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Reducing Childhood Admissions to the PICU for Poisoning (ReCAP²) by Predicting Unnecessary PICU Admissions After Acute Intoxication

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Abstract

Objective: To derive and validate clinical prediction models to identify children at low risk of clinically significant intoxications for whom intensive care admission is unnecessary.

Design: Retrospective review of data in the National Poison Data Systems from 2011 to 2014 and Georgia Poison Center cases from July to December 2016.

Setting: United States PICUs and poison centers participating in the American Association of Poison Control Centers from 2011 to 2016.

Patients: Children 18 years and younger admitted to a United States PICU following an acute intoxication.

Interventions: None.

Measurements and Main Results: The primary study outcome was the occurrence of clinically significant intoxications defined a priori as organ system-based clinical effects that require intensive care monitoring and interventions. We analyzed 70,364 cases. Derivation ($n = 42,240$; 60%) and validation cohorts ($n = 28,124$; 40%) were randomly selected from the eligible population and had similar distributions of clinical effects and PICU interventions. PICU interventions were performed in 1,835 children (14.1%) younger than 6 years, in 374 children (15.4%) 6–12 years, and in 4,446 children (16.5%) 13 years and older. We developed highly predictive models with an area under the receiver operating characteristic curve of 0.834 (< 6 yr),

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Drs. Patel, Stockwell, Kamat, and Grunwell conceived and developed the study and wrote the article. Mr. Travers conducted statistical analyses, aided with data interpretation, and edited the article. Drs. Numur and Geller acquired data, validated the model using Georgia Poison Center data, and edited the article. All authors read and approved the article.

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0.771 (6–12 yr), and 0.786 (< 13 yr), respectively. For predicted probabilities of less than or equal to 0.10 in the validation cohorts, the negative predictive values were 95.40% (< 6 yr), 94.9% (6–12 yr), and 95.1% (< 13 yr). An additional 700 patients from the Georgia Poison Center were used to validate the model and would have reduced PICU admission by 31.4% ($n = 110$).

Conclusions: These validated models identified children at very low risk of clinically significant intoxications for whom pediatric intensive care admission can be avoided. Application of this model using Georgia Poison Center data could have resulted in a 30% reduction in PICU admissions following intoxication.

Keywords

ingestion; intoxication; pediatric intensive care unit; poisoning; toxicology

Acute intoxications account for ~5% of annual PICU admissions, but 71% of these children do not undergo any intervention while in the PICU (1). There are currently no objective criteria to identify which children with intoxications need PICU admission. The goal of this study was to derive and validate generalizable prediction rules to identify children who are at minimal risk for clinically significant intoxication.

MATERIALS AND METHODS

Study Design and Data Collection

We performed a retrospective review of prospectively collected data from the American Association of Poison Control Centers (AAPCC) National Poison Data System (NPDS) database with approval from the Children's Healthcare of Atlanta and Emory University Institutional Review Boards, as well as the Data Access Committee and Board of Directors of the AAPCC (2). All AAPCC member poison centers use electronic health record collection systems with mandatory common data elements and reporting requirements. During normal AAPCC member poison center operations, data is entered by staff in real-time as cases are being managed (3). Follow-up phone calls are made to the health systems caring for the patient to confirm disposition of the patient. We reviewed records of cases in the NPDS from January 2011 to December 2014. We then validated the model using an additional 700 Georgia Poison Center (GPC) patients for which we had access to the call transcripts from July to December 2016 using only facts known from the preadmission evaluation. Subsequent patient information after admission through discharge was used to ensure that children who required PICU care were not inappropriately triaged for general inpatient admission or discharge.

Inclusion and Exclusion Criteria

Children 18 years and younger admitted to a United States PICU for acute intoxications were included. We excluded subjects who were bitten, had food poisoning, were exposed to plants, were pregnant, had an effect unrelated to the acute intoxication, had no outcome or age recorded, or had no known exposure (Fig. 1). An unrelated effect is defined as one in which the exposure was probably not responsible for the effect (4).

Outcome Measures

The definition of “clinical effect” is any sign, symptom, or clinical finding that is recorded in the NPDS database (4). Clinical effects are stratified into clinically significant intoxications and nonclinically significant intoxications in Supplementary Table 1 (Supplemental Digital Content 1, <http://links.lww.com/PCC/A579>). We defined clinically significant intoxications a priori as clinical effects that required monitoring and interventions that could only be performed in a PICU as defined in Supplementary Tables 1 and 2 (Supplemental Digital Content 1, <http://links.lww.com/PCC/A579>).

