HHS Public Access

Author manuscript

Pediatrics. Author manuscript; available in PMC 2015 November 18.

Published in final edited form as:

Pediatrics. 2014 October ; 134(4): e1009–e1016. doi:10.1542/peds.2014-0840.

Emergency Hospitalizations for Unsupervised Prescription Medication Ingestions by Young Children

Maribeth C. Lovegrove, M.P.H.[a], **Justin Mathew, Pharm.D.**[b], **Christian Hampp, Ph.D.**[b], **Laura Governale, Pharm.D., M.B.A.**[b,c], **Diane K. Wysowski, Ph.D.**[b], and **Daniel S. Budnitz, M.D., M.P.H.**[a]

[a]Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention (CDC), Atlanta, GA

[b]Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, Food and Drug Administration (FDA), Silver Spring, MD

[c]AstraZeneca, Patient Safety, Gaithersburg, MD

Abstract

Background—Emergency department visits and subsequent hospitalizations of young children following unsupervised ingestions of prescription medications are increasing despite widespread use of child-resistant packaging and caregiver education efforts. Data on the medications implicated in ingestions are limited, but could help identify prevention priorities and intervention strategies.

Methods—We used nationally-representative adverse drug event data from the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance project and national retail pharmacy prescription data from IMS Health to estimate the frequency and rates of emergency hospitalizations for unsupervised prescription medication ingestions by young children (2007 through 2011).

Address correspondence to: Maribeth C. Lovegrove, M.P.H., Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, 1600 Clifton Road, NE, Mailstop A-24, Atlanta, GA 30333, Phone: 404-639-4089; Fax: 404-639-2647; mlovegrove@cdc.gov.

Financial disclosures: The authors have no financial relationships relevant to this article to disclose.

Potential Conflict of Interest disclosures: The authors have no conflicts of interest relevant to this article to disclose.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the Food and Drug Administration.

Contributors' Statement

Maribeth C. Lovegrove: conceptualized and designed the study, conducted the analyses, contributed to interpretation of data, drafted the initial manuscript, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Justin Mathew: participated in study concept and design, contributed to acquisition, analysis, and interpretation of data, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Christian Hampp: participated in study concept and design, contributed to interpretation of data, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Laura Governale: participated in study concept and design, contributed to acquisition and interpretation of data, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Diane K. Wysowski: participated in study concept and design, contributed to interpretation of data, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Daniel S. Budnitz: conceptualized and designed the study, contributed to acquisition and interpretation of data, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Results—Based on 1,513 surveillance cases, 9,490 estimated emergency hospitalizations (95% confidence interval, 6,420 to 12,560) occurred annually in the United States for unsupervised prescription medication ingestions among children < 6 years from 2007 through 2011; 75.4% involved 1- or 2-year old children. Opioids (17.6%) and benzodiazepines (10.1%) were the most commonly implicated medication classes. The most commonly implicated active ingredients were buprenorphine (7.7%) and clonidine (7.4%). The top twelve active ingredients, alone or in combination with others, were implicated in nearly half (45.0%) of hospitalizations. Accounting for the number of unique patients who received dispensed prescriptions, the hospitalization rate for unsupervised ingestion of buprenorphine products was significantly higher than rates for all other commonly implicated medications and 97-fold higher than the rate for oxycodone products (200.1 vs. 2.1 hospitalizations per 100,000 unique patients).

Conclusions—Focusing unsupervised ingestion prevention efforts on medications with the highest hospitalization rates may efficiently achieve large public health impact.

Keywords

poisoning; unintentional overdose; pediatric hospitalization; buprenorphine; opioids; sulfonylureas; prescription drugs; drug packaging

In the decades since the 1970 Poison Prevention Packaging Act (PPPA) was enacted, child-resistant (CR) packaging and education on safe medication storage have saved thousands of children's lives.[1,2] Despite these interventions, unsupervised medication ingestions (young children accessing medications without adult permission or oversight) remain an important cause of preventable pediatric harm, leading to over 60,000 emergency department (ED) visits by children < 6 years and approximately 500,000 calls to poison centers annually in the United States.[3–5] Serious unsupervised ingestions have been increasing and most hospitalizations for unsupervised ingestions involve prescription medications.[6]

In the United States, nearly all prescription medications are dispensed in bottles with CR caps that patients or caregivers must correctly re-secure after each and every use. Even when correctly secured, CR packaging is not intended to be impenetrable, but rather to delay young children from opening the container and obtaining a toxic amount.[7] Circumstances leading to unsupervised ingestions are multifactorial, but leaving medications in locations accessible to young children, even temporarily, as well as failing to fully re-secure CR caps are known contributors.[8–11]

Enhancing safety packaging with elements beyond those currently required by the PPPA holds promise for reducing the incidence and severity of pediatric medication ingestions, but may add marginal cost and inconvenience for adults.[3,6,8,12,13] Data on the specific medications involved in serious unsupervised ingestions by young children may help prioritize products for enhanced safety packaging. We used nationally-representative surveillance data to characterize emergency hospitalizations for unsupervised prescription medication ingestions by children < 6 years and to identify the prescription medications with the highest frequencies and rates of hospitalization.

