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ORIGINAL ARTICLE

The Toxicology Investigators Consortium Case Registry—the 2017 Annual Report

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Abstract

The Toxicology Investigators Consortium (ToxIC) Case Registry was established by the American College of Medical Toxicology in 2010. The Registry collects data from participating sites with the agreement that all bedside medical toxicology consultations will be entered. The objective of this eighth annual report is to summarize the Registry's 2017 data and activity with its additional 7577 cases. Cases were identified for inclusion in this report by a query of the ToxIC database for any case entered from 1 January to 31 December 2017. Detailed data was collected from these cases and aggregated to provide information which includes demographics (e.g., age, gender, race, ethnicity), reason for medical toxicology evaluation (e.g., intentional pharmaceutical exposure, envenomation, withdrawal from a substance), agent and agent class, clinical signs and symptoms (e.g., vital sign abnormalities, organ system dysfunction), treatments and antidotes administered, fatality, and life support withdrawal data. Females were involved in 50.4% of cases. Transgender demographic information collection was initiated in 2017 to better represent the population and there were 36 cases involving transgender patients. Adults aged 19–65 were the most commonly reported age group. Non-opioid analgesics were the most commonly reported agent class, with acetaminophen again the most common agent reported. There were 93 fatalities reported in 2017. Treatment interventions were frequently reported with 30.6% receiving specific antidotal therapy. Major trends in demographics and exposure characteristics remained similar to past years' reports. While treatment interventions were commonly required, fatalities were rare.

Keywords Poisonings · Overdose · Surveillance · Epidemiology · Medical toxicology

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Introduction

The year 2017, the eighth full year of operation of the Toxicology Investigators Consortium (ToxIC), was marked by a number of achievements and continued robust data collection. A summary of the data collected is provided in the body of this report. Major changes and achievements are described below.

On January 1, 2017, ToxIC moved to the REDCap data collection platform. This provided an even greater level of data security than we had with our previous interface and allowed for the incorporation of two factor authentication of identity before the database was accessed for data entry or searching.

Given the growth of ToxIC and large amount of associated information, policies, and background information, a unique ToxIC website was developed throughout 2016 and went live in 2017 at https://www.toxicregistry.org. The reader of this Annual Report is referred to this website for additional information about ToxIC.

In light of the evolving complexity of ToxIC, it was felt that it was necessary to embark on a long-term strategic plan. That plan was completed in 2017 and its implementation was initiated. Continued implementation is expected throughout 2018. It is hoped that the implementation of the strategic plan will lead to further sophistication of our data collection and analysis, research, post-marketing surveillance, and toxicovigilance activities. It is also hoped that the strategic plan implementation will serve as a direction to ensure the continued long-term sustainability of the ToxIC program.

In 2017, there were 7577 novel cases entered from 40 separate sites comprising 63 separate facilities. The year 2017 saw the closure of three projects, the evolution and growth of existing efforts, and the launch of three of new focused sub-Registries.

A study, in the form of a sub-Registry, on diagnostic modalities in caustic ingestions, which collected data for nearly the entire 8 years of ToxIC's existence, was completed and the sub-Registry was closed by virtue of not being migrated to the REDCap platform. Data analysis collected in this project is now underway.

The focused data collection, also in the form of a sub-Registry, on electrocardiographic QRS widening and the antidotal use of sodium bicarbonate was also closed in 2017. The analysis of data from this project is also underway. Hypotheses emerging from this analysis will be potentially tested once this data analysis is completed.

Our data collection of prescription opioid misuse was closed by virtue of it not being migrated to REDCap. With the continued and growing concern about opioid toxicity, it was felt that a new and more robust approach to this critical problem was necessary. The epidemic of opioid abuse and misuse is a major public health concern and new efforts related to this problem by ToxIC are in development. As described below, one such project relating to pediatric opioid exposures has already been instituted.

Our study on the use of lipid resuscitation therapy continues and currently represents the largest known prospective collection of patients treated with this modality. Data analysis for this project is also underway; however, patient accrual is still ongoing. Following our preliminary analysis, the need for objective definable end-points became apparent and were instituted in our mid-2017 database modifications.

The North American Snakebite sub-Registry continues to thrive and currently represents the largest prospective collection of data on these snakebites in existence. The publications and published abstracts from presentations at national professional meetings deriving from this sub-Registry are listed on https://www.toxicregistry.org.

Our extracorporeal substance removal sub-Registry continues to collect unique data on drug clearances by these techniques. Also continuing is the data collection of prognostic factors following drug overdose, now in its fourth year.

Two of our new sub-Registries deal with critical issues related to pediatric exposures: opioids and marijuana. Both of these projects went live with the launch of REDCap on January 1, 2017. Also at that time a sub-Registry on plant and mushroom exposures was initiated. These uncommon but extremely important exposures are very hard to study given the few cases encountered. By aggregating the prospective experience of the network of ToxIC investigators, it is anticipated that a robust series of cases on individual plant and mushroom exposures will be characterized.

There were eight peer-reviewed publications derived from the ToxIC Registry and published by ToxIC investigators in 2017. In addition, there were 17 published abstracts from professional meetings in 2017.

In 2017, ToxIC continued to be supported by a grant on cardiovascular toxicity from the National Institutes of Health, the continuation of our contract with the US Food and Drug Administration, and further unrestricted grant support from BTG International. The latter was used to support the North American Snake Bite Registry.

Ongoing investigator-initiated research projects can be found on the ToxIC website.

This eighth ToxIC Annual Report summarizes the main points of the data collected in our main Registry in 2017. Data from our sub-Registries are published separately.

Methods

A detailed description of the creation and design of the ToxIC Registry has been previously reported [1]. To be part of the consortium, all medical toxicologists at participating institutions agree to enter data into the ToxIC Registry on all medical

toxicology consultations performed. Cases are entered on a password-protected encrypted online data collection form. The site uses the REDCap (Research Electronic Data Capture) interface and is hosted by Vanderbilt University. The content of the database is maintained with oversight by the ToxIC Leadership Group. The Registry is compliant with the Health Insurance Portability and Accountability Act and does not collect any protected health information or otherwise identifying fields. Registry participation is pursuant to the participating institutions' Institutional Review Board approval and compliant with their policies and procedures. The Registry has also been independently reviewed by the Western IRB and determined not to meet the threshold of human subject research under federal regulation 45 CFR 46 and associated guidance.

Data collected on each case includes presenting signs and symptoms, clinical course, treatments, limited patient demographics, outcome, laboratory values, and circumstances of, and reasons for, the toxicological exposure. As in prior reports, the term consultation is used in this report to describe any in-person encounter with a medical toxicologist in which a formal evaluation was conducted and placed in the medical record. Such encounters may include admission to a medical toxicology inpatient service, or evaluation by a medical toxicologist as a consulting physician in an emergency department, inpatient unit, or outpatient clinic. The online data collection interface is formatted to ensure data entry remains organized and searchable. Free text entry fields allow providers to provide further detail or supplementary information. As part of the Registry's toxicosurveillance mission, one component of the standard data form is a continuously monitored sentinel detection field that signals novel or unusual cases.

For this report a search of the database was performed to identify cases recorded from January 1, 2017, through December 31, 2017. This descriptive report summarizes case demographics, source and location of consultation, and reasons for encounter and provides case frequencies by individual agent class and treatment provided. We also have included several more focused analyses of particular interest. These dealt with pediatric exposures, marijuana edibles, the use of extracorporeal membrane oxygenation (ECMO), coingestants associated with opioid exposures, and gabapentinoid misuse.

In the tables describing individual agents or agent classes, unless otherwise indicated, cells with fewer than five occurrences were not listed as separate items but are further grouped as "miscellaneous." Percentages noted in tables for individual agents represent their relative proportion within their respective agent class.

For clinical signs or symptoms, the tables provide the percentage of individual signs or symptoms relative to the total number of Registry cases in 2017. Signs and symptoms include the presence or absence of a toxidrome, vital sign abnormalities, and a variety of organ system-based derangements which may arise from a toxic exposure. For each subheading in the data collection instrument, investigators are required to either select an abnormality, or "None," to improve the accuracy of data collection and to avoid missing data fields. In the detailed treatment tables, percentages for each treatment modality represent the relative frequency among all treatments rendered.

Results

In 2017, there were a total of 7577 cases reporting toxicologic exposures to the ToxIC Registry. This is a decrease from the prior 2 years (Fig. 1). Table 1 lists all individual sites that contributed cases in 2017.

Demographics

Tables 2 and 3 summarize selective demographics including gender, age, race, and ethnicity. In 2017, 50.4% of cases involved female patients. Sixty patients (0.8%) were pregnant (Table 2). New fields were added in 2017 to better represent the population and include transgender patient data. There were 14 male-to-female transgender patients and 22 female-to-male, making up 0.5% of patients in the database.

Age distribution in 2017 was similar to past years [2–8]. The majority of patients were adults age 19–65 (63.4%), followed by adolescents age 13–18 (19.4%). Children age 12 and under made up 11.8% of cases.

The most commonly reported race was Caucasian (59.4%), followed by Black/African (13.2%) and Asian (4.6%) (Table 3). Unknown or uncertain race was reported in 19.2% of cases, similar to 2016 data [8]. Hispanic ethnicity was reported in 11.3% of cases (Table 3). Nineteen percent of cases reported unknown ethnicity. Race and ethnicity are self-reported by patients, or in cases where a patient is unable to report, it may be reported by the examining medical toxicologist to the best of their ability.

Table 4 summarizes the referral sources of inpatient and outpatient medical toxicology encounters. The majority of inpatient cases (56.7%) were generated from the Emergency Department. Only 0.3% of inpatient encounters were referred from poison centers. Outpatient toxicology evaluations were predominantly referred by primary care or other outpatient physicians (43.5%) or were self-referrals (37.1%).

Table 5 reports the reasons for medical toxicology encounters. Similar to prior years, intentional pharmaceutical exposures were the most common reason for encounter (54.7%).

Table 6 presents information on reasons for intentional pharmaceutical exposures. The majority of cases (67.6%) were an attempt at self-harm. Of these cases with an attempt at self-harm, 88.2% represented a suicide attempt.

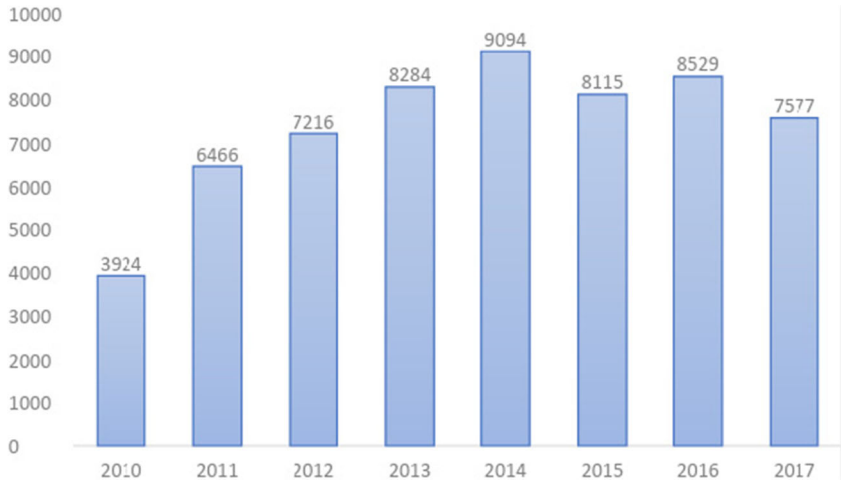

Fig. 1 ToxIC Registry total case count by year, 2010–2017

Agent Classes

Of the 7577 cases entered into the ToxIC Registry in 2017, 2340 cases involved multiple agents for a total of 10,606 individual agent entries. The non-opioid analgesic class was the most common (14.9%), followed by antidepressants (11.4%), opioids (10.4%), and sedative-hypnotic/muscle relaxants (9.2%). Table 7 presents the totals for each of the 40 agent classes in the Registry.

Pediatric Agent Classes

Table 8 presents the agent classes reported by age group. There were 3366 individual agent entries in 2017 for 2360 reported pediatric cases with 610 (25.8%) cases involving multiple agents. The top agent classes for all pediatric cases were analgesics (19.5%), followed by antidepressants (13.0%) and anticholinergic/antihistamine (9.2%). By age category, the most common exposures by agent class were opioids for children < 2 years old, cardiovascular drugs for ages 2–6, envenomations for ages 7–12, and analgesics for ages 13–18. Opioids were ranked sixth in agent class frequency for pediatrics with the majority of exposures involving 13–18 year olds, though they were the most common agent class in those under age 2. Envenomations were most commonly reported in the 7–12 year old age category, followed by 13–18 year olds. Caustic exposures were most often seen in 2–6 year olds.