Statistical Methods

Data were stratified into three age groups for analysis (< 6 yr, 6–12 yr, and ≥ 13 yr). Within each age group, derivation and validation cohorts were created using random, independent allocation for those who underwent a PICU procedure and those who did not undergo a PICU procedure at a 60:40 ratio. Descriptive statistics were calculated using counts and frequencies, medians, and interquartile ranges for nonnormally distributed variables, or means and SDs for patient demographics and intoxication-related drug categories (defined in Supplementary Table 3, Supplemental Digital Content 1, <http://links.lww.com/PCC/A579>), clinical effects and interventions. Associations of demographics, intoxication classification, and clinical effects with PICU procedures were tested using chi-square tests. Variables with significant associations were considered candidates for multivariable logistic regression. A step-wise backward selection was used to select a final model containing less than or equal to eight variables, maximizing the area under the receiver operating curve (AUROC).

Variable removal was stopped when reductions in AUROC were greater than 0.1. Significantly associated variables are presented as odds ratios with 95% CIs. Models were then dichotomized by selecting a threshold of predicted probabilities. Thresholds were selected to obtain a negative predictive value of greater than or equal to 95% while maximizing sensitivity to ensure that children with clinically significant intoxications were not misclassified as not requiring PICU admission. Model coefficients resulting from the derivation cohort were then used to calculate predicted probabilities in the validation cohort and model diagnostic statistics were assessed. Unless otherwise noted, statistical significance was assessed using a significance level of p value less than 0.05. Two-sided statistical tests are reported. All statistical analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC).

We suspected a coding error might explain some of the false negatives in our model. To explore this possibility, we reviewed the variables in the NPDS and our model. In the NPDS database, each case is assigned an organ system-based pediatric severity score (PSS): none (0), minor (1), moderate (2), severe (3), and fatal (4) (5). The PSS considers the entire clinical course using the most severe symptoms; therefore, it is usually done retrospectively. If the PSS is assigned before symptoms develop or interventions are required, this could lead to a coding error within the database. To see how our models would perform if these patients with PSS less than or equal to 1 were listed as not having a PICU procedure performed, we completed a sensitivity analysis where we assumed that the PSS is the gold standard, but procedure(s) listed was incorrect.

Simplified Model Validation

We simplified the model to recommend PICU admission for any child who ingested an oral hypoglycemic agent, clonidine, or ethanol, or was exposed to carbon monoxide, and to those who had any clinically significant symptoms or abnormalities on examination greater than 2 hours after exposure. The 2-hour postexposure time was chosen because most oral medications are bioavailable 1–2 hours following ingestion and gastric decontamination with activated charcoal is not recommended if the ingestion occurred more than 1 hour prior to arrival at a medical facility (6). We applied this simplified model to the 700 GPC patients.

RESULTS

Of the 76,136 cases in the AAPCC NPDS from 2011 to 2014, we analyzed 70,364 cases (92.4%). The number of subjects in each age-stratified derivation and validation cohort is presented in Figure 1. Clinical effects, interventions, therapies, and PICU procedures for the derivation and validation cohorts were well-matched (Table 1). PICU procedures were reported in 1,835 of 12,997 children (14.1%) younger than 6 years, 374 of 2,429 children (15.4%) 6–12 years, and 4,446 of 26,814 children (16.5%) 13 years and older. The frequencies of most predictor variables differed significantly between children with and without clinically significant intoxications (Table 2).

Age-Stratified Multivariable Models

For all age-stratified models, specific organ system-based clinical effects were associated with increased odds of having an intervention, therapy, or PICU procedure performed. For children younger than 6 years old, fluids, electrolytes, nutrition, and gastrointestinal effects were associated with the highest odds of a PICU intervention or procedure. For children 6 years and older, respiratory effects were associated with the highest odds of having a PICU intervention or procedure performed. For children younger than 6 years, renal effects and ingestion of clonidine or diabetic medications were also associated with higher odds of clinically significant intoxication (Table 3). In the multivariable model for children 6–12 years old, ingestion of clonidine or alcohol and carbon monoxide exposure were associated with increased odds of requiring a PICU intervention (Table 4). In children 13 years and older, being male, renal effects, and ingestion of diabetic medication or alcohol were associated with higher odds of needing a PICU intervention (Table 5). The AUROC for the derivation and validation cohorts are reported in Tables 3–5. The age-stratified predictive formulas for requiring a PICU intervention are presented in Supplementary File 4 (Supplemental Digital Content 1, <http://links.lww.com/PCC/A579>). For children younger than 6 years, a predicted probability threshold of 0.091 was used, and for children 6 years and older, a predicted probability of 0.10 was used. Performance characteristics for the age-stratified multivariable models for the derivation and validation cohorts using the above predicted probabilities are reported in Table 6.