METHODS

Data Sources

National estimates of ED visits and subsequent hospitalizations for unsupervised medication ingestions were based on data from the National Electronic Injury Surveillance System – Cooperative Adverse Drug Event Surveillance (NEISS-CADES) project. NEISS-CADES is an ED-based public health active surveillance system based on a nationally-representative sample of hospitals in the United States and its territories with a minimum of six beds and a 24-hour ED, and has been described in detail.[14,15] Briefly, trained coders at 63 participating hospitals review the clinical diagnoses and supporting information in all ED visit medical records to identify adverse drug events, including unsupervised medication ingestions, diagnosed by treating clinicians. Coders report up to two medications implicated in each adverse event, verbatim diagnoses, and narrative descriptions of the event, including precipitating circumstances, clinical manifestations, treatments administered in the ED, and discharge disposition.

National estimates of dispensed prescriptions from outpatient retail pharmacies were obtained from the IMS Health, Vector One®: National (VONA) database and national estimates of unique patients receiving dispensed prescriptions were obtained from IMS Health, Vector One®: Total Patient Tracker (TPT).[16,17] The Vector One® database integrates retail pharmacy prescription activity from a sample of chain, independent, food store, and mass merchandiser pharmacies. Each year, Vector One® receives over 1.9 billion prescription claims, representing over 158 million unique patients and nearly half of all U.S. retail prescription activity.

Definitions

A surveillance case of an unsupervised ingestion was defined as hospitalization following an ED visit by a child < 6 years for accessing prescription medication without adult permission or oversight from January 1, 2007 through December 31, 2011, as documented by the treating clinician. Hospitalizations included inpatient admissions, transfers to another hospital, and observation admissions (time-limited assessment, treatment, and reassessment, typically lasting <24 to 48 hours). For this analysis, prescription medications included oral medications available only by prescription. Because detailed information about dosage strength and brand name was not consistently documented, cases involving medications commonly available in both prescription and over-the-counter formulations were not included (e.g., single-ingredient ibuprofen). When only a medication class was documented, only cases involving classes comprising solely prescription medications were included (e.g., opioid analgesics were included; unspecified non-steroidal anti-inflammatory drugs were excluded). Outpatient use of commonly implicated oral medications during the study period was estimated using two measures, numbers of dispensed outpatient prescriptions and numbers of unique patients receiving dispensed prescriptions, regardless of indication or intended recipient.

Outcome Measures

The primary outcome measure was hospitalization following an ED visit for unsupervised ingestion of an oral prescription medication by a child < 6 years. Secondary outcomes included rates of emergency hospitalizations for unsupervised prescription medication ingestions per 100,000 dispensed outpatient prescriptions and per 100,000 unique patients receiving dispensed prescriptions.

Statistical Analysis

Each NEISS–CADES case was assigned a sample weight based on the inverse probability of selection, adjusted for nonresponse and post-stratified to adjust for the number of annual hospital ED visits.[18] National estimates of ED visits, subsequent hospitalizations, and corresponding 95% confidence intervals (CIs) were calculated using the SURVEYMEANS procedure in SAS, version 9.2 (SAS Institute), to account for the sample weights and complex sample designs. Annual national estimates were calculated by dividing the NEISS–CADES estimates for the 5-year period from 2007 through 2011 by five. Estimates based on <20 cases, total estimates <1200 over the five-year study period, and estimates with a coefficient of variation greater than 30% may be statistically unreliable and are noted. IMS Health projects national estimates of dispensed outpatient prescriptions and unique patients from the Vector One® sample using proprietary analytical methods.

To calculate hospitalization rates for unsupervised ingestions, we divided the estimated number of emergency hospitalizations by both estimates of medication use (number of dispensed outpatient prescriptions and number of unique patients receiving dispensed prescriptions). Accompanying 95% CIs for rate estimates were calculated incorporating variance estimates for both numerator and denominator components.[19] Since these components were calculated from separate surveillance systems, they were treated as independent (i.e., having zero covariance).

RESULTS

Based on 3,638 surveillance cases, we estimated 34,503 ED visits (95% CI, 27,296 to 41,709) for unsupervised ingestion of oral prescription medications annually from 2007 through 2011 among children < 6 years. An estimated 27.5% of these ED visits (9,490 visits; 95% CI, 6,420 to 12,560) resulted in hospitalization; 5,887 hospitalizations (95% CI, 4,152 to 7,622) involved inpatient admission or transfer to another hospital and the remaining hospitalizations were observation admissions. Three-quarters of hospitalizations for unsupervised prescription medication ingestions involved 1- or 2-year old children (75.4%; 95% CI, 72.1 to 78.7) and one-fifth involved ingestion of 2 or more medications (21.9%; 95% CI, 18.3 to 25.5) (Table 1).

