

Medication-Related Emergency Department Visits and Hospital Admissions in Pediatric Patients: A Qualitative Systematic Review

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Objective To review and describe the current literature pertaining to the incidence, classification, severity, preventability, and impact of medication-related emergency department (ED) and hospital admissions in pediatric patients.

Study design A systematic search of PubMed, Embase, and Web of Science was performed using the following terms: *drug toxicity, adverse drug event, medication error, emergency department, ambulatory care, and outpatient clinic*. Additional articles were identified by a manual search of cited references. English language, full-reports of pediatric (≤ 18 years) patients that required an ED visit or hospital admission secondary to an adverse drug event (ADE) were included.

Results We included 11 studies that reported medication-related ED visit or hospital admission in pediatric patients. Incidence of medication-related ED visits and hospital admissions ranged from 0.5%-3.3% and 0.16%-4.3%, respectively, of which 20.3%-66.7% were deemed preventable. Among ED visits, 5.1%-22.1% of patients were admitted to hospital, with a length of stay of 24-72 hours. The majority of ADEs were deemed moderate in severity. Types of ADEs included adverse drug reactions, allergic reactions, overdose, medication use with no indication, wrong drug prescribed, and patient not receiving a drug for an indication. Common causative agents included respiratory drugs, antimicrobials, central nervous system drugs, analgesics, hormones, cardiovascular drugs, and vaccines.

Conclusion Medication-related ED visits and hospital admissions are common in pediatric patients, many of which are preventable. These ADEs result in significant healthcare utilization. (*J Pediatr* 2013;163:477-83).

Adverse drug events (ADEs) are unfavorable occurrences related to the use and misuse of medications.¹ It has been estimated that ADEs account for over 17 million emergency department (ED) visits and 8.7 million hospital admissions annually in the US.^{2,3} A cost-of-illness model estimated that between 1995 and 2000, costs associated with morbidity and mortality secondary to ADEs more than doubled from US\$76.6 billion to more than US\$177.4 billion and is likely even higher today.^{3,4} In recent years, ADEs have been extensively evaluated in ambulatory care,⁵⁻⁹ ED care,¹⁰⁻³¹ and in hospitalized patients.³²⁻⁴³ Studies have estimated that 5%-25% of all hospital admissions and up to 12% of ED visits are medication-related, of which 50%-70% are deemed preventable.³⁴⁻⁴⁴

The majority of research performed has provided data for medication-related hospital visits in adults, but this issue has not been well studied in pediatric patients. In the majority of studies published to-date, pediatric patients were either excluded or significantly under-represented among the study population. The incidence and classification of medication-related ADEs in pediatrics cannot be expected to be the same as in adults attributable in large part to the age-related prevalence of disease and spectrum and scope of medication use. As a result, approaches to identify and prevent ADEs in pediatric patients will also be unique.

Thus, there remains a significant knowledge gap in our understanding of the magnitude and impact of medication-related hospital visits in pediatric patients. The purpose of this report is to review the current literature pertaining to the incidence, classification, severity, preventability, and impact of medication-related ED and hospital admissions in pediatric patients.

ADE	Adverse drug event
ADR	Adverse drug reaction
ADRE	Adverse drug-related event
CNS	Central nervous system
ED	Emergency department
ICU	Intensive care unit

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Methods

A systematic search (to July 2012) was performed of PubMed, Embase, and Web of Science databases for full reports in English language and patients age ≤ 18 years. Additional published reports were identified through a manual search of references in retrieved articles and in review articles. Search terms included: *drug toxicity, adverse drug event, medication error, emergency department, ambulatory care, and outpatient clinic.*

Citations identified following literature review were evaluated independently by 2 authors for inclusion using title and abstract. Where uncertainty remained regarding eligibility for inclusion, full text was reviewed. Retrospective and prospective reports of medication-related visits to an ED or hospital admission in pediatric patients were included. Definition of a medication-related visit included any visit to the ED or admission to hospital that satisfied 1 or more of the 8 classes of drug-related problems as defined by Hepler and Strand, which include: adverse drug reaction (ADR), drug interaction, improper drug selection, untreated indication, subtherapeutic dosage, suprathreshold dosage, non-adherence, and drug use without indication.⁴⁵ Exclusion criteria included all case reports of medication-related visits, studies including oncology patients, and articles that specifically evaluated intentional overdose, poisoning, or substance abuse.