Misclassification of Children in the Age-Stratified Validation Groups

A small group of patients in the validation cohort were misclassified as false negatives—187 of 8,649 (2.2%) in the younger than 6-year-old group, 34 of 1,656 (2.1%) in the 6–12-year-old group, and 388 of 17,813 (2.2%) in the 13 years and older group. False negatives are

defined as patients who are scored as not needing a PICU intervention by our model, but were documented as requiring intubation (50–57%), ventilation (50%), and sedation (39–49%), even though these patients were not coded in the NPDS database as having respiratory failure, coma, extreme agitation, or any metabolic derangements (Supplementary Tables 5 and 6, Supplemental Digital Content 1, <http://links.lww.com/PCC/A579>).

In our cohort, 31% of the false negatives were assigned a PSS of none (0) or mild (1) by the NPDS that was inconsistent with the coded interventions that included intubation, ventilation, and sedation. A sensitivity analysis, where we assumed that the PSS was the gold standard, but the procedure(s) listed was incorrect resulted in the change of a false negative to a true negative in 64 cases in the younger than 6-year-old group, 10 cases in the 6–12-year-old group, and 113 cases in the 13 years and older group. Our model diagnostic statistics were minimally changed (compare Table 6 with Supplementary Table 7, Supplemental Digital Content 1, <http://links.lww.com/PCC/A579>).

Exposure-Related Mortality

In our entire cohort, there were 274 deaths (31% < 6 yr old, 11% 6–12 yr old, and 59% 13 yr old) with a male predominance (54%) (Supplementary Table 8, Supplemental Digital Content 1, <http://links.lww.com/PCC/A579>). The drug classes most highly associated with mortality included narcotics (22%), household/industrial products (20%), miscellaneous medications (15%), recreational drugs (14%), unknown drugs (12%), and antidepressants (11%).

Our model missed two patients who died. The first missed patient was an 18-year-old that ingested narcotics and benzodiazepine in a suspected suicide attempt, but no clinically significant effects or PICU procedures were reported. The second patient was an 11-year-old who required ventilation after an unknown drug intoxication associated with coagulopathy, renal failure, and acidosis. Given the clinical severity of these two cases, clinical judgment would determine the need for PICU admission.

Retrospective Validation of the Models With GPC Data

Of the 700 patients reviewed from the GPC, 414 were admitted to PICU (59.1%). The remaining 286 patients were admitted to a general pediatric ward. Only 64 of the 414 patients (15.5%) admitted to the PICU received one or more ICU-level interventions. Using only clinical findings documented in the emergency department, the model successfully predicted all 64 of the patients who required PICU intervention. Of the 350 remaining patients admitted to a PICU, our model correctly predicted 110 patients as not needing PICU intervention. Application of our model to these 350 patients could have reduced PICU admissions by 31.4%. Application of our simplified model to this cohort would have resulted in a 29.7% (104 of 350 children) reduction in PICU admissions without missing any child needing a PICU intervention.

DISCUSSION

We derived and validated age-stratified prediction rules for acute intoxications in a large, diverse population of children admitted to U.S. PICUs using data readily collected by the

NPDS with a high negative predictive value for clinically significant intoxications. We further tested our model using pediatric acute intoxication calls to the GPC and found that our model would have reduced PICU admission by 30% without missing any child needing a PICU intervention.

Data to guide clinical decision making for children following acute intoxications is urgently needed because pediatric poisonings are a leading cause of unintentional injury in young children (< 6 yr old) and death in adolescents (> 13 yr old) (7). Also, application of adult Glasgow Coma Scale-based prediction models for deterioration after acute intoxications is problematic in a nonverbal child (8). Although half of all children treated in a healthcare facility for intoxication are hospitalized in an ICU (9), the overwhelming majority of these children do not have clinical effects necessitating ICU-level monitoring or interventions. While the length of stay for the majority of children admitted for intoxication is only 1–2 days (1), admission to a PICU can be emotionally and physically traumatizing for the child and expensive for the family. While the safety and monitoring of children following intoxication is paramount, there are increasing demands for PICU services and limited bed availability (10); therefore, the use of PICU beds for noncritically ill children stresses PICU resources and may delay care for other critically ill children.

Previous single-center studies (11–16) have identified predictors similar to the findings in our model to determine whether children may be safely monitored in a short-stay observation unit outside of the PICU (17, 18). Clonidine and antidiabetic medications were significant in our multivariable models for children under 6 years old. Due to the lower body mass of young children, single adult doses of medications used to treat hypertension, diabetes, depression, and anxiety are likely to be toxic when ingested by a child (19).

Additionally, our model shows that there is an increased risk of PICU interventions following alcohol intoxication for children 6 years and older. This is not surprising, given that alcohol is the most widely abused drug in teenagers and is linked to increased accidental injuries and deaths (20). In contrast, despite the rising number of adults with opiate/opioid dependence and the prevalence of drugs used to treat narcotic addiction (15, 21), we were surprised that these medications were not associated with clinically significant intoxications in our final model. Perhaps, this finding is due to the use of naloxone as an antidote or that increased education and awareness of opioid intoxication has led to quicker recognition and treatment without the need for critical care interventions. Another possibility is that emerging abuse of synthetic opiate analogs may lead to fatal intoxication in children prior to reaching medical attention (22–24). Although not an ingestion, moderate-to-severe unintentional carbon monoxide poisoning—defined as requiring treatment due to prolonged or life-threatening symptoms—occurs in ~16% of children 18 years and younger (25).