Twelve medication classes, alone or in combination with others, were implicated in 79.1% (95% CI, 73.4 to 84.9) of hospitalizations for unsupervised prescription medication ingestions (Table 2). Opioid analgesics were implicated in a significantly higher proportion of hospitalizations (17.6%; 95% CI, 13.9 to 21.2) than any other medication class. Other commonly implicated classes included benzodiazepines (10.1%), sulfonylureas (8.2%), beta

blockers (8.0%), centrally-acting antiadrenergics (8.0%), and calcium channel blockers (7.8%). These 6 classes were implicated in 57.4% (95% CI, 51.8 to 63.1) of hospitalizations. Over half of ED visits for unsupervised ingestion of sulfonylureas (77.8%), calcium channel blockers (57.4%), and centrally-acting antiadrenergics (53.5%) resulted in hospitalization.

Twelve active ingredients, alone or in combination with others, were implicated in 45.0% (95% CI, 39.5 to 50.5) of hospitalizations for unsupervised prescription medication ingestions (Table 3). Buprenorphine and clonidine were most commonly implicated, accounting for 7.7% and 7.4% of hospitalizations, respectively. Nearly all hospitalizations for buprenorphine ingestions (97.2%; 95% CI, 93.5 to 100.0) involved a combination buprenorphine/naloxone product. The proportion of ED visits resulting in hospitalization for buprenorphine (62.4%) and clonidine (56.2%) was high and exceeded only by sulfonylureas.

Accounting for estimated numbers of dispensed outpatient prescriptions, the hospitalization rate for unsupervised ingestion of buprenorphine products (13.6 hospitalizations per 100,000 outpatient prescriptions) was significantly higher than the rate for all other commonly implicated medications except clonidine (6.0 hospitalizations per 100,000 outpatient prescriptions) (Figure 1A). Accounting for numbers of dispensed prescriptions, the hospitalization rate for buprenorphine products was 27 times higher than the rate for oxycodone products (0.5 hospitalizations per 100,000 outpatient prescriptions) and 67 times higher than the rate for hydrocodone products (0.2 hospitalizations per 100,000 outpatient prescriptions).

Similarly, accounting for estimated numbers of unique patients who received dispensed prescriptions, the hospitalization rate for unsupervised ingestion of buprenorphine products (200.1 hospitalizations per 100,000 unique patients) was significantly higher than the rate for all other commonly implicated medications (Figure 1B). The hospitalization rate for clonidine (47.4 hospitalizations per 100,000 unique patients) was significantly higher than the rate for all other medications except the two sulfonylureas. Accounting for numbers of unique patients, the hospitalization rate for buprenorphine products was 97 times higher than the rate for oxycodone products (2.1 hospitalizations per 100,000 unique patients) and 238 times higher than the rate for hydrocodone products (0.8 hospitalizations per 100,000 unique patients). The national estimate of hospitalizations for hydrocodone product ingestions used to calculate hospitalization rates had a coefficient of variation of 30.8%, a value on the border of statistical reliability.

DISCUSSION

Prescription medication ingestions by children < 6 years lead to over 9,000 estimated U.S. hospitalizations annually; 75% involve 1- or 2-year old children. While thousands of unique prescription medications are currently marketed in the United States, 12 active ingredients were implicated in 45% of estimated hospitalizations, with the top 2 ingredients (buprenorphine and clonidine) implicated in 15% of hospitalizations. Accounting for the estimated number of unique patients receiving dispensed prescriptions, buprenorphine had the highest rate of unsupervised ingestion hospitalizations compared with all other commonly implicated active ingredients and clonidine had the second highest

hospitalization rate. A targeted prevention approach that focuses on medications with the highest rates of unsupervised ingestion hospitalization, relative to outpatient use, has the potential to efficiently achieve large public health impact.

Efforts to prevent unsupervised prescription medication ingestions have largely been part of broader poisoning prevention initiatives. Child-resistant packaging and test protocols mandated by the PPPA apply equally to all specified products -- including household cleaners, pesticides, and medications -- based on the premise that they all have potential for significant toxicity if accessed by young children.[20] While a handful of prescription medications with low potential for toxicity are excluded from CR packaging requirements, other prescription medications that are potentially highly toxic to young children in small amounts, such as those identified on “one pill can kill” lists,[21,22] have no additional requirements. Similarly, a wide-range of potential poisons are typically included in educational programs on safe storage practices.[23,24] While existing efforts have been credited with preventing thousands of pediatric deaths from medication ingestions over several decades,[1,2] the finding of over 9,000 estimated hospitalizations annually resulting from prescription medication ingestions indicates that pediatric ingestions remain a serious, but preventable, public health concern.