Table 9 lists the most commonly reported agent classes involved in exposures in children aged 5 or younger. The cardiovascular agent class was the most commonly reported (15.6%), followed by opioids (8.4%). Diabetic medications (5.0%), herbal products/dietary supplements (3.8%), and metals (3.8%) were also reported more frequently in children aged 5 or younger compared to their representation in the Registry as a whole.

Individual Agents by Class

Tables 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26, 27, and 28 present the frequencies of individuals agents, organized by agent class as reported to the Registry in 2017. The organization follows past years for consistency with three agents—ethanol, lithium, and amphetamine-like hallucinogens—defined as their own agent class, but reported in conjunction with other agent classes (toxic alcohols, anticonvulsants and mood stabilizers, and psychoactives, respectively) for brevity. For agent classes with few overall entries (less than 100), or for which a single agent made up more than 75% of the cases, or for which the majority of cases were infrequent miscellaneous agents, the results are reported in Tables S1–S16 in the Supplemental Materials.

Analgesics

Table 10 presents the non-opioid analgesics, the largest class reported in the Registry. Acetaminophen, aspirin, and ibuprofen were the most frequently reported agents in 2017 similar to past years [2–8]. In 2017, gabapentin and pregabalin were moved from the sedative-hypnotics/muscle relaxants class into the analgesics class. In this largest agent class, gabapentin still made up 11.1% of the category.

Antidepressants

Table 11 describes the antidepressant agents. The other antidepressant category was again the most frequent, predominantly due to the frequent reporting of bupropion (21.0%) and trazodone (13.3%). The selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) were reported with similar agent frequencies to past years [7, 8].

Table 1 Participating institutions providing cases to ToxIC in 2017

- Arizona
  - Phoenix
    - Banner - University Medical Center Phoenix
    - Phoenix Children's Hospital
- California
  - Loma Linda
    - Loma Linda University Medical Center
  - Los Angeles
    - University of Southern California Verdugo Hills
    - Keck Medical Center of University of Southern California
  - San Francisco
    - San Francisco General Hospital
- Colorado
  - Denver
    - Children's Hospital Colorado
    - Denver Health Medical Center
    - Porter and Littleton Adventist Hospital
    - Swedish Medical Center
    - University of Colorado Medical Center
- Connecticut
  - Hartford
    - Hartford Hospital
- Georgia
  - Atlanta
    - Children's Healthcare of Atlanta Egelston
    - Children's Healthcare of Atlanta Hughes Spalding
    - Elmhurst Medical Center
    - Emory University Hospital
    - Grady Health System
    - Grady Memorial Hospital
- Illinois
  - Evanston
    - Evanston North-Shore University Health System
- Indiana
  - Indianapolis
    - IU-Eskenazi Hospital
    - IU-Indiana University Hospital
    - IU-Methodist Hospital-Indianapolis
    - IU-Riley Hospital for Children
- Massachusetts
  - Boston
    - Beth Israel Deaconess Medical Center Boston
    - Boston Children's Hospital
  - Worcester
    - University of Massachusetts Memorial Medical Center
- Michigan
  - Grand Rapids
    - Spectrum Health Hospitals
- Missouri
  - Kansas City
    - Children's Mercy Hospitals & Clinics
  - St. Louis
    - Washington University School of Medicine
- Nebraska
  - Omaha
    - University of Nebraska Medical Center
- New Mexico
  - Albuquerque
    - University of New Mexico
- New Jersey
  - New Brunswick
    - Robert Wood Johnson University Hospital
  - Newark
    - NJMS/Rutgers
- New York
  - Manhasset
    - North Shore University Hospital
  - New York
    - Bellevue Medical Center
    - Mount Sinai Hospital
    - NYU Langone Medical Center
  - Staten Island
    - Staten Island Hospital
    - Staten Island University Hospital
  - Rochester
    - Highland Hospital
    - Strong Memorial Hospital
  - Syracuse
    - Upstate Medical University-Downtown Campus
- North Carolina
  - Charlotte
    - Carolinas Medical Center
  - Greenville
    - Vidant Medical Center
- Oregon
  - Portland
    - Oregon Health & Science University Hospital
- Pennsylvania
  - Lehigh Valley
    - Lehigh Valley Hospital Cedar Crest
    - Lehigh Valley Hospital Muhlenberg
  - Philadelphia
    - Hahnemann University Hospital
    - Mercy Fitzgerald Hospital
    - Mercy Hospital of Philadelphia
    - St. Christopher's Hospital for Children
  - Pittsburgh
    - UPMC Magee Women's Hospital
    - UPMC Mercy Hospital
    - UPMC Presbyterian/Shadyside
- Texas
  - Dallas
    - Children's Medical Center Dallas
    - Parkland Memorial Hospital
    - University of Texas Southwestern Clinic
    - William P Clements University Hospital
  - Houston
    - Ben Taub General Hospital
    - Texas Children's Hospital
- Utah
  - Salt Lake City
    - Primary Children's Hospital
    - University of Utah Hospital
- Virginia
  - Charlottesville
    - University of Virginia Health Systems
  - Richmond
    - Virginia Commonwealth University Medical Center
- Wisconsin
  - Milwaukee
    - Children's Hospital of Wisconsin
    - Froedtert Memorial Lutheran Hospital
- Isreal
  - Haifa
    - Rambam Health Care Campus
- Canada
  - Toronto
    - Hospital for Sick Children
- Thailand
  - Bangkok
    - Vajira Hospital

Table 2 ToxIC case demographics—age and gender

	N (%)
Gender	
Male	3718 (49.1)
Female	3820 (50.4)
Transgender	
Male to female	14 (0.2)
Female to male	22 (0.3)
Not recorded	3 (0.0)
Pregnant	60 (0.8)
Age (years)	
< 2	268 (3.5)
2–6	371 (4.9)
7–12	253 (3.3)
13–18	1468 (19.4)
19–65	4803 (63.4)
66–89	376 (5.0)
> 89	13 (0.2)
Unknown	25 (0.3)
Total	7577 (100)

Opioids

Table 12 presents the opioid agent class. As in recent years, heroin was the most commonly reported opioid in the Registry in 2017 (28.9%). Oxycodone was again the second most frequently reported agent (14.5%), though its percent contribution to the class was slightly decreased from last year (17.8%)

Table 3 ToxIC case demographics—race and Hispanic ethnicity

	N (%)
Race	
Caucasian	4504 (59.4)
Unknown/uncertain	1456 (19.2)
Black/African	999 (13.2)
Asian	350 (4.6)
Mixed	136 (1.8)
American Indian/Alaska Native	111 (1.5)
Other	16 (0.2)
Native Hawaiian or Pacific Islander	5 (0.1)
Total	7577 (100)
Hispanic ethnicity[a]	
Hispanic	854 (11.3)
Non-Hispanic	5283 (69.7)
Unknown	1439 (19.0)
Total	7577 (100)

One case not recorded as Hispanic or non-Hispanic ethnicity

[a] Hispanic ethnicity as indicated exclusive of race

[8]. Overall, oxycodone has declined in its percent contribution to the opioid agent class each year [2–8]. Tramadol increased slightly from 2016, making up 9.6% of reported opioids [8]. Reported fentanyl exposures increased by more than 90% in 2017 making up 7.9% of the opioid class after being steady at 4.1% in both 2015 and 2016 [7, 8]. In the same years, unspecified opioids had increased from 6.5% in 2015 to 8.1% in 2016, but remained fairly stable in 2017 at 7.4%. This increase in fentanyl cases may be a reflection of increased awareness of and testing for fentanyl adulteration of heroin. Additionally, the opioid unspecified class which has had a trending increase since the Registry began in 2010, may be capturing additional cases of adulterated heroin when testing is not available [2–8]. In 2017, the miscellaneous opioids included more specific designer opioids not previously reported to the Registry including butanoyl-4-fluorofentanyl, fluorofentanyl, fluoroisobutyryl fentanyl (4- or para-), methyl norfentanyl, N-allyl norfentanyl, butyrylfentanyl (butyr-), and carfentanil. The designer opioid U47700 and methylfentanyl were also reported after being reported to the Registry for the first time in 2016.

Opioid Coingestants

In 2017, there were 988 total opioid agents reported in 718 unique case entries. The frequency of coingestion was high with 403 (56.1%) out of 718 unique cases having more than one primary agent reported. Coingestion rates varied widely; however, based on specific opioid ingested, ranging from a high of 84.4% of cases for which hydrocodone was reported to a low of 21% when buprenorphine was reported. There were 270 cases (37.6%) with more than one opioid reported as a primary agent. Heroin was the most common opioid reported in 2017 with 318 case entries. The most common coingestions included stimulants occurring in 72 (22.6%) of heroin cases. Cocaine was the most commonly reported stimulant reported with heroin occurring in 49 (15.4%) followed by methamphetamine in 23 (7.2%). Alprazolam was the most commonly reported benzodiazepine reported with heroin occurring in 14 (4.4%). Other opioids were reported in 26 (8.2%) of cases involving heroin. Tramadol was the second most commonly reported opioid in 2017 occurring in 104 case entries. Coingestion was reported in 34 (32.7%) of tramadol cases, and while there were some drugs reported more than once, coingestion involved a variety of other agents. There were 18 unique agents reported along with tramadol; THC, kratom, gabapentin, cyclobenzaprine, and alcohol were all reported more than twice. Oxycodone was reported in 100 case entries with coingestion occurring in 57 (57.0%). Acetaminophen was the most commonly reported drug ingested with oxycodone occurring in 13 cases (13.0%). Benzodiazepines were reported as coingestants in 22

(22.0%) of oxycodone cases and alprazolam was the most commonly reported benzodiazepine in 11 (11.0%) of cases. Fentanyl was reported in 87 case entries with 53 cases (60.9%) involving coingestion and cocaine was the single most common drug, occurring in 13 cases (14.9%). Opioids were the most frequent class of drug reported as coingestion for fentanyl reported for nearly a third of all fentanyl cases with co ingestion. Methadone was reported in 79 case entries with coingestion in 30 (37.9%) and other opioids reported most commonly occurring in 19 cases (24.1%) with heroin being the most common opioid reported with methadone. Other drugs reported with methadone included cocaine in 8 (10.1%) and alprazolam was the most commonly reported benzodiazepine reported in 5 cases (6.3%). Hydrocodone was reported in 77 cases with 39 (50.6%) involving coingestion with acetaminophen as ingestion of the coformulation products for hydrocodone and acetaminophen were common. Sedative ingestion was common with hydrocodone though a variety of sedatives were reported including gabapentin, clonazepam, lorazepam, baclofen, and alcohol and although alprazolam was the most common. Buprenorphine was reported in 66 cases with 16 (24.2%) having coingestion reported. Other opiates, sedatives, cocaine, and benzodiazepines were the most commonly reported substances with buprenorphine. Morphine was reported in 37 cases and 26 (70.3%) had coingestion with opioid coingestion occurring in 10 and oxycodone being the most commonly reported other opioid along with morphine. Non-specific opioids (opioids NOS) were reported in 82 unique entries and 13 cases included co ingestion with sedatives being reported in almost half of these cases. Several different benzodiazepines, alcohol, and gabapentin were reported when non-specified opioid ingestion occurred in case entries.

Overall, alprazolam, followed by clonazepam, were the most common benzodiazepines reported with an opioid reported as primary agent. Illicit opioids had other illicit drugs including cocaine, methamphetamine, fentanyl, or heroin reported as coingestion though commonly abused pharmaceuticals were also not uncommon for illicit opioid cases (e.g., sedatives including alprazolam, gabapentin, and baclofen). Coingestion with other opioids and sedatives was also commonly reported for the pharmaceutical opioids as were illicit drugs, though this was at lower rates than their illicit opioid counterparts.