While the NPDS database used information gathered through hospital discharge; in clinical practice, the patient disposition is determined solely on initial emergency department evaluation. We addressed this shortcoming by testing and further validating our models with GPC cases using information only from the initial presentation, and we found that our model did not miss any child needing a PICU intervention. After necessary clinical variables have been entered into the patient's electronic medical record, the formulas that comprise the age-

stratified models can be computed in the background at the poison control center during emergency department care. These clinical variables are part of the standard set of information requested on every poison center encounter in the United States and therefore are not burdensome or complicated to collect. We are currently testing implementation of this automated model scoring in real time at the GPC with the goal of recommending appropriate disposition of the child following acute intoxication. In the future, the model and/or formulas could also be incorporated into healthcare facility electronic medical record systems.

Our study has several limitations. The intensity and frequency of interventions cannot be quantified in the NPDS dataset limiting the ability to predict the need for PICU admission using retrospective analysis of information. We cannot control for the severity of illness in patients in this study as no pediatric severity of illness or mortality scores are calculated. Additionally, cases would be missed in our analysis if suspicion for intoxication, even if of an unknown substance, was not present. Also, the accuracy and completeness of the case record forms is inherent in any large data entry system. We noted a very small proportion of cases were coded as false negatives and a sensitivity analysis did not change our model statistics. Furthermore, introduction of systemic bias is not likely as inaccurate data entry and/or missing data likely occurred at random. Lastly, institution-specific differences in policies for PICU, step-down, observational unit, or general pediatric ward admission criteria lead to clinical practice differences across the country. Therefore, our prediction models can help guide decision making, but cannot substitute for clinical judgment, knowledge, and experience of the local institutional capabilities for managing children with intoxications. Despite these limitations, clinical implementation of these models in real-time upon initial GPC contact and automated predictive modeling is underway to predict which children are unlikely to have a clinically significant intoxication.

CONCLUSIONS

Using NPDS data, we developed highly predictive models to identify children with a low likelihood of clinically significant intoxications. Furthermore, we validated our models using GPC data and could have reduced PICU admission by almost one-third. A simplified model using only drug ingested and the presence of any clinically significant symptoms greater than 2 hours after exposure resulted in nearly identical results as the full age-stratified models. Implementation of our model across other U.S. poison centers will guide future prospective, multicenter studies to definitively develop criteria for which children need the PICU after acute intoxications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

- Patel MM, Travers CD, Stockwell JA, et al.: Analysis of interventions required in 12,021 children with acute intoxications admitted to PICUs. *Pediatr Crit Care Med* 2017; 18:e281–e289 [PubMed: 28481828]
- National Poison Data System: Process for Requesting Data. 2017 Available at: <http://www.aapcc.org/data-system/data-request-process/>. Accessed September 26, 2017
- System NPD. NPDS Elements. 2017 Available at: <http://www.aapcc.org/data-system/npds-elements/>. Accessed September 26, 2017
- Mowry JB, Spyker DA, Brooks DE, et al.: 2015 Annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 33rd Annual Report. *Clin Toxicol (Phila)* 2016; 54:924–1109 [PubMed: 28004588]
- Persson HE, Sjöberg GK, Haines JA, et al.: Poisoning severity score. Grading of acute poisoning. *J Toxicol Clin Toxicol* 1998; 36:205–213 [PubMed: 9656975]
- Bond GR: The role of activated charcoal and gastric emptying in gastrointestinal decontamination: A state-of-the-art review. *Ann Emerg Med* 2002; 39:273–286 [PubMed: 11867980]
- Centers for Disease Control and Prevention: CDC Childhood Injury Report: Pattern of Unintentional Injuries Among 0–19 Year Olds in the United States, 2000–2006. Atlanta, GA, Centers for Disease Control and Prevention, 2009
- Maignan M, Pommier P, Clot S, et al.: Deliberate drug poisoning with slight symptoms on admission: Are there predictive factors for intensive care unit referral? A three-year retrospective study. *Basic Clin Pharmacol Toxicol* 2014; 114:281–287 [PubMed: 23998644]
- Geller RJ: National Poison Data System. Atlanta, GA, System.ex1 NPD, 2016
- Fieldston ES, Li J, Terwiesch C, et al.: Direct observation of bed utilization in the pediatric intensive care unit. *J Hosp Med* 2012; 7:318–324
- Even KM, Armsby CC, Bateman ST: Poisonings requiring admission to the pediatric intensive care unit: A 5-year review. *Clin Toxicol (Phila)* 2014; 52:519–524 [PubMed: 24738737]
- Fazen LE, 3rd, Lovejoy FH, Jr, Crone RK: Acute poisoning in a children's hospital: A 2-year experience. *Pediatrics* 1986; 77:144–151 [PubMed: 3945527]
- Hon KL, Leung TF, Hung CW, et al.: Ingestion-associated adverse events necessitating pediatric ICU admissions. *Indian J Pediatr* 2009; 76:283–286 [PubMed: 19347668]
- Lacroix J, Gaudreault P, Gauthier M: Admission to a pediatric intensive care unit for poisoning: A review of 105 cases. *Crit Care Med* 1989; 17:748–750 [PubMed: 2486553]
- Martin TC, Rocque MA: Accidental and non-accidental ingestion of methadone and buprenorphine in childhood: A single center experience, 1999–2009. *Curr Drug Saf* 2011 ; 6:12–16 [PubMed: 21047302]
- Ozdemir R, Bayrakci B, Tekçam O, et al.: Thirty-three-year experience on childhood poisoning. *Turk J Pediatr* 2012; 54:251–259 [PubMed: 23094535]
- Plumb J, Dudley NC, Herman BE, et al.: Utilization of a pediatric observation unit for toxicologic ingestions. *Pediatr Emerg Care* 2012; 28:1169–1172 [PubMed: 23114240]
- Judge BS, Ouellette LM, VandenBerg M, et al.; Toxicology Investigators Consortium (ToxIC) Case Registry: Utilization of observation units for the care of poisoned patients: Trends from the Toxicology Investigators Consortium Case Registry. *J Med Toxicol* 2016; 12:111–120 [PubMed: 26275996]
- Matteucci MJ: One pill can kill: Assessing the potential for fatal poisonings in children. *Pediatr Ann* 2005; 34:964–968 [PubMed: 16419734]