Interventions to reduce unsupervised ingestions by young children should focus on the medications that most commonly lead to harm. In this study, opioids, benzodiazepines, sulfonylureas, and 3 classes of antiadrenergic agents (beta blockers, calcium channel blockers, and centrally-acting antiadrenergics) were implicated in nearly 60% of hospitalizations. Previous studies have also identified these classes as significant contributors to pediatric medication ingestions.[6,13,25–28] Recently, there has been growing concern for harm from pediatric buprenorphine ingestions[8,29,30] and we previously noted a marked increase in estimated buprenorphine ingestion ED visits over several years.[31] What has not been previously reported is that just 12 active ingredients, alone or in combination with other medications, were implicated in nearly half of all hospitalizations for unsupervised ingestions of prescription medications, and two ingredients, buprenorphine and clonidine, were implicated in 15% of hospitalizations.

The finding that buprenorphine and clonidine were the leading contributors to unsupervised ingestion hospitalizations likely reflects the interplay of pharmacological properties, clinical presentation, medication dose forms, availability, and other factors. Emergency hospitalization rates among pharmacologically similar medications (e.g., buprenorphine vs. other opioids) varied greatly. Recent studies have shown an association between increased use of specific prescription medications, including opioids, and increases in child exposures.[25,26,28] However, in this study, estimated numbers of both prescriptions and unique patients were highest for oxycodone- and hydrocodone-containing analgesics, while estimated rates of unsupervised ingestion hospitalizations were significantly higher for buprenorphine products and clonidine. After adjusting for medication utilization during the study period, one child was hospitalized for an unsupervised ingestion per 500 unique patients receiving buprenorphine, compared with one child hospitalized per 48,500 unique patients receiving oxycodone and one child hospitalized per 119,000 unique patients receiving hydrocodone.

Passive safety features can augment existing child-resistant packaging by addressing a key limitation - reliance on patients or caregivers to properly cap and safely store medications immediately after every use. For example, adding flow restrictors to the neck of liquid medication bottles has been shown to be efficacious in delaying preschool-aged children from accessing bottle contents and limiting the amount accessed even when safety caps are not re-applied.[32] Flow restrictors are currently used in conjunction with CR caps to provide a secondary layer of protection on infants' and children's acetaminophen.[33]

The prescription medications most commonly implicated in unsupervised ingestion hospitalizations, however, are largely available in solid dosage forms (i.e., tablets, capsules, or films). Unit-dose packaging, in which each individual dose has CR protection, is another passive approach to limiting unsupervised ingestions of solid medications,[3,6,8,12] and may provide benefits in addition to enhanced child safety.[34] Unlike multi-dose bottles which rely on users to keep medications in original bottles and fully re-secure caps after every use, there is no need to re-secure safety barriers of unit-dose packaging, which remain in place for unused doses. Additionally, if a child opens a CR cap or finds a bottle that was left open, all contents are readily accessible; however, with unit-dose packaging, each unit must be opened individually.

Unit-dose packaging has begun to be implemented for buprenorphine products. A study of calls to poison centers (from October 2009–March 2012) found that rates of child exposure to buprenorphine/naloxone tablets packaged in multi-dose bottles were significantly higher than rates of child exposure to buprenorphine/naloxone film packaged in unit-dose pouches,[8] although exposure rates may have been affected by differences in formulation as well as differences in packaging. In 2013, all branded buprenorphine/naloxone products transitioned to unit-dose packaging,[35,36] but generic buprenorphine/naloxone tablets packaged in multi-dose bottles became available. In 2014, the U.S. Food and Drug Administration (FDA) approved amended applications allowing two manufacturers to transition generic buprenorphine/naloxone products to unit-dose packaging.[37] Although complicated by the staggered implementation of unit-dose packaging, continued monitoring and further investigations should assess the impact of unit-dose packaging designs on pediatric ingestions.

Study findings should be interpreted in the context of the limitations of public health surveillance data, which likely underestimate the burden of unsupervised medication ingestions. First, the ED is the most appropriate setting to identify hospitalizations for unsupervised medication ingestions; however, NEISS-CADES does not include hospitalizations for children who were directly admitted for treatment or transferred from another hospital without undergoing ED evaluation. While some hospitalizations may reflect provider precaution rather than symptom severity, hospitalization is itself a serious and costly event. Additionally, NEISS-CADES does not include adverse events resulting in death prior to or during ED evaluation. Second, hospitalizations for unsupervised ingestion of non-oral prescription medications (e.g., fentanyl patches) were not included. Third, because narrative details about adverse events are collected in an emergency setting from distressed caregivers, when timely diagnosis and treatment are the priority, detailed information about medication formulation, dosage strength, or brand name and precipitating