Table 4 ToxIC registry case referral sources by inpatient/outpatient status

	N (%)
Emergency Department (ED) or inpatient (IP)[a]	
ED	4066 (56.7)
Admitting service	1726 (24.1)
Outside hospital transfer	932 (13.0)
Request from another hospital service (not ED)	239 (3.3)
Self-referral	180 (2.5)
Poison Center	24 (0.3)
Primary care provider or other outpatient treating physician	4 (0.1)
Employer/Independent medical evaluation	2 (0.0)
ED/IP total	7173 (100)
Outpatient (OP)/clinic/office consultation[b]	
Primary care provider or other OP physician	175 (43.5)
Self-referral	149 (37.1)
Employer/Independent medical evaluation	35 (8.7)
Poison Center	24 (6.0)
ED	10 (2.5)
Admitting service	3 (0.7)
Outside hospital transfer	3 (0.7)
Request from another hospital service (not ED)	3 (0.7)
OP total	402 (100)

Two cases not recorded inpatient or outpatient location

[a] Percentage based on the total number of cases ($N = 7173$) seen by a medical toxicologist as consultant (ED or IP) or as attending (IP)

[b] Percentage based on the total number of cases ($N = 402$) seen by a medical toxicologist as outpatient, clinic visit, or office consultation

Table 5 Reason for medical toxicology encounter

	N (%)
Intentional exposure—pharmaceutical	4144 (54.7)
Intentional exposure—non-pharmaceutical	921 (12.2)
Unintentional exposure—pharmaceutical	610 (8.1)
Unintentional exposure—non-pharmaceutical	322 (4.2)
Envenomation—snake	297 (3.9)
Organ system dysfunction	256 (3.4)
Withdrawal—opioid	217 (2.9)
Withdrawal—ethanol	149 (2.0)
Ethanol abuse	132 (1.7)
Interpretation of toxicology data	123 (1.6)
Environmental evaluation	122 (1.6)
Occupational evaluation	80 (1.1)
Envenomation—spider	55 (0.7)
Malicious/criminal	41 (0.5)
Envenomation—other	38 (0.5)
Withdrawal—sedative-hypnotic	35 (0.5)
Withdrawal—other	16 (0.2)
Withdrawal—cocaine/amphetamine	6 (0.1)
Envenomation—scorpion	5 (0.1)
Marine/fish poisoning	5 (0.1)
Not recorded	3 (0.0)
Total	7577 (100)

Sedative-Hypnotics/Muscle Relaxants

Table 13 presents the sedative-hypnotics/muscle relaxants class. Benzodiazepines remained the most commonly reported subclass of sedative-hypnotics/muscle relaxants in 2017. Alprazolam (22.8%) and clonazepam (18.6%) were again the most frequent agents both for the benzodiazepine subclass, as well as for the agent class as a whole. Of note, in 2016, gabapentin was reclassified from the sedative-hypnotics/muscle relaxants class to the non-opioid analgesic class, so is summarized in Table 10. The number of gabapentin cases was approximately stable from 2016. The muscle relaxants baclofen and cyclobenzaprine were reported with equal frequency (10.0%) in 2017. Barbiturates were again infrequently reported with butalbital making up the majority of these (1.8%).

Toxic Alcohols and Ethanol

Table 14 presents data on ethanol and toxic alcohols. As in prior years, ethanol is considered its own agent class. There were 723 ethanol exposures in 2017. Among the non-ethanol alcohols and glycols, isopropanol (37.3%) and ethylene glycol (34.7%) were similarly reported.

Anticholinergics

Table 15 shows the anticholinergics and antihistamines agent class. As in past years, diphenhydramine (59.1%) made up the majority of the agent class, with hydroxyzine (14.9%) following.

Table 6 Detailed reason for encounter—intentional pharmaceutical exposure

	N (%)
Reason for intentional pharmaceutical exposure subgroup[a]	
Attempt at self-harm	2803 (67.6)
Misuse/abuse	718 (17.3)
Therapeutic use	328 (7.9)
Unknown	294 (7.1)
Not recorded	1 (0.0)
Total	4144 (100)
Attempt at self-harm- suicidal intent subclassification[b]	
Suicidal intent	2473 (88.2)
Suicidal intent unknown	248 (8.8)
No suicidal intent	79 (2.8)
Not recorded	3 (0.1)
Total	2803 (100)

[a] Percentage of total number of cases ($N = 4144$) indicating primary reason for encounter due to intentional pharmaceutical exposure

[b] Percentage of number of cases indicating attempt at self-harm ($N = 2803$)

Table 7 Agent classes involved in medical toxicology consultation

	N(%)[a]
Analgesic	1582 (14.9)
Antidepressant	1207 (11.4)
Opioid	1101 (10.4)
Sedative-hypnotic/muscle relaxant	972 (9.2)
Ethanol	723 (6.8)
Anticholinergic/antihistamine	669 (6.3)
Sympathomimetic	658 (6.2)
Cardiovascular	597 (5.6)
Antipsychotic	556 (5.2)
Anticonvulsant	399 (3.8)
Envenomation and marine	375 (3.5)
Psychoactive	223 (2.1)
Diabetic medication	172 (1.6)
Lithium	121 (1.1)
Toxic alcohol	118 (1.1)
Metals	115 (1.1)
Cough and cold products	112 (1.1)
Herbal products/dietary supplements	111 (1.0)
Gases/irritants/vapors/dusts	94 (0.9)
Caustic	89 (0.8)
Hydrocarbon	75 (0.7)
Household products	68 (0.6)
Plants and fungi	65 (0.6)
Antimicrobial	60 (0.6)
Endocrine	38 (0.4)
Chemotherapeutic/immunological	35 (0.3)
Other non-pharmaceutical product	33 (0.3)
Gastrointestinal agents	30 (0.3)
Anesthetic	27 (0.3)
Insecticide	27 (0.3)
Anticoagulant	24 (0.2)
Other pharmaceutical product	18 (0.2)
Amphetamine-like hallucinogen	12 (0.1)
Herbicide	10 (0.1)
WMD/riot agent/radiological	7 (0.1)
Anti-parkinsonism drugs	6 (0.1)
Rodenticide	6 (0.1)
Ingested foreign body	5 (0.0)
Pulmonary	4 (0.0)
Fungicide	NR (0.0)
Unknown agent	62 (0.6)
Total	10,606 (100)

NR no cases reported

[a] Percentages are out of total number of reported agent entries in 2017; 2340 cases (30.9%) reported multiple agents

Table 8 ToxIC 2017—agent classes for pediatric cases by age group

	Exposure rank	Totals	%[a]	Age < 2	Age 2–6	Age 7–12	Age 13–18
Analgesic	1	658	19.5%	23	20	30	585
Antidepressant	2	436	13.0%	13	25	20	378
Anticholinergic/antihistamine	3	309	9.2%	10	24	30	245
Unknown/blank	4	234	7.0%	36	62	36	100
Cardiovascular	5	224	6.7%	36	82	25	81
Opioid	6	172	5.1%	37	20	5	110
Envenomation	7	171	5.1%	6	37	71	57
Antipsychotic	8	158	4.7%	5	10	8	135
Sympathomimetic	9	155	4.6%	31	24	12	88
Sedative-hypnotic/muscle relaxant	10	148	4.4%	9	16	14	109
Anticonvulsant	11	110	3.3%	8	16	14	72
Psychoactive	12	67	2.0%	8	14	3	42
Herbal/dietary supp/vitamins	13	61	1.8%	9	17	4	31
Diabetic med	14	59	1.8%	14	23	1	21
Ethanol	14	59	1.8%	5	2	2	50
Cough/cold	15	50	1.5%	1	7	2	40
Metals	16	48	1.4%	8	19	5	16
Household product	17	26	0.8%	11	6	1	8
Hydrocarbons	18	24	0.7%	13	9	0	2
Lithium	19	23	0.7%	1	1	2	19
Antimicrobial	20	22	0.7%	4	3	2	13
Caustic	21	19	0.6%	5	10	1	3
Toxic alcohols	22	18	0.5%	5	3	2	8
Endocrine	23	16	0.5%	1	7	1	7
GI Agent	24	15	0.4%	3	2	1	9
Chemotherapeutic/immune	25	14	0.4%	3	2	3	6
Gases/vapors/irritants/dusts	25	14	0.4%	5	2	3	4
Plants/fungi	26	12	0.4%	3	4	3	2
Anesthetic	27	10	0.3%	3	1	2	4
Other non-pharmaceutical	28	9	0.3%	2	2	1	4
Other pharmaceutical	29	7	0.2%	1	1	0	5
Amphetamine-like hallucinogen	30	4	0.1%	0	1	1	2
Anticoagulant	31	3	0.1%	2	1	0	0
Ingested foreign body	31	3	0.1%	1	1	0	1
Insecticide	32	2	0.1%	2	0	0	0
Pulmonary	32	2	0.1%	0	1	0	1
Rodenticide	32	2	0.1%	1	1	0	0
Parkinson's med	33	1	0.0%	0	1	0	0
WMD	33	1	0.0%	1	0	0	0
Totals		3366	100.0%				

[a] Percentages are out of total number of reported agent entries per year; 610 cases (25.8%) reported multiple agents

Sympathomimetics

Table 16 summarizes the sympathomimetics agent class. Cocaine (38.8%) was the leading agent reported. Methamphetamine (27.4%) and amphetamine (9.6%) were the next most commonly reported, consistent with prior years.

Cardiovascular Agents

Table 17 presents the cardiovascular agent class. In 2017, the sympatholytic subclass was the most commonly reported (25.1%), outnumbering beta blockers (23.3%) for the first time in the Registry. Among all of the cardiovascular agents,

Table 9 Most frequent exposures by agent class- age ≤ 5 years

	N (%)[a]
Cardiovascular	106 (15.6)
Opioid	57 (8.4)
Sympathomimetic	52 (7.7)
Analgesic	43 (6.3)
Envenomation	38 (5.6)
Antidepressant	34 (5.0)
Diabetic medication	34 (5.0)
Anticholinergic/antihistamine	33 (4.9)
Herbal products/dietary supplements	26 (3.8)
Metals	26 (3.8)
Sedative-hypnotics/muscle relaxant	24 (3.5)
Anticonvulsant	24 (3.5)
Psychoactive	22 (3.2)
Hydrocarbon	22 (3.2)
Household	17 (2.5)
Antipsychotic	15 (2.2)
Caustic	15 (2.2)
Class total	678 (100)

[a] Percentages are out of total number of agent exposures reported in children aged 5 or younger in 2017 (*N* = 678)

clonidine was the most commonly reported agent (18.9%), followed by amlodipine (9.9%), lisinopril (8.4%), and metoprolol (7.7%). Other cardiovascular agent subclasses—other antihypertensives and vasodilators, antidysrhythmics and other cardiovascular agents, cardiac glycosides, diuretics, and angiotensin receptor blockers—each made a smaller contribution to the class, altogether accounting for about one-quarter of the agents.

Table 10 Analgesics

	N (%)
Acetaminophen	901 (57.0)
Aspirin	202 (12.8)
Ibuprofen	183 (11.6)
Gabapentin	176 (11.1)
Naproxen	57 (3.6)
Pregabalin	25 (1.6)
Salicylic acid	10 (0.6)
Analgesic unspecified	6 (0.4)
Meloxicam	5 (0.3)
Miscellaneous[a]	17 (1.1)
Class total	1582 (100)

[a] Includes aminophenazone, diclofenac, etoricoxib, ketorolac, mefenamic acid, unspecified NSAID, other analgesic, phenylbutazone, salicylamide, and salsalate

Table 11 Antidepressants

		N (%)
Other antidepressants		476 (39.4)
	Bupropion	252 (21.0)
	Trazodone	161 (13.3)
	Mirtazapine	43 (3.6)
	Vilazodone	9 (0.7)
	Antidepressant unspecified	8 (0.7)
	Miscellaneous[a]	< 5 (< 0.4)
Selective serotonin reuptake inhibitors (SSRIs)		445 (36.9)
	Sertraline	128 (10.6)
	Fluoxetine	116 (9.6)
	Citalopram	96 (8.0)
	Escitalopram	80 (6.6)
	Paroxetine	25 (2.1)
Tricyclic antidepressants (TCAs)		166 (13.8)
	Amitriptyline	105 (8.7)
	Nortriptyline	28 (2.3)
	Doxepin	25 (2.1)
	Miscellaneous[b]	8 (0.7)
Serotonin-norepinephrine reuptake inhibitors (SNRIs)		120 (9.9)
	Venlafaxine	80 (6.6)
	Duloxetine	30 (2.5)
	Desvenlafaxine	6 (0.5)
	Miscellaneous[c]	< 5 (< 0.4)
	Class Total	1207 (100)

[a] Includes phenelzine and vortioxetine

[b] Includes imipramine, clomipramine, amoxapine, and dosulepin

[c] Includes fluvoxamine

Antipsychotics

Table 18 shows the antipsychotic agent class. Distribution of agents was similar to prior years. Quetiapine made up early half of the agent class (47.5%). Olanzapine was the next most common (14.6%), followed by risperidone (7.2%) and aripiprazole (7.0%).