20. National Institute on Alcohol Abuse and Alcoholism: Underage Drinking. 2016 Available at: <https://pubs.niaaa.nih.gov/publications/UnderageDrinking/UnderageFact.htm>. Accessed March 11, 2017
21. Burghardt LC, Ayers JW, Brownstein JS, et al.: Adult prescription drug use and pediatric medication exposures and poisonings. *Pediatrics* 2013; 132:18–27 [PubMed: 23733792]
22. Prekupec MP, Mansky PA, Baumann MH: Misuse of novel synthetic opioids: A deadly new trend. *J Addict Med* 2017; 11:256–265 [PubMed: 28590391]
23. Gladden RM, Martinez P, Seth P: Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths-27 states, 2013–2014. *MMWR Morb Mortal Wkly Rep* 2016; 65:837–843 [PubMed: 27560775]
24. Rudd RA, Aleshire N, Zibbell JE, et al.: Increases in drug and opioid overdose deaths-United States, 2000–2014. *MMWR Morb Mortal Wkly Rep* 2016; 64:1378–1382 [PubMed: 26720857]
25. Bronstein A, Clower JH, Iqbal S, et al.: Carbon Monoxide Exposures-United States, 2000–2009. *Morbidity and Mortality Weekly Report (MMWR)*. 2011 Available at: <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6030a2.htm>. Accessed March 11, 2017

Figure 1.

Flow diagram of children included and excluded in the final derivation and validation cohort analysis. NPDS = National Poison Data System.

TABLE 1.

