessment of whether month of the year influenced alert rates. Some dose rule customization did occur in February and late April, but the goal of this study was not to analyze the effect of customization efforts. Exclusion criteria included: outpatient prescriptions, orders for formula and breast milk, formula thickeners, water for oral administration, non-medicated bandages, and any orders where the medication could not be identified in the data set (common with some non-formulary items). The reports included the date of the order, ordered medication, alert description, patient age, and route of administration. Since dosing alerts could be presented to multiple practitioners for one order, duplicate alerts for the same order were excluded.

**Table 1 – Medication route categories.**

| Category title | All included routes |
|---|---|
| Intermittent injectables | Intravenous, intracatheter, intrathecal, plasmapherisis, intraarticular, subcutaneous, intradermal, intramuscular, sclerotherapy |
| Continuous infusion | Intravenous, intracatheter, intrathecal |
| Enteral | Oral, sublingual, gastric tube |
| Inhalation | Intranasal, intratracheal, aerosolized, inhalation |
| Rectal | Rectal |
| Topical | Topical, ophthalmic, otic, transdermal, mucous membranes, irrigations |

The medication orders and the alerted orders were categorized based on American Hospital Formulary Service (AHFS) Pharmacologic-Therapeutic Classifications [20]. Minor changes were made to the AHFS classes to best describe the medication categories used in pediatric patients. Intravenous (IV) magnesium sulfate was categorized as a respiratory tract agent or an electrolyte, caloric, and water balance agent (based on the order). This is because it is not generally used as an anticonvulsant in pediatrics (which is how the AHFS categorizes it). The AHFS "miscellaneous" class was further divided into immunosuppressive agents, disease-modifying antirheumatic agents, and other miscellaneous medications for clarity. Additionally, the central nervous system (CNS) agents were divided into non-opioid related CNS analgesics (e.g., acetaminophen and ibuprofen), opioid related CNS agents (e.g., morphine and oxycodone) and non-analgesic CNS agents (e.g., amphetamines, antidepressants, and anticonvulsants). Medication classes with less than 150 orders were combined with other AHFS classes (e.g., smooth muscle relaxants were combined with non-analgesic CNS agents). Medication classes were broken down further by active ingredient regardless of concentration and unique medication (e.g., acetaminophen 160 mg/5 mL oral suspension). When determining the most frequently alerted medications, medications were excluded if they had less than 124 orders (one order every day).

Medication orders and alerted orders were also categorized based on the month of order and route of administration for the medication. Details regarding the route categories are provided in Table 1, some categories included multiple related routes. The orders and alerts were also categorized based on the age of the patient, using previously described pediatric