Anticonvulsants, Mood Stabilizers, and Lithium

Table 19 presents the anticonvulsants and mood stabilizers, along with lithium. As in past years, lithium is considered its own agent class, but for brevity, is presented along with the anticonvulsants and mood stabilizers. There were 121 cases reporting lithium exposure in 2017. The distribution of anticonvulsants and mood stabilizers followed a similar trend to past years. Lamotrigine was the most common agent in the class (27.1%), followed by valproic acid (22.8%). Carbamazepine and topiramate were equally reported (9.5%).

Table 12 Opioids

	N (%)
Heroin	318 (28.9)
Oxycodone	160 (14.5)
Tramadol	106 (9.6)
Fentanyl	87 (7.9)
Opioid unspecified	82 (7.4)
Methadone	79 (7.2)
Hydrocodone	78 (7.1)
Buprenorphine	67 (6.1)
Morphine	38 (3.5)
Hydromorphone	17 (1.5)
Codeine	15 (1.4)
Loperamide	12 (1.1)
Naltrexone	9 (0.8)
Oxymorphone	6 (0.5)
Miscellaneous[a]	27 (2.5)
Class total	1101 (100)

[a] Includes U47700 (designer opioid), butanoyl-4-fluorofentanyl, methylfentanyl (3- or alpha), diphenoxylate, fluorofentanyl, fluoroisobutyryl fentanyl (4- or para-), methyl norfentanyl, N-allyl norfentanyl, butyrylfentanyl (butyr-), carfentanil, naloxone, normethadone, opium (raw, latex), Papaver somniferum (plant parts), and tapentadol

Table 13 Sedative-hypnotics/muscle relaxants by sub-type

	N (%)
Benzodiazepines	571 (58.8)
Alprazolam	220 (22.8)
Clonazepam	181 (18.6)
Lorazepam	80 (8.2)
Diazepam	42 (4.3)
Benzodiazepine unspecified	23 (2.4)
Temazepam	11 (1.1)
Chlordiazepoxide	6 (0.6)
Miscellaneous[a]	8 (0.8)
Muscle relaxants	259 (26.7)
Baclofen	97 (10.0)
Cyclobenzaprine	97 (10.0)
Carisoprodol	22 (2.3)
Tizanidine	22 (2.3)
Methocarbamol	15 (1.5)
Metaxalone	5 (0.5)
Miscellaneous[b]	< 5 (< 0.5)
Non-benzodiazepine agonists ("Z" drugs)	63 (6.5)
Zolpidem	58 (6.0)
Miscellaneous[c]	5 (0.5)
Other Sedatives	52 (5.3)
Sedative-hypnotic unspecified	19 (1.9)
Buspirone	17 (1.8)
Phenibut	5 (0.5)
Miscellaneous[d]	11 (1.1)
Barbiturates	27 (2.8)
Butalbital	17 (1.8)
Phenobarbital	7 (0.7)
Miscellaneous[e]	3 (0.3)
Class total	972 (100)

[a] Includes clorazepate, midazolam, flunitrazepam, and oxazepam
[b] Includes orphenadrine
[c] Includes eszopiclone and zopiclone
[d] Includes propofol, chlorzoxazone, etizolam, and clomethiazole
[e] Includes butabarbital and barbiturate unspecified

Envenomations and Marine Poisonings

Table 20 summarizes the envenomations and marine poisonings. *Agkistrodon* species exposures slightly outnumbered *Crotalus* species exposures in 2017 (28.8% vs 25.3%). Unspecified snake exposures were the next most common (10.1%). *Loxosceles* exposures increased from 2016 when they made up 4.2% of the agent class, making up 8.5% of the class in 2017 [8]. *Chilopoda* species exposures also were reported more frequently than in past years with 15 cases, making up 4% of the agent class.

Psychoactives

Table 21 presents the psychoactive agents and the amphetamine-like hallucinogen methylenedioxymethamphetamine (molly). Molly was reported in 12 cases in 2017, an increase from 2016 when 6 cases were reported [7]. In 2017, the number of marijuana cases surpassed the number of synthetic cannabinoids after a 2-year trend of synthetic cannabinoids being reported more frequently [7, 8].

Marijuana Edibles

Figure 2 presents annual data on exposures to marijuana edible agents from 2012 through 2017, reported by age range. In 2012, there were no cases of oral marijuana ingestion in children aged 0–6. There were 10 cases reported in this age group in 2017 and 8 in 2017. Use among those aged 66–89 was low with only 1 case reported over the timeframe.

Pediatric Exposures to Drugs of Abuse

Tables 22 A–J present more detailed information about cases involving pediatric exposures to agents that are commonly used as drugs of abuse. If a case was identified reporting a drug of abuse, then additional agents in a polypharmacy exposure were also included in the analysis. Overall, 123 cases

Table 14 Ethanol and toxic alcohols

	N (%)
Ethanol[a]	723 (100)
Non-ethanol alcohols and glycols	
Isopropanol	44 (37.3)
Ethylene glycol	41 (34.7)
Methanol	18 (15.3)
Acetone	5 (4.2)
Miscellaneous[b]	10 (8.5)
Class total	118 (100)

[a] Ethanol is considered a separate agent class

[b] Includes benzyl alcohol, butyl ethylene glycol, diethyl ether, diethylene glycol, dipropylene glycol, glycol ethers, propylene glycol, and toxic alcohol unspecified

involving pediatrics exposed to drugs of abuse were identified. Tables 22 A, B, C, and D present the distribution of these patients by overall race and ethnicity, as well as race and ethnicity broken down by gender. Overall, 59.3% of patients were Caucasian and 21.1% were African American. Tables 22 E and F compare the numbers of single agent exposures and multiple agent exposures overall and by gender. Single agent exposures were more common (61.8%). Table 22 G and H show the most common agent classes involved in these exposures overall and by gender. The top agent classes were psychoactives, sympathomimetics, opioids, and antidepressants. These remained similarly reported among both male and female genders. Table 22 I and J show the reasons for medical

Table 15 Anticholinergics and antihistamines

	N (%)
Diphenhydramine	413 (61.7)
Hydroxyzine	85 (12.7)
Doxylamine	32 (4.8)
Chlorpheniramine	22 (3.3)
Benztropine	21 (3.1)
Cetirizine	18 (2.7)
Promethazine	14 (2.1)
Loratadine	9 (1.3)
Trihexyphenidyl	8 (1.2)
Dicyclomine	7 (1.0)
Dimenhydrinate	7 (1.0)
Meclizine	5 (0.7)
Miscellaneous[a]	28 (4.2)
Class total	669 (100)

[a] Includes anticholinergic unspecified, antihistamine unspecified, atropine, brompheniramine, buclizine, cyproheptadine, fexofenadine, homatropine, hyoscyamine, mirabegron, oxybutynin, pheniramine, pyrilamine, scopolamine, and triprolidine

Table 16 Sympathomimetics

	N (%)
Cocaine	255 (38.8)
Methamphetamine	180 (27.4)
Amphetamine	63 (9.6)
Methylphenidate	36 (5.5)
Dextroamphetamine	30 (4.6)
Lisdexamfetamine	16 (2.4)
Sympathomimetic unspecified	15 (2.3)
Methylenedioxy-*N*-methamphetamine	10 (1.5)
Pseudoephedrine	9 (1.4)
Phentermine	8 (1.2)
Atomoxetine	7 (1.1)
Dexmethylphenidate	5 (0.8)
Phenylephrine	5 (0.8)
Miscellaneous[a]	19 (2.9)
Class total	658 (100)

[a] Includes clenbuterol, epinephrine, 2C series drugs, 25I-NBOMe, 3-fluoroethamphetamine, 4-fluoroamphetamine, butylone, cathinone, ephedrine, ethylphenidate, isometheptine, MDPV, norpseudoephedrine, phenylpropanolamine, and tetrahydrozoline

toxicology encounters overall and broken down by gender. Intentional non-pharmaceutical exposures were the most commonly reported (38.2%), followed by intentional pharmaceutical exposures (27.6%).

Diabetic Agents

Table 23 shows diabetic medications. There were 172 diabetic medications reported to the Registry. Metformin was the most commonly reported agent (33.1%). In 2017, glipizide (23.3%) was reported more frequently than insulin (22.1%), a change from prior years.

Metals

Table 24 presents the metal agent class. There were 115 agents reported in 2017, with the top agents and frequencies similar to past years. Lead was the most commonly reported (27.8%), followed by iron (22.6%). Cobalt (8.7%) and chromium (5.2%) entries have continued to decrease since they peaked in 2011, coincident with the discontinued use of certain metal-on-metal hip joint prostheses [2–8].

Herbal Products and Dietary Supplements

Table 25 shows the herbal products and dietary supplements agent class. Similar to past years, this category included a diverse group of products, many of which were infrequently

Table 17 Cardiovascular agents by sub-type

	N (%)
Sympatholytics	150 (25.1)
Clonidine	113 (18.9)
Guanfacine	34 (5.7)
Miscellaneous[a]	< 5 (< 0.8)
Beta blockers	139 (23.3)
Metoprolol	46 (7.7)
Propranolol	39 (6.5)
Carvedilol	24 (4.0)
Atenolol	19 (3.2)
Labetalol	9 (1.5)
Miscellaneous[b]	< 5 (< 0.8)
Calcium channel antagonists	104 (17.4)
Amlodipine	59 (9.9)
Diltiazem	24 (4.0)
Verapamil	10 (1.7)
Nifedipine	9 (1.5)
Miscellaneous[c]	< 5 (< 0.8)
ACE inhibitors	58 (9.7)
Lisinopril	50 (8.4)
Enalapril	5 (0.8)
Miscellaneous[d]	< 5 (< 0.8)
Other antihypertensives and vasodilators	40 (6.7)
Prazosin	26 (4.1)
Hydralazine	5 (0.8)
Miscellaneous[e]	9 (1.5)
Antidysrhythmics and other cardiovascular agents	38 (6.4)
Atorvastatin	8 (1.3)
Amiodarone	7 (1.2)
Cardiovascular agent unspecified	5 (0.8)
Sotalol	5 (0.8)
Miscellaneous[f]	13 (2.2)
Cardiac glycosides	30 (5.0)
Digoxin	28 (4.7)
Digitoxin	2 (0.3)
Diuretics	29 (4.9)
Hydrochlorothiazide	14 (2.3)
Furosemide	8 (1.3)
Spironolactone	5 (0.8)
Miscellaneous[g]	< 5 (< 0.8)
Angiotensin receptor blockers	9 (1.5)
Losartan	6 (1.0)
Miscellaneous[h]	< 5 (< 0.8)
Class total	597 (100)

[a] Includes dexmetetomidine and methyldopa

[b] Includes nadolol

[c] Includes felodipine and lercanidipine

[d] Includes benazepril and quinipril

[e] Includes nitroglycerin, doxazosin, isosorbide, tamsulosin, and terazosin

[f] Includes flecainide, gemfibrozil, midodrine, simvastatin, disopyramide, ivabradine, lovastatin, and rosuvastatin

[g] Includes chlorthalidone and pamabrom

[h] Includes valsartan

reported with less than 5 cases. Caffeine was again the most common agent (25.6%), followed by melatonin (21.4%). Unspecified herbals/dietary supplements/vitamins were the next most common (9.4%).

Table 18 Antipsychotics

	N (%)
Quetiapine	264 (47.5)
Olanzapine	81 (14.6)
Risperidone	40 (7.2)
Aripiprazole	39 (7.0)
Haloperidol	31 (5.6)
Chlorpromazine	19 (3.4)
Clozapine	19 (3.4)
Ziprasidone	17 (3.1)
Lurasidone	13 (2.3)
Antipsychotic unspecified	7 (1.3)
Paliperidone	5 (0.9)
Miscellaneous[a]	21 (3.8)
Class total	556 (100)

[a] Includes asenapine, brexpiprazole, fluphenazine, loxapine, perphenazine, prochlorperazine, thiothixene, and trifluoperazine

Gases, Irritants, Vapors, and Dusts

Table 26 shows the gases, irritants, vapors, and dusts category. Carbon monoxide was the most commonly reported agent (53.2%), consistent with prior years [5–8]. Chlorine and natural gas were reported with equal frequency (4.3%). In 2017, a number of infrequently reported miscellaneous compounds made up a large portion of the agent class (35.1%).

Household Agents

Table 27 presents the household product agent class. Cleaning solutions and disinfectants were most commonly reported (25.0%), followed by sodium hypochlorite at a concentration less than or equal to 6% (19.1%). Laundry detergent pod exposures decreased slightly, making up 11.8% of the class in 2017 as compared to 13.3% in 2016.