Characteristics of Derivation and Validation Cohorts by Age

Cohort Characteristics	< 6 Yr Old (n = 21,646)		6–12 Yr Old (n = 4,085)		13 Yr Old (n = 44,633)	
	Derivation (n = 12,997) (%)	Validation (n = 8,649) (%)	Derivation (n = 2,429) (%)	Validation (n = 1,656) (%)	Derivation (n = 26,814) (%)	Validation (n = 17,819) (%)
Clinical effects						
Cardiac	2,229 (17.2)	1,522 (17.6)	761 (31.3)	556 (33.6)	8,322 (31.0)	5,547 (31.1)
Respiratory	1,502 (11.6)	1,054 (12.2)	184 (7.6)	138 (8.3)	1,480 (5.5)	1,023 (5.7)
Neurologic	1,368 (10.5)	938 (10.9)	675 (27.8)	457 (27.6)	7,746 (28.9)	5,180 (29.1)
FEN/GI	1,000 (7.7)	625 (7.2)	155 (6.4)	105 (6.3)	2,448 (9.1)	1,610 (9.0)
Renal	447 (3.4)	316 (3.7)	144 (5.9)	108 (6.5)	1,970 (7.4)	1,236 (6.9)
Hepatic	77 (0.6)	36 (0.4)	33 (1.4)	15 (0.9)	538 (2.0)	350 (2.0)
Miscellaneous	443 (3.4)	302 (3.5)	116 (4.8)	72 (4.4)	962 (3.6)	656 (3.7)
Intervention/therapies						
Cardiac	371 (2.9)	276 (3.2)	116 (4.8)	86 (5.2)	1,025 (3.8)	669 (3.8)
Respiratory	2,023 (15.6)	1,361 (15.7)	379 (15.6)	286 (17.3)	4,405 (16.4)	2,923 (16.4)
Neuro	2,910 (22.4)	2,035 (23.5)	659 (27.1)	436 (26.3)	7,425 (27.7)	4,985 (28.0)
FEN/GI	7,541 (58.0)	5,045 (58.3)	1,586 (65.3)	1,079 (65.2)	20,012 (75.4)	13,324 (74.8)
Renal	207 (1.6)	129 (1.5)	105 (4.3)	60 (3.6)	2,570 (9.6)	1,583 (8.9)
Hepatic	195 (1.5)	126 (1.5)	149 (6.1)	94 (5.7)	4,063 (15.2)	2,741 (15.4)
Miscellaneous	2,078 (16.0)	1,398 (16.2)	276 (11.4)	207 (12.5)	1,568 (5.9)	1,021 (5.7)
PICU procedure	1,835 (14.1)	1,228 (14.2)	374 (15.4)	275 (16.6)	4,446 (16.6)	2,993 (16.8)

FEN/GI = fluid, electrolytes, nutrition and gastrointestinal.

TABLE 2.

Bivariable Analysis for Intoxications

Children < 6 Yr Old (Derivation)	Clinically Significant (n = 1,835) (%)	Nonclinically Significant (n = 11,162) (%)	p
Gender: male	1,002 (54.7)	5,958 (53.5)	0.339
Intentional	8 (0.4)	36 (0.3)	0.438
Clinical effects			
Cardiac	614 (33.5)	1,615 (14.5)	<0.001
Respiratory	659 (35.9)	843 (7.6)	<0.001
Neurologic	488 (26.6)	880 (7.9)	<0.001
FEN/GI	537 (29.3)	463 (4.2)	<0.001
Renal	204 (11.1)	243 (2.2)	<0.001
Hepatic	45 (2.5)	32 (0.3)	<0.001
Miscellaneous	111 (6.1)	332 (3.0)	<0.001
Poly-intoxication	363 (19.8)	2,300 (20.6)	0.418
Drug class			
Tylenol	30 (1.6)	354 (3.2)	<0.001
Nonsteroidal anti-inflammatory drugs	52 (2.8)	430 (3.9)	0.032
Narcotics	119 (6.5)	1,251 (11.2)	<0.001
Anesthetics, analgesics	45 (2.5)	170 (1.5)	0.004
Antihistamines	69 (3.8)	562 (5.0)	0.019
Cough/cold medications	9 (0.5)	121 (1.1)	0.018
Antidepressants, anxiolytics and antipsychotics	162 (8.8)	1,719 (15.4)	<0.001
Clonidine	342 (18.6)	1,206 (10.8)	<0.001
Antihypertensives ^a	150 (8.2)	2,004 (18.0)	<0.001
Diuretics	15 (0.8)	196 (1.8)	0.003
Bronchodilators	1 (0.1)	43 (0.4)	0.024
Benzodiazepines	57 (3.1)	686 (6.2)	<0.001
Stimulants	57 (3.1)	598 (5.4)	<0.001
Diabetic medications	298 (16.2)	578 (5.2)	<0.001
Alcohol	41 (2.2)	146 (1.3)	0.002

Nutrients, vitamins, minerals	44 (2.4)	433 (3.9)	0.002
Recreational drugs	52 (2.8)	215 (1.9)	0.011
Gastrointestinal medications	38 (2.1)	410 (3.7)	0.001
Hematology and oncology medications	11 (0.6)	130 (1.2)	0.030
Antihyperlipidemics	24 (1.3)	136 (2.1)	0.022
Alkalis	43 (2.3)	131 (1.2)	< 0.001
Laundry and dish detergents	97 (5.3)	333 (3.0)	< 0.001
^b Misc 1: pesticides, herbicides, fertilizer	26 (1.4)	81 (0.7)	0.002
^b Misc 2: disc batteries	17 (0.9)	37 (0.3)	< 0.001
^b Misc 5: nonpharmaceuticals	224 (12.2)	937 (8.4)	< 0.001
Miscellaneous unknown drug	102 (5.6)	461 (4.1)	0.005
Carbon monoxide	32 (1.7)	33 (0.3)	< 0.001
Children 6–12 Yr Old (Derivation)	Clinically Significant (n = 374)	Nonclinically Significant (n = 2,055)	p
Gender: male	192 (51.3)	981 (47.8)	0.203
Intentional	155 (41.4)	895 (43.6)	0.449
Clinical effects			
Cardiac	170 (45.5)	591 (28.8)	< 0.001
Respiratory	108 (28.9)	76 (3.7)	< 0.001
Neurologic	173 (46.3)	502 (24.4)	< 0.001
FEN/GI	53 (14.2)	102 (5.0)	< 0.001
Renal	57 (15.2)	87 (4.2)	< 0.001
Hepatic	12 (3.2)	21 (1.0)	0.001
Miscellaneous	34 (9.1)	82 (4.0)	< 0.001
Poly-intoxication	112 (30.0)	548 (26.7)	0.190
Drug class			
Tylenol	18 (4.8)	193 (9.4)	0.004
Diabetic medications	13 (3.5)	31 (1.5)	0.009
Alcohol	15 (4.0)	39 (1.9)	0.011
^b Misc 3: other medications/pharmaceuticals	35 (9.4)	127 (6.2)	0.024
^b Misc 5: nonpharmaceuticals	51 (13.6)	113 (5.5)	< 0.001