circumstances may not be completely documented. We did not differentiate extended-release or long-acting formulations from immediate-release or short-acting formulations (e.g., OxyContin® vs. immediate-release oxycodone). This information could guide targeted educational efforts, such as the educational components of Risk Evaluation and Mitigation Strategies (REMS) currently required for specified medications, including oral buprenorphine products.[38] Similarly, information on indication and intended recipient of ingested medications was not consistently documented but could be useful for targeting interventions to specific audiences. Fourth, for ingestions involving more than one medication (22%), we did not attempt to prioritize the contribution of individual medications to hospitalization. Fifth, the IMS Health sample is limited to outpatient retail pharmacy settings. Medications obtained from other settings (e.g., mail-order/specialty pharmacies) were not included; however, buprenorphine and the other commonly implicated medications are primarily distributed in the outpatient retail pharmacy setting. Lastly, IMS estimates do not account for medication diversion; medication safeguarding practices; psychosocial or behavioral characteristics; or presence of young children in medication recipients' households, which may differ by medication. However, these factors do not nullify the multi-fold higher hospitalization rates for buprenorphine and clonidine ingestions, and do not negate the need to address these harms to young children.

CONCLUSION

To efficiently achieve large public health impact, strategies to reduce harm from unsupervised pediatric ingestions of prescription medications, such as implementation of enhanced child safety packaging and patient/caregiver education, should target specific medications with the highest frequencies and highest rates of emergency hospitalizations.

Acknowledgements

We thank Kathleen Rose, R.N., B.S.N., Nina Weidle, Pharm.D. (contractors for the Centers for Disease Control and Prevention) and Kelly Weidenbach, Dr.P.H. (contractor for the Centers for Disease Control and Prevention at the time of data collection), and Joel Friedman, B.A., Herman Burney, M.S., and Ray Colucci, R.N. of the U.S. Consumer Product Safety Commission for assistance with data collection and processing.

Funding source: No external funding was secured for this study

Abbreviations and Acronyms

CI	confidence interval
CR	child-resistant
ED	emergency department
FDA	U.S. Food and Drug Administration
NEISS-CADES	National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance
PPPA	Poison Prevention Packaging Act

References

1. Rodgers GB. The safety effects of child-resistant packaging for oral prescription drugs: two decades of experience. JAMA. 1996; 275(21):1661–1665. [PubMed: 8637140]
2. US Consumer Product Safety Commission. Poison prevention packaging: a guide for healthcare professionals. Washington, DC: US Consumer Product Safety Commission; 2005.
3. Budnitz DS, Salis S. Preventing medication overdoses in young children: an opportunity for harm elimination. Pediatrics. 2011; 127(6):e1597–e1599. [PubMed: 21555494]
4. Bronstein AC, Spyker DA, Cantilena LR Jr, Rumack BH, Dart RC. 2011 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 29th Annual Report. Clin Toxicol (Phila). 2012; 50(10):911–1164. [PubMed: 23272763]
5. Bronstein AC, Spyker DA, Cantilena LR Jr, Green JL, Rumack BH, Dart RC. 2010 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 28th Annual Report. Clin Toxicol (Phila). 2011; 49(10):910–941. [PubMed: 22165864]
6. Bond GR, Woodward RW, Ho M. The growing impact of pediatric pharmaceutical poisoning. J Pediatr. 2012; 160(2):265–270.e1. [PubMed: 21920539]
7. Code of Federal Regulations. 16 CFR §1700.1.
8. Lavonas EJ, Banner W, Bradt P, et al. Root causes, clinical effects, and outcomes of unintentional exposures to buprenorphine by young children. J Pediatr. 2013; 163(5):1377. 1383.e1-3. [PubMed: 23993129]
9. Schoenewald S, Ross S, Bloom L, et al. New insights into root causes of pediatric accidental unsupervised ingestions of over-the-counter medications. Clin Toxicol (Phila). 2013; 51(10):930–936. [PubMed: 24283302]
10. Lembersky RB, Nichols MH, King WD. Effectiveness of child-resistant packaging on toxin procurement in young poisoning victims. Vet Hum Toxicol. 1996; 38(5):380–383. [PubMed: 8888549]
11. Jacobson BJ, Rock AR, Cohn MS, Litovitz T. Accidental ingestions of oral prescription drugs: a multicenter survey. Am J Public Health. 1989; 79(7):853–856. [PubMed: 2660604]
12. Budnitz DS, Lovegrove MC. The last mile: taking the final steps in preventing pediatric pharmaceutical poisonings. J Pediatr. 2012; 160(2):190–192. [PubMed: 22056349]
13. Schillie SF, Shehab N, Thomas KE, Budnitz DS. Medication overdoses leading to emergency department visits among children. Am J Prev Med. 2009; 37(3):181–187. [PubMed: 19666156]
14. Jhung MA, Budnitz DS, Mendelsohn AB, Weidenbach KN, Nelson TD, Pollock DA. Evaluation and overview of the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance project (NEISS-CADES). Med Care. 2007; 45 Supl 2(10):S96–S102. [PubMed: 17909391]
15. Budnitz DS, Pollock DA, Weidenbach KN, Mendelsohn AB, Schroeder TJ, Annest JL. National surveillance of emergency department visits for outpatient adverse drug events. JAMA. 2006; 296(15):1858–1866. [PubMed: 17047216]
16. IMS Health. Vector One® National (VONA). January 2007 through December 2011. Extracted August 2013.
17. IMS Health. Vector One® Total Patient Tracker (TPT). January 2007 through December 2011. Extracted September 2013.
18. National Electronic Injury Surveillance System All Injury Program: sample design and implementation. Washington, DC: Consumer Product Safety Commission; 2002.
19. Kish, L. Survey sampling. New York: Wiley Interscience; 1995.
20. Code of Federal Regulations. 16 CFR §1700.14.
21. Bar-Oz B, Levichek Z, Koren G. Medications that can be fatal for a toddler with one tablet or teaspoonful: a 2004 update. Paediatr Drugs. 2004; 6(2):123–126. [PubMed: 15035652]
22. Michael JB, Sztajnkrycer MD. Deadly pediatric poisons: nine common agents that kill at low doses. Emerg Med Clin North Am. 2004; 22(4):1019–1050. [PubMed: 15474780]
23. Poison Prevention Week Council. Available from: http://www.poisonprevention.org/index.htm.