Plants and Fungi

Table 28 summarizes the plants and fungi agent class. There were 65 agents entered with unspecified mold species being the predominant agent in the category (44.6%). Other or unknown mushroom species was the next most common entry (12.3%). Kratom (*Mitragyna speciosa*) entries remained stable from 2016 (9.2%) [8]. Infrequent miscellaneous agents made up 26.2% of the class.

Supplemental Tables

Tables S1–S16 can be found in the Supplemental Materials. They present the less frequently reported agent classes, or those agent classes with little diversity, such as fewer than five

Table 19 Anticonvulsants and mood stabilizers, and lithium

	N (%)
Lithium[a]	121 (100)
Lamotrigine	108 (27.1)
Valproic acid	91 (22.8)
Carbamazepine	38 (9.5)
Topiramate	38 (9.5)
Oxcarbazepine	31 (7.8)
Phenytoin	30 (7.5)
Levetiracetam	24 (6.0)
Divalproex	10 (2.5)
Lacosamide	9 (2.3)
Zonisamide	5 (1.3)
Miscellaneous[b]	15 (3.8)
Class total	399 (100)

[a] Lithium is considered a separate agent class

[b] Includes anticonvulsant unspecified, clobazam, felbamate, fosphenytoin, perampanel, primidone, rufinamide, and tiagabine

agent types, or where one agent made up a vast majority of the class. They are briefly described below.

Cough and Cold Preparations

Table S1 presents the 112 cough and cold product agent entries. As in prior years, dextromethorphan made up the majority of the category (84.8%). Unspecified cough and cold products were the next most common (8.0%).

Table 20 Envenomations and marine poisonings

	N (%)
Agkistrodon spp.	108 (28.8)
Crotalus spp.	95 (25.3)
Snake unspecified	38 (10.1)
Loxosceles spp.	32 (8.5)
Trimeresurus spp. (Asian pit vipers)	25 (6.7)
Chilopoda spp. (centipedes)	15 (4.0)
Envenomation unspecified	14 (3.7)
Latrodectus spp.	10 (2.7)
Micrurus spp.	9 (2.4)
Hymenoptera	7 (1.9)
Miscellaneous[a]	19 (5.1)
Class total	375 (100)

[a] Includes *Centruroides* spp., *Vipera palaestinae*, *Homalopsis* spp. (water snakes), *Naja kaouthia*, spider unspecified, *Acanthanter plasti* (Crown of Thorns starfish), animal bite unspecified, ciguetera poisoning, marine toxin unspecified, *Micruroides* spp., *Scolopendra* spp. (giant centipedes), scombroid poisoning, scorpion unspecified, and stingrays

Table 21 Psychoactives

	N (%)
Molly—amphetamine-like hallucinogen[a]	12 (100)
Marijuana	73 (32.7)
Cannabinoid synthetic	49 (22.0)
LSD	15 (6.7)
Cannabinoid non-synthetic	14 (6.3)
Phencyclidine	11 (4.9)
Ketamine	10 (4.5)
Gamma hydroxybutyrate	9 (4.0)
Methylenedioxymethamphetamine	9 (4.0)
Delta-9-tetrahydrocannabinol	8 (3.6)
Miscellaneous[b]	25 (11.2)
Class total	223 (100)

LSD lysergic acid diethylamide

[a] Amphetamine-like hallucinogens are considered a separate agent class

[b] Includes 1,4-Butanediol, 3-methoxyphencyclidine, cannabidiol, disulfiram, donepezil, ethylone, gamma butyrolactone, hallucinogen unspecified, Ipracetin (4-acetoxy-DiPT, 4-acetoxy-N,N-diisopropyltryptamine), nicotine, pharmaceutical tetrahydrocannabinol (THC), psychoactive unspecified, and thujone

Caustics

Table S2 details the caustics agent class. In 2017, cleaning agents and formaldehyde were the most frequently reported agents (10.1%). Miscellaneous caustics, each reported 4 or fewer times, made up more than one-third of the agent class (36.0%).

Hydrocarbons

Table S3 presents the hydrocarbons agent class. Unspecified hydrocarbons were the most frequently reported (21.3%), similar to prior years. In 2017, lamp oil and petroleum distillates each made up 8% of the agent class, an increase from the past few years [6–8].

Antimicrobials

Table S4 presents the antimicrobial agent class. The class is subdivided into antibiotics, antivirals, and other antimicrobial agents. In 2017, the top antibiotic agents were again amoxicillin (10.0%) and dapsone (8.3%), with isoniazid (5.0%) and levofloxacin (5.0%) following. Among the other antimicrobials, quinine was the most commonly reported (10.0%). The antiviral subclass made up 16.7% of the agent class with amantadine (5.0%) being the most common agent.

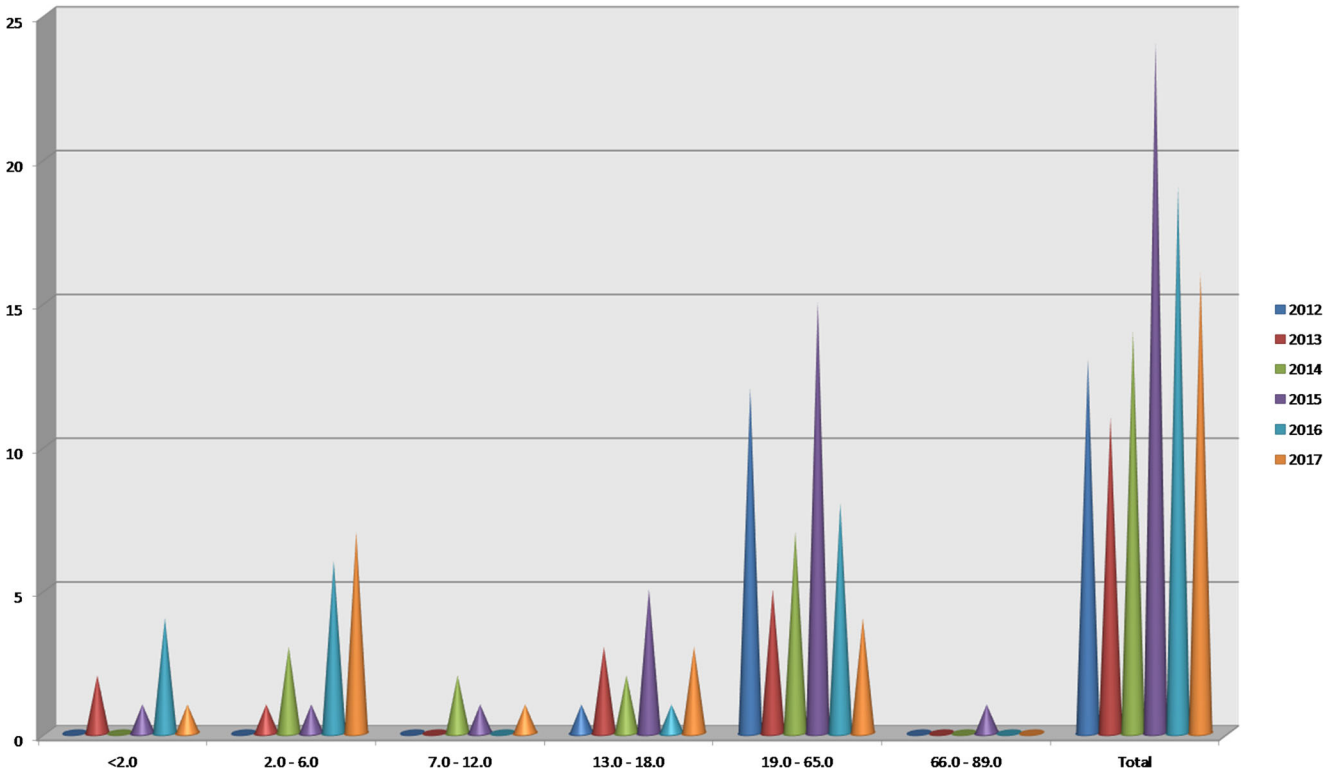

Fig. 2 Marijuana edibles from 2012 to 2017 by age group

Endocrine

Table S5 summarizes the 38 endocrine agents. Levothyroxine was the most commonly reported agent, making up 31.6% of the agent class. Prednisone was the next most commonly reported (15.8%).

Chemotherapeutic and Immunological Agents

Table S6 summarizes the 35 chemotherapeutic and immunological agents. Methotrexate was again the most commonly reported agent (22.9%). The majority of the class (54.3%) was made up of infrequently reported miscellaneous agents.

Other Non-pharmaceuticals

Table S7 presents the 38 other non-pharmaceutical agents. Perfluoro and polyfluoroalkyl substances (PFASs) were the most commonly reported (18.2%). Miscellaneous agents made up 51.5% of the agent class.

Gastrointestinal Agents

Table S8 presents the 30 gastrointestinal agents. Omeprazole (30.0%) and ondansetron (10.0%) were the most commonly reported specific agents. Miscellaneous agents made up 60.0% of the class.

Anesthetics

Table S9 shows the anesthetic agent class. There were 27 anesthetic agents reported with almost half of the class (48.1%) being made up of miscellaneous items. Lidocaine was the most commonly reported agent (29.6%).

Insecticides, Herbicides, Rodenticides, and Fungicides

Table S10 presents the insecticide, rodenticide, and herbicide agent classes. There were no fungicide agents reported in 2017. There were 27 insecticide agent entries. Unspecified pyrethroids were the most commonly reported agents, making up 22.2% of the class. Miscellaneous agents made up 33.3% of the class. Rodenticides and herbicides were infrequently reported.

Anticoagulants

Table S11 summarizes the 24 entries in the anticoagulant class. Warfarin was again the most commonly reported agent and made up the majority of the class (58.3%).

Other Pharmaceuticals

Table S12 presents the other pharmaceutical agent class. There were 18 entries in this category, with no agent contributing more than 3 cases. Hydrogen peroxide less than or equal to

Table 22 Pediatric exposures to drugs of abuse

A. Ethnicity				
Ethnicity	Total number of pediatric patients		% of total	
Hispanic	20		16.2	
Non-Hispanic	50		40.6	
Unknown	53		43.1	
B. Ethnicity by gender				
Ethnicity by gender	Male	% of males	Female	% of females
Hispanic	15	22.4	5	8.9
Non-Hispanic	45	67.2	5	8.9
Unknown	7	10.4	46	82.1
C. Race				
Race	Total # of pediatric patients		% of total	
Caucasian	73		59.3	
African American	26		21.1	
Asian	2		1.6	
American Indian/Alaska Native	1		0.8	
Mixed	2		1.6	
Unknown	19		15	
D. Race by gender				
Race by Gender	Male	% of males	Female	% of female
Caucasian	37	55.2	36	64.3
African American	13	19.4	13	23.2
Asian	2	3.0	0	0
American Indian/Alaska Native	0	0	1	1.8
Mixed	2	3.0	0	0
Unknown	13	19.4	6	10.7
E. Single and multiple ingestions				
Single vs multiple ingestion	Total number of pediatric patients		% of total	
Single agent	76		61.8	
Multiple agents	47		38.2	
F. Single and multiple ingestions by gender				
Single vs multiple agents	Males	% of males	Females	% of females
Single	44	65.7	32	57.1
Multiple	23	34.3	24	42.9
G. Agent classes involved in pediatric exposures to drugs of abuse				
Agent class	Total number of pediatric patients		% of total	
Psychoactive	57		46.3	
Sympathomimetic	54		43.9	
Opioid	29		23.6	
Antidepressant	10		8.1	
Sedative-hypnotic/muscle relaxant	7		5.7	
Anticholinergic/antihistamine	4		3.3	
Amphetamine-like hallucinogen	4		3.3	
Antipsychotic	4		3.3	
Herbals/dietary supplements	3		2.4	
Analgesics	3		2.4	
Cardiovascular	2		2.4	
Alcohol-ethanol	2		2.4	
H. Agent classes involved in pediatric exposures to drugs of abuse by gender				
Agent class	Males	% of males	Females	% of females
Psychoactive	32	47.7	25	44.6
Sympathomimetic	30	44.8	24	42.8
Opioid	16	23.9	13	23.2
Antidepressant	3	4.5	1	1.8
Sedative-hypnotic/muscle relaxant	3	4.5	4	7.1
Anticholinergic/antihistamine	3	4.5	1	1.8
Antipsychotic	2	2.9	2	3.6
Herbals/dietary supplements	2	2.9	1	1.8
Analgesics	0	0	3	5.4
Cardiovascular	1	1.5	4	7.1
Alcohol-ethanol	1	1.5	1	1.8
I. Reason for medical toxicology encounter				
Reason for encounter	Total number of pediatric patients		% of total	
Intentional pharmaceutical	34		27.6	
Attempt at self-harm	16		13.0	

Table 22 (continued)

Misuse/abuse	12		9.8	
Therapeutic use	2		1.6	
Unknown	4		3.3	
Intentional non-pharmaceutical	47		38.2	
Attempt at self-harm	1		0.8	
Misuse/abuse	26		21.1	
Use for therapeutic intent	1		0.8	
Drug concealment	1		0.8	
Unknown	18		14.6	
Unintentional pharmaceutical	13		10.6	
Unintentional non-pharmaceutical	27		21.9	
Malicious/criminal	1		0.8	
Interpretation of tox data	1		0.8	
J. Reason for medical toxicology encounter by gender				
Reason for encounter by gender	Male	% of males	Female	% of female
Intentional pharmaceutical	20	29.8	14	25.0
Attempt at self-harm	8	11.9	8	14.3
Misuse/abuse	9	13.4	3	5.4
Therapeutic use	1	1.5	1	1.8
Unknown	2	2.9	2	3.6
Intentional non-pharmaceutical	28	41.8	19	33.9
Attempt at self-harm	0	0	1	1.8
Misuse/Abuse	24	35.8	2	3.6
Use for therapeutic intent	1	1.5	0	0
Drug concealment	1	1.5	0	0
Unknown	2	2.98	16	28.6
Unintentional Pharmaceutical	8	11.9	5	8.9
Unintentional non-pharmaceutical	10	14.9	17	30.3
Malicious/criminal	1	1.5	0	0
Interpretation of tox data	0	0	1	1.8

10% and sumatriptan were the most commonly reported, each accounting for 16.7% of the class.