Carbon monoxide	22 (5.9)	18 (0.9)	< 0.001
Children 13 Yr (Derivation)	Clinically Significant (n = 4,446)	Nonclinically Significant (n = 22,368)	p
Gender: male	1,989 (44.7)	6,982 (31.2)	< 0.001
Intentional	4,034 (90.7)	21,124 (94.4)	< 0.001
Clinical effects			
Cardiac	2,229 (50.1)	6,093 (27.2)	< 0.001
Respiratory	931 (20.9)	549 (2.5)	< 0.001
Neurologic	2,378 (53.5)	5,368 (24.0)	< 0.001
FEN/GI	827 (18.6)	1,621 (7.3)	< 0.001
Renal	838 (18.9)	1,132 (5.1)	< 0.001
Hepatic	193 (4.3)	345 (1.5)	< 0.001
Miscellaneous	247 (5.6)	715 (3.2)	< 0.001
Poly-intoxication	2,309 (51.9)	9,284 (41.5)	< 0.001
Drug class			
Tylenol	453 (10.2)	4,804 (21.5)	< 0.001
Nonsteroidal anti-inflammatory drugs	500 (11.3)	4,002 (17.9)	< 0.001
Narcotics	460 (10.4)	1,675 (7.5)	< 0.001
Anesthetics, analgesics	173 (3.9)	634 (2.8)	< 0.001
Antihistamines	669 (15.1)	3,013 (13.5)	0.005
Clonidine	148 (3.3)	583 (2.6)	0.007
Antihypertensives ^a	306 (6.9)	962 (4.3)	< 0.001
Diuretics	34 (0.8)	115 (0.5)	0.040
Benzodiazepines	478 (10.8)	1,677 (7.5)	< 0.001
Barbiturates	17 (0.4)	33 (0.2)	0.001
Muscle relaxants	306 (6.9)	675 (3.0)	< 0.001
Antiepileptic drugs	416 (9.4)	1,560 (7.0)	< 0.001
Diabetic medications	185 (4.2)	175 (0.8)	< 0.001
Anti-infectives	125 (2.8)	502 (2.2)	0.022
Alcohols	468 (10.5)	1,050 (4.7)	< 0.001
Nutrients, vitamins, minerals	74 (1.7)	583 (2.6)	< 0.001
Recreational drugs	513 (11.5)	1,245 (5.6)	< 0.001

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Cardiovascular medications	23 (0.5)	41 (0.2)	< 0.001
Hematology and oncology medications	26 (0.6)	41 (0.2)	< 0.001
Antihyperlipidemics	45 (1.0)	106 (0.5)	< 0.001
Misc ^b 1: pesticides, herbicides, fertilizer	15 (0.3)	28 (0.1)	0.001
Misc ^b 4: other medications/pharmaceuticals	393 (8.8)	1,101 (4.9)	< 0.001
Misc ^b 5: nonpharmaceuticals	156 (2.5)	449 (2.0)	< 0.001
Carbon monoxide	25 (0.6)	20 (0.1)	< 0.001

FEN/GI — fluid, electrolytes, nutrition and gastrointestinal.

^a Antihypertensives include beta blockers and calcium channel blockers.

^b Miscellaneous.

TABLE 3.