24. National Capital Poison Center. Quills Up – Stay Away. Available from: http://www.poison.org/prevent/preschool.asp.
25. Burghardt LC, Ayers JW, Brownstein JS, Bronstein AC, Ewald MB, Bourgeois FT. Adult prescription drug use and pediatric medication exposures and poisonings. Pediatrics. 2013; 132(1): 18–27. [PubMed: 23733792]
26. Wang GS, Le Lait MC, Heard K. Unintentional pediatric exposures to central alpha-2 agonists reported to the National Poison Data System. J Pediatr. 2014; 164(1):149–152. [PubMed: 24094880]
27. Lung DD, Olson KR. Hypoglycemia in pediatric sulfonylurea poisoning: an 8-year poison center retrospective study. Pediatrics. 2011; 127(6):e1558–e1564. [PubMed: 21606145]
28. Bailey JE, Campagna E, Dart RC. RADARS System Poison Center Investigators. The underrecognized toll of prescription opioid abuse on young children. Ann Emerg Med. 2009; 53(4):419–424. [PubMed: 18774623]
29. Buprenorphine prescribing practices and exposures reported to a poison center--Utah, 2002–2011. MMWR Morb Mortal Wkly Rep. 2012; 61(49):997–1001. [PubMed: 23235296]
30. Kim HK, Smiddy M, Hoffman RS, Nelson LS. Buprenorphine may not be as safe as you think: a pediatric fatality from unintentional exposure. Pediatrics. 2012; 130(6):e1700–e1703. [PubMed: 23129079]
31. Emergency department visits and hospitalizations for buprenorphine ingestion by children--United States, 2010–2011. MMWR Morb Mortal Wkly Rep. 2013; 62(3):56. [PubMed: 23344700]
32. Lovegrove MC, Hon S, Geller RJ, et al. Efficacy of flow restrictors in limiting access of liquid medications by young children. J Pediatr. 2013; 163(4):1134–1139.e1. [PubMed: 23896185]
33. OTC industry announces voluntary transition to one concentration of single-ingredient pediatric liquid acetaminophen medicines [press release]. Washington, DC: Consumer Healthcare Products Association; 2011 May 4. Available from: http://www.chpa.org/05_04_11_PedAcet.aspx. [Accessed March 18, 2014]
34. Institute for Safe Medication Practices. Simple packaging change can reduce Rx drug diversion. Available from: http://www.consumermedsafety.org/medication-safety-articles/item/721-simple-packaging-change-can-reduce-rx-drug-diversion.
35. Reckitt Benckiser Pharmaceuticals Inc. to Voluntarily Discontinue the Supply of Suboxone® Tablets (buprenorphine and naloxone sublingual tablets [CIII]) [press release]. Reckitt Benckiser Pharmaceuticals Inc.; 2012 Sep 25. Available from: http://www.rb.com/site/rkbr/templates/mediainvestorsgeneral2.aspx?pageid=1328&&cc=gb. [Accessed May 27, 2014]
36. Orexo provides update on reimbursement and launch preparations for Zubsolv® [press release]. Uppsala, Sweden: Orexo AB; 2013 Sep 5. Available from: http://www.orexo.com/en/Investor-Relations/Press-releases/?guid=803851. [Accessed March 18, 2014]
37. Drugs@FDA. Silver Spring, MD: US Food and Drug Administration; 2014. Available from: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. [Accessed June 5, 2014]
38. US Food and Drug Administration. [Accessed March 18, 2014] Currently Approved Shared System REMS. Available from: http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm111350.htm#Shared.

What's Known on This Subject

Despite child-resistant packaging requirements for most medications and education on safe storage of all medicines, tens of thousands of young children are brought to emergency departments and thousands are hospitalized after ingesting prescription medications. Targeted prevention efforts may be needed.