Weapons of Mass Destruction

Table S13 summarizes the potential weapons of mass destruction/riot agents/ radiological agents class. There were 7 entries with 42.9% being botulinum toxin.

Table 23 Diabetic medications

	N (%)
Metformin	57 (33.1)
Glipizide	40 (23.3)
Insulin	38 (22.1)
Glimepiride	15 (8.7)
Glyburide	12 (7.0)
Miscellaneous[a]	10 (5.8)
Class total	172 (100)

[a] Includes diabetic medication unspecified, sitagliptin, alogliptin, exenatide, and liraglutide

Anti-Parkinsonism Agents

Table S14 presents the 6 entries for the anti-parkinsonism agent class. Levodopa/carbidopa and pramipexole were reported in equal numbers each making up 33.3% of the agent class.

Table 24 Metals

	N (%)
Lead	32 (27.8)
Iron	26 (22.6)
Mercury	11 (9.6)
Cobalt	10 (8.7)
Arsenic	6 (5.2)
Chromium	6 (5.2)
Miscellaneous[a]	24 (20.9)
Class total	115 (100)

[a] Includes magnesium, cadmium, copper, gadolinium, manganese, aluminum, antimony, beryllium, cesium, metal unspecified, selenium, titanium, and zinc

Table 25 Herbal products and dietary supplements

	N (%)
Caffeine	30 (25.6)
Melatonin	25 (21.4)
Herbals/dietary supplements/vitamins unspecified	17 (14.5)
Multiple vitamin	5 (4.3)
Vitamin D	5 (4.3)
Eucalyptus oil	5 (4.3)
Limonene	3 (2.6)
Miscellaneous[a]	27 (23.1)
Class total	117 (100)

[a] Includes aloin (aloe vera extract or outer leaves), ashwangandha, black cohosh, Brazil seed (*Bertholletia excelsa*), citronella oil, dietary supplement unspecified, eugenol (clove oil), herbal (dietary) multibotanical, minerals unspecified, omega-3-acid ethyl esters, orange oil, potassium, senna, sodium chloride, tryptophan, vitamin A, vitamin B1 (thiamine), vitamin B3 (niacin), vitamin B6 (pyridoxine), vitamin C (ascorbic acid), and yohimbine

Foreign Bodies

Table S15 presents the ingested foreign bodies agent class. These were infrequently reported with 5 entries, 2 of which were batteries (40.0%).

Pulmonary Agents

Table S16 reports the 4 pulmonary agent entries. Albuterol made up 50.0% of the category.

Clinical Signs and Symptoms

The various clinical signs and symptoms categories report information on a diverse range of abnormal clinical findings. In order to be reported as being present, it must meet predefined criteria. For example, tachycardia is defined as a heart rate greater than 140 beats per minute. Additionally, each case may report more than one abnormality within a group or across groups. For example, a single case entry may have more than one vital sign abnormality, or may have both a vital sign abnormality and a neurological abnormality. The percentages for these categories are calculated relative to the total number of Registry cases. It is possible for the total to be more than 100%.

Table 26 Gases, irritants, vapors, and dusts

	N (%)
Carbon monoxide	50 (53.2)
Chlorine	4 (4.3)
Natural gas	4 (4.3)
Hydrogen sulfide	3 (3.2)
Miscellaneous[a]	33 (35.1)
Class total	94 (100)

[a] Includes acetonitrile, asbestos, bromine, carbon dioxide, chloramine, cyanide, diesel exhaust, dust, duster (canned air), fumes/vapors/gases unspecified, gases/vapors/irritants/dusts unspecified, halon, metal dust unspecified, nitric oxide, nitrogen oxides, ozone, petroleum vapors, polyurethane vapors, radon, smoke, sulfur dioxide, volatile organic compounds (VOC) unspecified, welding fumes, and wood dusts

Table 27 Household products

	N (%)
Cleaning solutions and disinfectants	17 (25.0)
Sodium hypochlorite ≤ 6%	13 (19.1)
Soaps and detergents	11 (16.2)
Laundry detergent pod	8 (11.8)
Hair product	4 (5.9)
Paint	4 (5.9)
Miscellaneous[a]	11 (16.2)
Class total	68 (100)

[a] Includes brake fluid, dishwasher detergent, dishwasher detergent pod, fabric softener, household product unspecified, phenylenediamine (hair dye), rubber cement, and sunscreens

Toxidromes

Table 29 summarizes the 2779 toxidrome entries in the Registry in 2017. The frequency of reported toxidromes remained consistent with prior years with the sedative-hypnotic toxidrome being by far the most commonly reported (15.7%). The anticholinergic toxidrome was the next most common (7.3%), followed by sympathomimetic (5.1%), opioid (3.7%), and serotonin syndrome (2.9%).

Table 28 Plants and fungi

	N (%)
Mold unspecified	29 (44.6)
Mushroom, other/unknown	8 (12.3)
Mitragyna speciosa (kratom)	6 (9.2)
Mushroom, psilocibin	5 (7.7)
Miscellaneous[a]	17 (26.2)
Class total	65 (100)

[a] Includes *Aesculus hippocastanum* (horse chestnut), Akuamma (*Picralima nitida*), *Amanita phalloides*, *Datura stramonium* (jimsonweed), *Hydrastis canadensis* (goldenseal), *Lupinus* (lupini beans), moonflower, *Nerium oleander*, strychnine, *Toxicoscordion venenosum* (death camas), Valerian root, and *Vicia faba* (fava bean)

Major Vital Sign Abnormalities

Table 30 summarizes the 2001 recorded major vital sign abnormalities. This represents 26.4% of the Registry, though cases may be associated with more than one major vital sign abnormality. The vital sign abnormalities remained similar in number to prior years. Tachycardia was the most commonly reported (11.8%). Hypotension was the next most common (6.2%).

Clinical Signs and Symptoms—Neurological

Table 31 presents the 6138 entries recording neurological signs and symptoms (81.0%). Coma/central nervous system depression remained the most commonly reported sign (33.3%). Agitation (16.5%) and delirium (11.1%) were the next most common.

Clinical Signs—Cardiovascular and Pulmonary

Table 32 presents the cardiovascular and pulmonary clinical signs. The most frequently reported cardiovascular sign was prolonged QTc (6.1%) followed by prolonged QRS (1.8%) and myocardial injury or infarction (1.5%). Among pulmonary signs, respiratory depression was the most commonly reported (10.4%) and made up the majority of this category.

Clinical Signs—Other Organ Systems

Table 33 presents the other organ system clinical signs. Among these additional categories, metabolic abnormalities were most frequently reported (12.4%). Cases reporting an elevated anion gap (5.2%) and a metabolic acidosis (4.7%) made up the majority of this category. The renal/musculoskeletal category was the next most common and cases were fairly evenly distributed between rhabdomyolysis (5.1%) and acute kidney injury (4.1%). Hematological signs made up 6.7% of the other organ systems. Coagulopathy (2.5%) and leukocytosis (1.8%) were the most commonly reported hematological signs. Among the gastrointestinal/hepatic signs, hepatotoxicity (3.2%) was the most common, followed by gastrointestinal bleeding (0.7%) and pancreatitis (0.6%). Dermatological signs were the least commonly reported category (4.5%). Rash (2.1%) and blister/bullae (1.1%) were the most common dermatological signs reported.

Fatalities

Tables 34 and 35 summarize cases which reported fatalities. Table 34 includes cases involving single agent exposures, and Table 35 presents those fatalities involving multiple agents. Table S17 in the Supplementary materials presents those fatalities in which it is unknown whether there was a related toxicological exposure.

There were a total of 93 fatalities in 2017, involving 1.2% of Registry cases. Forty-seven cases involved single agent exposures, 21 involved multiple agents, and 25 cases were unknown. The number of fatality cases decreased from 2016, though was similar to the years prior to that [6–8].

Seventeen fatality cases involved at least one opioid agent. Eight cases involved heroin. Two additional cases involved fentanyl or a fentanyl derivative, and 1 case involved U47700. There were 6 opioid fatalities in which only the single opioid agent was involved, the remainder were polypharmacy exposures, and some involved multiple opioids. Sedative-hypnotics/muscle relaxants, including gabapentinoids, were involved in 14 fatality cases. There were five cases that involved both a sedative-hypnotics/muscle relaxant and an opioid.

In 2017, there were 10 pediatric (age 0–18 years) deaths related to toxicologic exposures. The age range for these was 11 months to 18 years. Six of these were single agent exposures and 4 involved multiple agents. Two deaths were single agent exposures to acetaminophen, both in 14 year olds. One death involved an 18 year-old with a bupropion exposure that resulted in hypotension, ventricular dysrhythmia, QRS prolongation, QTc prolongation, myocardial injury, respiratory depression, metabolic acidosis, and central nervous system depression. He was treated with sodium bicarbonate, lipid resuscitation, vasopressors, intubation, and cardiopulmonary resuscitation. There was a death in an 11 month old related to cocaine and methamphetamine who had clinical signs of hypotension, tachycardia, agitation, and reactive airway disease and was treated with benzodiazepines. A 16 year old died related to an unspecified opioid after life support was withdrawn.

There were 38 fatality cases in which life support was withdrawn (0.5% of Registry cases). An additional, 7 cases were unknown whether life support was withdrawn. Brain death was declared in 12 cases, though there were 19 cases in which it was unknown if brain death was declared.

Adverse Drug Reactions

Table 36 presents the drugs most frequently associated with adverse drug reactions (ADRs). Lithium was again the most commonly reported agent in 2017 (4.1%), as it has been in past years. The next most commonly reported agents—valproic acid (3.8%), haloperidol (2.9%), and bupropion (2.7%)—have also been reported in past years. Digoxin was less frequently reported in 2017 and was not one of the top 10 agents as it has been in prior years [5–8]. The sedatives clonazepam (2.4%) and baclofen (2.1%) were among the most commonly reported agents associated with ADRs in 2017. This was a change from prior years, though in 2015, lorazepam was the second most commonly reported ADR [7].

Table 29 Toxidromes

	N (%)[a]
Sedative-hypnotic	1192 (15.7)
Anticholinergic	550 (7.3)
Sympathomimetic	387 (5.1)
Opioid	280 (3.7)
Serotonin syndrome	217 (2.9)
Alcoholic ketoacidosis	58 (0.8)
Sympatholytic	37 (0.5)
NMS	17 (0.2)
Washout syndrome	16 (0.2)
Overlap syndromes (MCS, chronic fatigue, etc.)	13 (0.2)
Anticonvulsant hypersensitivity	5 (0.1)
Miscellaneous[b]	7 (0.1)
Total	2779 (36.7)

NMS neuroleptic malignant syndrome

[a] Percentage equals number cases reporting specific toxidrome relative to total number of Registry cases in 2017 (*N* = 7577)

[b] Includes cholinergic, fume fever

Treatment

Antidotal Therapy Administered

Table 37 summarizes antidotal therapies reported to the Registry. Similar to prior years, N-acetylcysteine was the most commonly reported antidote (28.3%), followed by naloxone/nalmefene (21.9%) and sodium bicarbonate (11.8%).