Multivariable Model for < 6 Year Olds

Model Variable	Derivation (<i>n</i> = 13,313)			Validation (<i>n</i> = 8,881)		
	OR (95% CI)	<i>p</i>	AUC	OR (95% CI)	<i>p</i>	AUC
Cardiac effects	2.48 (2.14–2.87)	< 0.001		2.71 (2.27–3.22)	< 0.001	
Respiratory effects	7.57 (6.59–8.68)	< 0.001		7.10 (6.00–8.40)	< 0.001	
Neurological effects	3.94 (3.39–4.59)	< 0.001		4.22 (3.51–5.08)	< 0.001	
Fluid, electrolytes, nutrition and gastrointestinal effects	9.91 (8.37–11.73)	< 0.001	0.836 (0.825–0.846)	11.00 (8.88–13.63)	< 0.001	0.834 (0.821–0.847)
Renal effects	2.53 (1.98–3.24)	< 0.001		1.92 (1.42–2.61)	< 0.001	
Clonidine	1.82 (1.53–2.16)	< 0.001		1.93 (1.57–2.37)	< 0.001	
Diabetic medication	3.58 (2.95–4.35)	< 0.001		3.39 (2.64–4.35)	< 0.001	

AUC = area under the curve, OR = odds ratio.

TABLE 4.

Multivariable Model for 6 – 12 Year Olds

Model Variable	Derivation (<i>n</i> = 2,763)			Validation (<i>n</i> = 1,831)		
	OR (95% CI)	<i>p</i>	AUC	OR (95% CI)	<i>p</i>	AUC
Cardiac effects	2.15 (1.67–2.78)	< 0.001		2.42 (1.79–3.27)	0.002	
Respiratory effects	10.77 (7.64–15.21)	< 0.001		8.54 (5.70–12.81)	< 0.001	
Neurological effects	2.52 (1.96–3.25)	< 0.001		2.58 (1.91–3.48)	< 0.001	
Fluid, electrolytes, nutrition and gastrointestinal effects	2.74 (1.83–4.10)	< 0.001	0.779 (0.753–0.805)	3.41 (2.12–5.48)	0.012	0.771 (0.739–0.803)
Clonidine	3.91 (1.91–7.99)	0.014		5.55 (2.57–12.01)	0.480	
Alcohol	3.19 (1.63–6.24)	< 0.001		2.67 (1.00–7.17)	0.004	
Carbon monoxide	9.48 (4.69–19.19)	< 0.001		19.22 (8.10–45.63)	0.116	

AUC = area under the curve, OR = odds ratio.

TABLE 5.

Multivariable Model for 13 Year Olds

Model Variable	Derivation (n = 27,139)			Validation (n = 18,048)		
	OR (95% CI)	p	AUC	OR (95% CI)	p	AUC
Male gender	1.42 (1.32–1.53)	< 0.001		1.49 (1.36–1.62)	< 0.001	
Cardiac effects	2.23 (2.07–2.40)	< 0.001		2.21 (2.02–2.42)	< 0.001	
Respiratory effects	8.16 (7.22–9.22)	< 0.001		7.86 (6.78–9.10)	< 0.001	
Neurological effects	2.80 (2.60–3.01)	< 0.001		2.85 (2.61–3.11)	< 0.001	
Fluid, electrolytes, nutrition and gastrointestinal effects	1.94 (1.74–2.16)	< 0.001	0.784 (0.776–0.791)	2.13 (1.87–2.42)	< 0.001	0.786 (0.777–0.795)
Renal effects	2.47 (2.21–2.76)	< 0.001		2.47 (2.15–2.84)	< 0.001	
Diabetic medication	7.31 (5.80–9.21)	< 0.001		5.96 (4.53–7.86)	< 0.001	
Alcohol	2.07 (1.82–2.36)	< 0.001		2.18 (1.86–2.55)	< 0.001	

AUC = area under the curve, OR = odds ratio.

TABLE 6.

Diagnostic Characteristics of Models

Age	Dataset	Sensitivity	Specificity	Positive Predictive Value	Positive Likelihood Ratio	Negative Predictive Value	Negative Likelihood Ratio	Accuracy
<6yr ^{a,b}	Derivation	85.6	65.9	29.2	2.51	96.5	0.22	68.7
	Validation	84.8	65.8	29.1	2.48	96.3	0.23	68.5
6–12 yr ^{c,d}	Derivation	88.8	47.5	23.5	1.69	95.9	0.24	53.8
	Validation	87.6	46.1	24.5	1.47	94.9	0.27	53.0
13–19 yr ^{d,e}	Derivation	86.9	50.9	26.0	1.77	95.1	0.26	56.9
	Validation	87.0	50.9	26.4	1.77	95.1	0.25	57.0

^aModel includes cardiac, respiratory, neurological, fluid, electrolytes, nutrition and gastrointestinal (FEN/GI) and renal effects, as well as ingestion of clonidine or diabetic medications.

^bPredicted probability cutoff of 0.091.

^cModel includes cardiac, respiratory, neurological, and FEN/GI, as well as ingestion of diabetic medications, alcohol, or carbon monoxide poisoning.

^dPredicted probability cutoff of 0.010.

^eModel includes male gender, cardiac, respiratory, neurological, FEN/GI and renal effects, as well as ingestion of alcohol or diabetic medications.