What This Study Adds

Twelve medications were implicated in nearly half of hospitalizations for prescription medication ingestions. Buprenorphine and clonidine were most commonly implicated and had the highest hospitalization rates when accounting for outpatient use. Prevention efforts should focus on most commonly implicated medications.

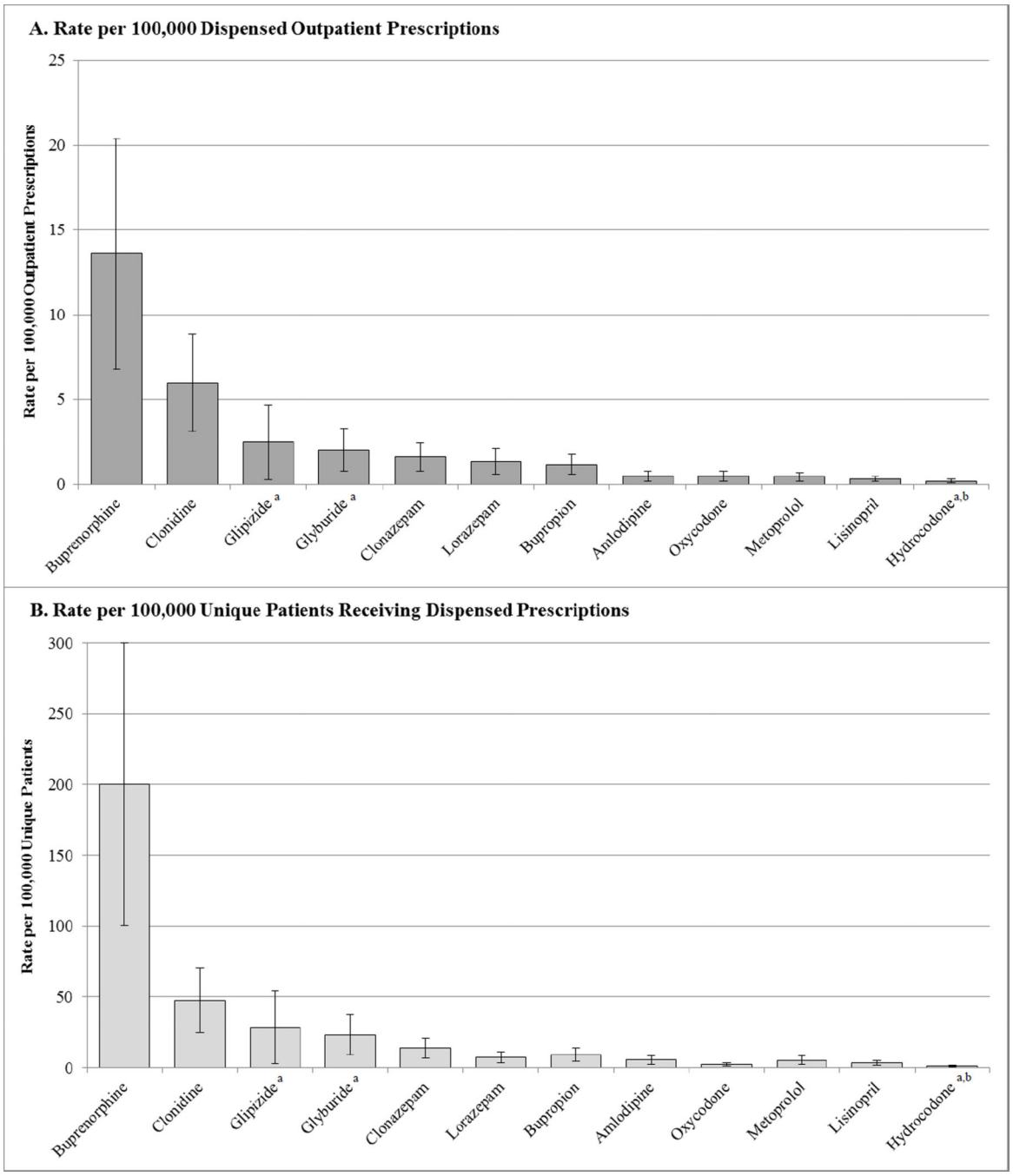

Figure 1. Estimated Rates of Emergency Hospitalizations for Unsupervised Oral Prescription Medication Ingestions by Children < 6 Years, United States, 2007–2011

Estimates of emergency hospitalizations for unsupervised oral prescription medication ingestions based on the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance project, 2007–2011. Estimates of numbers of dispensed outpatient prescriptions and numbers of unique patients receiving dispensed prescriptions based on data from IMS Health, Vector One®, extracted August and September, 2013,

respectively. [a]Coefficient of variation greater than 30%. [b]Excludes antitussive combination products.