Antivenom Therapy Administered

Table 38 summarizes the antivenom therapies reported in 2017. Similar to prior years, Crotalidae polyvalent immune fab (ovine) was the most commonly reported antivenom (92.0%). Other snake venoms were the next most common and made up 3.7% of the category.

Table 30 Major vital sign abnormalities

	N (%)[a]
Tachycardia (HR > 140)	896 (11.8)
Hypotension (systolic BP < 80 mmHg)	471 (6.2)
Bradycardia (HR < 50)	264 (3.5)
Bradypnea (RR < 10)	205 (2.7)
Hypertension (systolic BP > 200 mmHg and/or diastolic BP > 120 mmHg)	123 (1.6)
Hyperthermia (temp > 105 °F)	42 (0.6)
Total	2001 (26.4)[b]

HR heart rate, *BP* blood pressure, *RR* respiratory rate

[a] Percentage equals the number of cases relative to the total number of Registry cases in 2017 (*N* = 7577)

[b] Total reflects cases reporting at least one major vital sign abnormality. Cases may be associated with more than one major vital sign abnormality

Table 31 Clinical signs and symptoms—neurological

	N (%)[a]
Coma/CNS depression	2524 (33.3)
Agitation	1251 (16.5)
Delirium	843 (11.1)
Hyperreflexia/myoclonus/tremor	480 (6.3)
Seizures	427 (5.6)
Hallucinations	312 (4.1)
Dystonia/rigidity/extrapyramidal symptoms	106 (1.4)
Numbness/paresthesia	93 (1.2)
Weakness/paralysis	76 (1.0)
Peripheral neuropathy	26 (0.3)
Total	6138 (81.0)[a,b]

CNS central nervous system

[a] Percentage equals number cases relative to total number of Registry cases in 2017 (*N* = 7577)

[b] Total reflects cases reporting at least one neurological symptom. Cases may be associated with more than one neurological symptom

Pharmaceutical Supportive Care

Table 39 presents the pharmacological supportive care interventions that were reported in 2017. There were 3574 pharmacological interventions recorded. As in past years, benzodiazepines made up approximately half of the reported

Table 32 Clinical signs—cardiovascular and pulmonary

	N (%)[a]
Cardiovascular	
Prolonged QTc (≥ 500 ms)	460 (6.1)
Prolonged QRS (≥ 120 ms)	138 (1.8)
Myocardial injury or infarction	115 (1.5)
Ventricular dysrhythmia	71 (0.9)
AV Block (> 1st degree)	29 (0.4)
Total	813 (10.7)[b]
Pulmonary	
Respiratory depression	785 (10.4)
Aspiration pneumonitis	197 (2.6)
Acute lung injury/ARDS	110 (1.5)
Asthma/reactive airway disease	49 (0.6)
Total	1141 (15.1)[b]

ARDS acute respiratory distress syndrome

[a] Percentage equals number cases reporting signs of symptoms relative to total number of Registry cases in 2017 (N = 7577)

[b] Total reflects cases reporting at least one cardiovascular or pulmonary symptom. Cases may be associated with more than one symptom

Table 33 Clinical signs—other organ systems

	N (%)[a]
Metabolic	
Elevated anion gap (> 20)	394 (5.2)
Metabolic acidosis (pH < 7.2)	357 (4.7)
Hypoglycemia (glucose < 50 mg/dL)	131 (1.7)
Elevated osmole gap (> 20)	60 (0.8)
Total	942 (12.4)[b]
Renal/Musculoskeletal	
Rhabdomyolysis (CPK > 1000 IU/L)	383 (5.1)
Acute kidney injury (creatinine > 2.0 mg/dL)	309 (4.1)
Total	692 (9.1)[b]
Hematological	
Coagulopathy (PT > 15 s)	188 (2.5)
Leukocytosis (WBC > 20 K/μL)	139 (1.8)
Thrombocytopenia (platelets < 100 K/μL)	83 (1.1)
Hemolysis (Hgb < 10 g/dL)	62 (0.8)
Methemoglobinemia (MetHgb ≥ 2%)	21 (0.3)
Pancytopenia	16 (0.2)
Total	509 (6.7)[b]
Gastrointestinal/hepatic	
Hepatotoxicity (AST ≥ 1000 IU/L)	243 (3.2)
Gastrointestinal bleeding	54 (0.7)
Pancreatitis	46 (0.6)
Corrosive injury	34 (0.4)
Intestinal ischemia	3 (0.03)
Total	380 (5.0)[b]
Dermatological	
Rash	162 (2.1)
Blister/bullae	81 (1.1)
Angioedema	54 (0.7)
Necrosis	45 (0.6)
Total	342 (4.5)[b]

AST aspartate aminotransferase, *PT* prothrombin time, *WBC* white blood cells, *Hgb* hemoglobin, *CPK* creatine phosphokinase

[a] Percentage equals the number of cases reporting specific clinical signs compared to the total number of Registry cases in 2017 (*N* = 7577)

[b] Total reflects cases reporting at least one sign in the category. Cases may be associated with more than one symptom

pharmacologic interventions (49.1%). Opioids (14.3%) and vasopressors (8.4%) were the next most commonly reported. There were 2501 cases (33.0%) that involved at least one form of pharmacological supportive care.

Non-pharmaceutical Supportive Care

Table 40 presents the non-pharmacological supportive care interventions. The majority of this category was made up of intravenous fluid resuscitation (72.3%). Intubation/ventilatory management was the next most common intervention (22.9%). Additional interventions were less common with none making up more than 2% of the category. Overall, 3141 Registry cases (41.5%) reported at least one non-pharmacological intervention.

Chelation Therapy Administered

Table 41 summarizes chelation therapy reported to the Registry in 2017. There were 31 total chelator agents reported in 2017. Twenty-five cases involved the delivery of a single chelating agent, while 5 cases involved two or more agents. The most commonly administered chelator was dimercaptosuccinic acid (DMSA) (38.7%). Deferoxamine was the next most common (25.8%).

Decontamination Interventions Administered

Table 42 presents decontamination interventions. Activated charcoal remained by a large margin the most commonly reported decontamination measure (79.6%). External irrigation (8.1%) and whole bowel irrigation (7.7%) were the next most commonly reported. Gastric lavage was an uncommon intervention (4.6%). Overall, there were 264 cases that reported at least one kind of intervention (3.5%). Some cases reported more than one decontamination method.

Enhanced Elimination Interventions Administered

Table 43 describes enhanced elimination techniques reported to the Registry. Urinary alkalinization was the most commonly reported intervention (26.4%). Hemodialysis for toxin removal was the next most common (24.8%) and hemodialysis for any other indication made up an additional 18.6% of the treatments in this group. Continuous renal replacement therapy made up 24.8% of the enhanced elimination techniques. There were 226 cases (3.0% of the Registry) reporting at least one enhanced elimination method. Some cases reported more than one.

Table 44 presents more detailed information about cases in which extracorporeal membrane oxygenation ECMO was delivered from 2013 through 2017. During the 5-year period of data collection, there were 62 cases reporting the use of ECMO. The mean age of patients was 22 years. Most cases involved intentional ingestions.

Discussion

The data collection in this eighth year of the ToxIC case registry has been characterized by continued strong data collection and a number of important observations related to new trends and findings. Although the slight reduction in the

Table 34 2017 fatalities reported in ToxIC Registry with known toxicological exposure: single agent

Age/ gender[a]	Agents involved	Clinical findings	Life support withdrawn	Brain death confirmed	Treatment[b]
51F	Acetaminophen	ALI, AGT, CNS, DLM, RFX, MA, AG, HPT, HYS, GIB, PLT, AKI	Yes	Unknown	NAC, vasopressors, continuous renal replacement, intubation, IV fluids
14F	Acetaminophen	None listed	No	No	NAC
34F	Acetaminophen	HTN, TC, RD, CNS, MA, HPT, CPT, AKI	No	No	NAC, vitamin K, vasopressors, continuous renal replacement, intubation
35M	Acetaminophen	HT, TC, CNS, MA, HPT, CPT	No	No	NAC, vitamin K, continuous renal replacement, intubation
53F	Acetaminophen	CNS, MA, HPT, CPT, AKI	Yes	No	NAC, vasopressors, corticosteroids, continuous renal replacement, intubation
37M	Acetaminophen	HT, TC, AP, CNS, DLM, MA, AG, HPT, GIB, CPT, WBC, AKI	Yes	Unknown	NAC, hemodialysis, intubation, IV fluids
38M	Acetaminophen	HPT, OTH2	Yes	No	NAC, thiamine, vasopressors, benzodiazepines, neuromuscular blockers, opioids, continuous renal replacement, intubation, IV fluids, transfusion
14F	Acetaminophen	HPT	No	No	NAC
55F	Amitriptyline	HT, QRS, QTC, RD, CNS, SZ, AKI	No	No	$NaHCO_3$, benzodiazepines, intubation, IV fluids
52F	Amlodipine	HT, BC, RD, CNS, MA	No	No	Calcium, glucagon, insulin-euglycemic therapy, methylene blue, vasopressors, neuromuscular blockers, opioids, continuous renal replacement, CPR, intubation, IV fluids
60M	Amphetamine	MI, ALI, AGT, DLM, RFX, MA, AG, HPT, PLT, AKI, RBM	Yes	No	Fomepizole, NAC, vasopressors, bronchodilators, antiarrhythmics, benzodiazepines, neuromuscular blockers, opioids, continuous renal replacement, CPR, aortic balloon pump
18M	Bupropion	HT, VD, QRS, QTC, MI, RD, CNS, MA	Yes	Yes	Lipid resuscitation, $NaHCO_3$, vasopressors, CPR, intubation, IV fluids
71M	Carbon monoxide	ALI, CNS, AG	No	No	Hydroxocobalamin
48F	Carbon monoxide	HT, QTC, MI, RD, CNS, MA	No	No	Vasopressors, CPR, intubation
33F	Clonazepam	CNS	No	No	None listed
47M	Cocaine	HT, HYT, VD, CNS, MA, GIB, AKI	Unknown	Unknown	Vasopressors, activated charcoal, hemodialysis, continuous renal replacement, CPR, intubation, IV fluids
43F	Cocaine	CNS, MA, AG, HPT, AKI, RBM	No	No	Calcium, lipid resuscitation, naloxone, $NaHCO_3$, intubation, IV fluids
51M	Cocaine	MI, RD, AGT, DLM, SZ, WBC, RBM	Yes	No	Vasopressors, antihypertensives, CPR, intubation, IV fluids
65F	Colchicine	HT, BC, MI, CNS, MA, PCT, AKI, OTH2	No	No	None listed
23M	Digitoxin	HT, BC, VD, QRS, MA, AG, AKI	Yes	No	Digoxin Fab
18F	Diphenhydramine	AGT	No	No	Physostigmine, benzodiazepines, IV fluids
19M	Diphenhydramine	AGT, DLM	No	No	Benzodiazepines, IV fluids
47F	Doxepin	HT, TC, BP, HYT, VD, QRS, MI, RD, CNS, MA, HYS, CPT, WBC, AKI, RBM	Yes	Unknown	$NaHCO_3$, vasopressors, intubation, IV fluids
49M	Ethanol	RD, CNS, HGY, MA, AG, OG, PNC, GIB, HYS, CPT, PLT, PCT, WBC	Yes	No	Fomepizole, vasopressors, benzodiazepines, glucose, opioids, continuous renal replacement, intubation, IV fluids, transfusion
32M	Ethanol	CNS	No	No	Folate, thiamine, IV fluids
30M	Ethanol	RD, CNS	Unknown	Unknown	Intubation, IV fluids
31F	Ethanol	CNS	Unknown	Unknown	None listed
60M	Ethanol	HT, AP, CNS, HCN, MA, AG, PNC, CPT	Yes	Unknown	Vasopressors, antiarrhythmics, antihypertensives, antipsychotics, benzodiazepines, opioids, intubation, IV fluids
48F	Heroin	HT, VD, CNS, MA, HPT, AKI	Yes	No	NAC, vasopressors, CPR, intubation, IV fluids
25M	Heroin	HT, AP, RD, CNS	Yes	Yes	Naloxone, vasopressors, benzodiazepines, intubation
32M	Heroin	HT, RD, CNS	Unknown	Unknown	Naloxone, vasopressors, CPR, intubation, IV fluids
35M	Heroin	None listed	No	No	Opioids
66M	Metaxalone	HT, CNS, DLM, RFX, AKI	Yes	Yes	Benzodiazepines, intubation, IV fluids
50M	Metformin	HT, RD, CNS, MA, AKI	Yes	Yes	Vasopressors, continuous renal replacement, intubation, IV fluids
67M	Metformin	HT, QTC, ALI, RD, CNS, MA, AG, GIB, CPT, WBC, AKI	Yes	Unknown	Calcium, methylene blue, $NaHCO_3$, thiamine, vasopressors, benzodiazepines, neuromuscular blockers, opioids, corticosteroids, continuous renal replacement, intubation, IV fluids
> 89F	Metformin	HT, QTC, CNS, MA, AG, AKI	Unknown	Unknown	IV fluids
57M	Methamphetamine	HT, TC, MI, RD, CNS, MA, AG	Yes	No	None listed