Data extraction included the characterization of study type, reported incidence of medication-related visits, and incidence of hospitalization. Each type of drug-related problem was classified. Patient demographics as well as the therapeutic classes of agents most commonly associated with the ADE were extracted. We describe the nature of the event, severity as defined by each of the individual studies (eg, mild, moderate, severe), and documented the reported proportion deemed to be preventable. Finally, the impact of medication-related visit was extracted in terms of clinical, economic, or humanistic outcomes and described when available. Data were analyzed qualitatively and are summarized in **Tables I and II.**

Results

Nine papers met the inclusion criteria of this review following electronic database search (**Figure**). Upon a manual search of selected citations, 2 additional studies were identified. Among the 11 selected papers, 5 are prospective studies and 6 are retrospective studies (**Tables I and II**).^{16,46-55}

Among the 11 studies included, 7 reported medication-related ED visits and 4 reported hospital admissions as a result of an ADE. Medication-related ED visits ranged from 0.5%-3.3%^{16,49,51-55} and hospital admissions as a result of an ADE ranged from 0.16%-4.3%.^{46-48,50}

Severity, as defined by each study, was reported in 5 studies and was most commonly described as mild, moderate, or

severe.^{16,46,48,49,55} Approximately one-half (42.2%-62.5%) of ADEs reported were identified as being moderate in severity, followed by mild (4.8%-35.7%), and severe (8.3%-38.1%) events. One study reported that 91.3% of ADEs were "significant" causing symptoms harmful to that patient but posed little to no threat to the patient's life.⁵⁵

Preventability of ADEs was reported in 4 studies.^{47,49,50,55} In two ED visit studies, medication-related visits were deemed preventable in 20.3% and 51.5% of patients, respectively.^{49,54} In two studies evaluating hospitalization, admission was determined to be preventable in 46.9% and 66.7%, respectively.^{47,50}

Classification and definition of ADEs were similar but not standardized across the studies. Reported ADEs included medication overdose, ADR, nonadherence, patient receiving a drug with no indication, patient not receiving a drug for an indication, low dose, high dose, drug interaction, and allergy. The most common ADEs were patient receiving drug with no indication (17.2%-36.2%),^{47,49,50} not receiving prescribed drug (8.9% and 46.6%),^{47,49} and ADR (17.2%-42.1%).^{47,49,50}

The most common drugs causing ADEs resulting in a ED visit or hospital admission varied across studies. Antibiotics were the most common drug class and were reported as causing 25%-60.3% of medication-related visits.^{46-52,55} Other common drug classes reported included respiratory agents (10.6%-35%),^{46,47,49-51} and central nervous system (CNS) agents (3.5%-17.5%).^{47-52,55} Common classes described included analgesics, vaccines, hormones, cough-and-cold products, cardiovascular drugs, and dermatologic drugs.

ADEs resulted in various clinical manifestations. Common systems affected by ADEs were dermatologic, gastrointestinal, CNS, endocrine, respiratory, and cardiovascular. Other specific reactions that occurred were facial edema, syncope, fever, general malaise, and local reactions.

Approximately one-half of the patients presenting to the ED required treatment with medication.⁵² Five percent to 22.1% of ED patients required admissions to hospital for further treatment.^{49,52} One study also reported that 1.1% of ED patients required admission to the intensive care unit (ICU).⁴⁹ In studies of patients admitted to hospital, length of stay varied. One study reported a mean length of stay of 2.6 days.⁴⁷ Another study describes approximately one-half of patients having a length of stay between 24 and 72 hours, and approximately one-quarter of patients requiring a length of stay longer than 72 hours.⁴⁸ Two studies described rates of admission to ICU and found that from among all admitted patients, 6.3% and 6.9% were to the ICU.^{47,50}

An Australian study of 3 EDs described the economic impact of medication-related visits.⁴⁹ They report that 280 medication-related visits cost the hospital AUS\$137 088, of which AUS\$44 455 was associated with ADEs classified as preventable. Another study of 2 Australian hospitals described the economic impact of hospital admissions.⁵⁰ Drug-related admissions cost the hospitals an estimated £100 707, of which £61 543 was associated with preventable events.

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