Table 1

National Estimates of Emergency Hospitalizations for Unsupervised Oral Prescription Medication Ingestions by Children < 6 Years, United States, 2007–2011[a]

Patient and Case Characteristics	Surveillance Cases	Annual National Estimate of Hospitalizations			Proportion of ED Visits Resulting in Hospitalization
	No.	No.	%	95% CI	%
Age (years)					
<1	103	641	6.8	(4.9 – 8.6)	33.7
1	526	3,266	34.4	(30.0 – 38.9)	27.3
2	582	3,887	41.0	(35.6 – 46.3)	28.4
3	186	1,053	11.1	(8.7 – 13.5)	23.6
4	80	442	4.7	(2.9 – 6.4)	23.6
5	36	--	--	--	--
Sex					
Female	709	4,555	48.0	(44.0 – 52.0)	28.5
Male	804	4,935	52.0	(48.0 – 56.0)	26.7
No. of Implicated Medications					
1	1,136	7,412	78.1	(74.5 – 81.7)	25.8
2 or more[b]	377	2,078	21.9	(18.3 – 25.5)	36.1
Total	**1,513**	**9,490**	**100.0**		**27.5**

Abbreviations: ED, emergency department

[a] Surveillance cases and estimates based on the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance project, 2007–2011. Hospitalizations included inpatient admissions, transfers to another hospital, and observation admissions (time-limited assessment, treatment, and reassessment, typically lasting <24 to 48 hours). The proportion of emergency department visits resulting in hospitalization is the ratio of hospitalizations to total emergency department visits for unsupervised ingestions of medications for each patient or case characteristic. Estimates that do not meet the criteria for statistical reliability are not shown.

[b] Includes cases in which >1 oral prescription medication was implicated and cases in which both an oral prescription medication and an over-the-counter or a non-oral medication were implicated.

Table 2

National Estimates of Medication Classes Most Commonly Implicated in Emergency Hospitalizations for Unsupervised Oral Prescription Medication Ingestions by Children < 6 Years, United States, 2007–2011[a]

Medication Class	Annual National Estimate of Hospitalizations			Proportion of ED Visits Resulting in Hospitalization
	No.	%	95% CI	%
Opioid analgesics	1,666	17.6	(13.9 – 21.2)	36.5
Benzodiazepines	960	10.1	(8.0 – 12.3)	23.9
Sulfonylureas	774[b]	8.2	(4.4 – 11.9)	77.8
Beta blockers	760	8.0	(5.8 – 10.2)	32.1
Centrally-acting antiadrenergics[c]	759	8.0	(5.5 – 10.5)	53.5
Calcium channel blockers[d]	739	7.8	(4.4 – 11.2)	57.4
Atypical antipsychotics	629	6.6	(4.8 – 8.4)	36.7
Selective serotonin reuptake inhibitors (SSRIs)	457	4.8	(2.6 – 7.0)	22.3
Anticonvulsants	438	4.6	(3.2 – 6.1)	26.1
Angiotensin-converting enzyme (ACE) inhibitors[d]	388	4.1	(2.8 – 5.3)	28.0
Skeletal muscle relaxants	294	3.1	(1.9 – 4.2)	20.9
Amphetamine-related stimulants	292[b]	3.1	(1.5 – 4.7)	17.2

Abbreviations: ED, emergency department

[a] Estimates based on the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance project, 2007–2011.

[b] Coefficient of variation greater than 30%.

[c] Includes clonidine, guanfacine, and methyldopa.

[d] Three surveillance cases involving hospitalizations for unsupervised ingestion of calcium channel blocker/ACE inhibitor combination products are included in national estimates for both medication classes.

Table 3

National Estimates of Active Ingredients Most Commonly Implicated in Emergency Hospitalizations for Unsupervised Oral Prescription Medication Ingestions by Children < 6 Years, United States, 2007–2011[a]

Active Ingredient	Annual National Estimate of Hospitalizations			Proportion of ED Visits Resulting in Hospitalization
	No.	%	95% CI	%
Buprenorphine	734	7.7	(3.9 – 11.5)	62.4
Clonidine	701	7.4	(4.9 – 9.8)	56.2
Glipizide	386[b]	4.1[b]	(1.0 – 7.2)	74.2
Clonazepam	368	3.9	(2.3 – 5.5)	24.0
Metoprolol	314	3.3	(1.8 – 4.8)	34.5
Lorazepam	309	3.3	(1.7 – 4.8)	38.4
Lisinopril	298	3.1	(2.0 – 4.3)	28.9
Amlodipine	295	3.1	(1.3 – 4.9)	51.4
Bupropion	265	2.8	(1.5 – 4.1)	56.2
Glyburide	257[b]	2.7	(1.2 – 4.2)	75.1
Hydrocodone[c]	252[b]	2.7	(1.4 – 3.9)	30.5
Oxycodone	249	2.6	(1.5 – 3.8)	26.1

Abbreviations: ED, emergency department

[a] Estimates based on the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance project, 2007–2011.

[b] Coefficient of variation greater than 30%.

[c] Excludes 5 surveillance cases involving hospitalizations for unsupervised ingestion of antitussive combination products.