Table 34 (continued)

Age/ gender[a]	Agents involved	Clinical findings	Life support withdrawn	Brain death confirmed	Treatment[b]
35M	Methamphetamine	HT, TC, QRS, MI, SZ, MA, HPT, CPT, AKI, RBM	Yes	No	Vasopressors, benzodiazepines, intubation, IV fluids
55M	Methanol	SZ, MA, AG, OG	Yes	Unknown	Fomepizole, antiarrhythmics, benzodiazepines, hemodialysis, intubation, IV fluids
84F	Methylene chloride	None listed	No	No	None listed
29M	Methylfentanyl	HT, TC, HYT, MI, RD, CNS, MA, HPT, CPT, AKI, RBM	Yes	No	Naloxone, vasopressors, benzodiazepines, opioids, intubation, IV fluids
16M	Opioid unspecified	HTN, HT, TC, ALI, CNS, MA, HPT	Yes	No	Atropine, naloxone, $NaHCO_3$, vasopressors, antihypertensives, benzodiazepines, opioids, CPR, intubation
54M	Quetiapine	QTC, RD, CNS	No	No	IV fluids
71M	Rasburicase	HT, ALI, CNS, MA, MET, HYS, AKI	No	No	Methylene blue, vasopressors, glucose, continuous renal replacement, intubation, IV fluids, transfusion
65F	Sodium hydroxide	RD, CNS, CRV, INT, OTH2	Yes	Yes	Vasopressors, opioids, intubation, IV fluids
58F	Verapamil	HT, BC, AVB, AP, RD, CNS, MA, PNC, AKI	No	No	None listed
17M	Vitamin A	HT, TC, VD, RD, CNS, MA, HYS, PLT, WBC	Yes	Unknown	Calcium, insulin-euglycemic therapy, lipid resuscitation, vasopressors, benzodiazepines, CPR, ECMO, intubation

Fatalities reported with known toxicological exposure: based on response from medical toxicologist "Did the patient have a toxicological exposure?" equals yes with known agent(s)

wk weeks, *m* months, *AG* anion gap, *AGT* agitation, *AKI* Acute kidney injury, *ALI* acute lung injury/ARDS, *AP* aspiration pneumonia, *AVB* AV block, *BC* bradycardia, *BP* bradypnea, *CNS* coma/CNS depression, *CPT* coagulopathy, *CRV* corrosive injury, *DLM* delirium, *EPS* dystonia/rigidity, *GIB* GI bleeding, *HCN* hallucinations, *HGY* hypoglycemia, *HPT* hepatoxicity, *HT* hypotension, *HTN* hypertension, *HYS* hemolysis, *HYT* hyperthermia, *INT* intestinal ischemia, *MA* metabolic acidosis, *MET* methemoglobinemia, *MI* myocardial injury/ischemia, *NP* neuropathy, *OG* osmole gap, *OTH1* rash, *OTH2* skin blisters, necrosis, *PCT* pancytopenia, *PLT* thrombocytopenia, *PNC* pancreatitis, *PST* paresthesia, *QRS* QRS prolongation, *QTc* QTc prolongation, *RAD* asthma/reactive airway disease, *RBM* rhabdomyolysis, *RD* respiratory depression, *RFX* hyperreflexia/tremor, *SZ* seizures, *TC* tachycardia, *VD* ventricular dysrhythmia, *WBC* leukocytosis, *WKN* weakness/paralysis, *BAL* dimercaprol, *CPR* cardiopulmonary resuscitation, *ECMO* extracorporeal membrane oxygenation, *NAC* n-acetyl cysteine, *$NaHCO_3$* sodium bicarbonate

[a] Age in years unless otherwise stated

[b] Pharmacological and non-pharmacological support as reported by medical toxicologist

number of cases entered is multifactorial, probably a major reason is our continued quality assurance efforts and dropping poorly performing sites from the Consortium.

The Registry serves as a large source of information on poisoning cases as evaluated by bedside medical toxicologists. Although the Toxic Registry is not technically population based, it does have multiple sites broadly around the USA. As such, it may be used in conjunction with other types of registries such as poison centers and health agencies to produce a more detailed understanding of poisoning trends, novel exposures, and their public health implications.

Information on novel exposure surveillance is not included with this annual report, but is being analyzed with results to be reported separately.

Overall, this annual report finds that the most common agent classes, agents, demographics, types of encounters, toxidromes, and treatments remain similar year-to-year. Some notable trends in the Registry as well as trends in a larger national context are discussed.

Use of Extracorporeal Membrane Oxygenation

The ToxIC case registry has been gathering data on extracorporeal membrane oxygenation (ECMO) since 2013. Analysis of these cases is presented in Table 44. Over 5 years, a total of 62 patients were recorded as receiving ECMO, accounting for a very small percentage of patients in the overall registry. The number of cases per year was relatively consistent, other than in 2015 where there were more cases than typically seen. ECMO patients were relatively younger compared to the total registry sample, with an overall mean age of 22 years. Most of the cases were likely to be related to a toxicologic exposure, with intentional exposures predominating. The most frequently encountered agent classes were analgesics, opioids, cardiovascular agents, psychiatric medications, or a diabetic medication, specifically metformin. Though ECMO is generally considered only in the most critically ill patients, the majority of the patients (76%) survived. This may be related to the superior prognosis of critically ill poisoned patients as compared to patients who are ill from other medical causes.

Table 35 2017 fatalities reported in ToxIC Registry with known toxicological exposure: multiple agents

Age/ gender[a]	Agents involved	Clinical findings	Life support withdrawn	Brain death confirmed	Treatment[b]
52F	Acetaminophen, hydrocodone	None listed	No	No	None listed
86F	Acetaminophen, ibuprofen	TC	Yes	Unknown	NAC,
60F	Alprazolam, clonazepam, quetiapine	RD, CNS	No	No	Intubation, IV fluids
43F	Alprazolam, gabapentin	QRS, QTC, MI, RD, MA, AG	Yes	Yes	$NaHCO_3$, vasopressors, continuous renal replacement, CPR, intubation, IV fluids
35F	Amitriptyline, buprenorphine, pregabalin, lorazepam	HT, TC, QRS, RD, CNS, MA, AG	No	No	Calcium, dantrolene, lipid resuscitation, naloxone, $NaHCO_3$, vasopressors, opioids, intubation, IV fluids
33M	Amitriptyline, clonazepam	TC, QRS, QTC, ALI, AP, RD, CNS, AG, CPT, RBM	No	No	$NaHCO_3$, intubation, IV fluids
29F	Amlodipine, nifedipine, metoprolol	HT, BC, VD, RD, CNS, SZ, HGY, MA, AG, HPT, HYS	No	No	Calcium, glucagon, insulin-euglycemic therapy, $NaHCO_3$, vasopressors, benzodiazepines, glucose, opioids, hemodialysis, CPR, intubation
75M	Atenolol, diltiazem, amiodarone	HT, BC, VD, QRS, RD, EPS	Yes	Yes	Calcium, glucagon, vasopressors, benzodiazepines, neuromuscular blockers, continuous renal replacement, intubation, IV fluids
52F	Chlorzoxazone, amitriptyline, tramadol	CNS, HPT	Unknown	Unknown	NAC
26F	Clonazepam, doxepin, fluoxetine, quetiapine, trazodone, bupropion	HT, BC, VD, RD, CNS, MA	No	No	Naloxone, vasopressors, antiarrhythmics, CPR, cardioversion, intubation, IV fluids, therapeutic hypothermia
11m M	Cocaine, methamphetamine	HT, TC, RAD, AGT	No	No	Benzodiazepines
12F	Diazepam, gabapentin	HT, TC, BP, HYT, RD, CNS, MA, AG	No	No	Naloxone, neuromuscular blockers, intubation, IV fluids
39F	Digoxin, diltiazem, cardiovascular agent unspecified, warfarin	HT, VD, ALI, RD, CNS, MA, CPT, AKI	Yes	Unknown	Calcium, digoxin Fab, glucagon, insulin-euglycemic therapy, lipid resuscitation, $NaHCO_3$, vasopressors, antiarrhythmics, glucose, CPR, cardioversion, intubation, IV fluids, pacemaker
41F	Ethanol, lorazepam	CNS	Unknown	Unknown	Antipsychotics, benzodiazepines,
30F	Fentanyl, quinine, buclizine, methyl norfentanyl	BP, MI, AP, CNS, MA, AKI, RBM	Yes	No	Naloxone, opioids, intubation, IV fluids
34M	Heroin, cocaine, levamisole	HT, BC, AP, RD, WBC	Yes	Yes	CPR, IVF, therapeutic hypothermia
26F	Heroin, cocaine	AVB, CNS, AG, HPT, RBM	Yes	Yes	$NaHCO_3$, vasopressors, opioids, intubation
25M	Heroin, ethanol, alprazolam, cocaine	HT, MI, RD, CNS, MA, AG, HPT, PNC, AKI	Yes	Yes	Vasopressors, CPR, ECMO, intubation, IV fluids, therapeutic hypothermia
20F	Ibuprofen, citalopram, trazodone, penicillin, ethanol	CNS	No	No	NAC, IVF
56M	Imipramine, cyclobenzaprine, hydrocodone	QTC, RD, CNS	No	No	Benzodiazepines, intubation, IV fluids
52M	Methamphetamine, amphetamine	HT, MI, AP, RD, AGT, CNS, MA, HPT, WBC, AKI, RBM	Yes	Unknown	None listed
31M		None listed	Yes	No	None listed

Table 35 (continued)

Age/ gender[a]	Agents involved	Clinical findings	Life support withdrawn	Brain death confirmed	Treatment[b]
	MDMA, hydromorphone, methadone, marijuana				
57M	Nortriptyline, gabapentin	QRS, MI, RD, CNS	No	No	$NaHCO_3$, intubation, IV fluids
52M	Olanzapine, hydrochlorothiazide	TC, DLM	No	No	Benzodiazepines, IV fluids
14F	Propofol, ketamine	HT, BC, MI, RD, SZ, MA, AG	Yes	Unknown	Vasopressors, hemodialysis, ECMO, intubation
63M	Propranolol, citalopram	HT, BC, AVB, RD, CNS	No	No	Glucagon, vasopressors, antiarrhythmics, benzodiazepines, neuromuscular blockers, CPR, intubation, IV fluids
33F	Propranolol, escitalopram, lamotrigine	HT, TC, BC, HYT, VD, QRS, QTC, AVB, MI, RD, AGT, CNS, DLM, EPS, RFX, SZ, HGY, MA, AG, PLT, RBM	Yes	No	Anticoagulation reversal, calcium, facto replacement, glucagon, insulin-euglycemic therapy, $NaHCO_3$, vasopressors, antiarrhythmics, benzodiazepines, glucose, intubation, IV fluids, transfusion
13F	Quetiapine, acetaminophen	HT, ALI, CNS, MA, AG, AKI	Yes	Yes	NAC, hemodialysis, ECMO, intubation, IV fluids
47F	Trazodone, ethanol, heroin	QTC, RFX, GIB	Yes	Unknown	CPR, intubation, IV fluids, transfusion
39F	U47700 (designer opioid), venlafaxine, gabapentin, doxepin	BP, ALI, AP, RD, CNS, MA	Yes	Yes	IV fluids

Fatalities reported with known toxicological exposure: based on response from medical toxicologist "Did the patient have a toxicological exposure?" equals yes with known agent(s)

wk weeks, *m* months, *AG* anion gap, *AGT* agitation, *AKI* Acute kidney injury, *ALI* acute lung injury/ARDS, *AP* aspiration pneumonia, *AVB* AV block, *BC* bradycardia, *BP* bradypnea, *CNS* coma/CNS depression, *CPT* coagulopathy, *CRV* corrosive injury, *DLM* delirium, *EPS* dystonia/rigidity, *GIB* GI bleeding, *HCN* hallucinations, *HGY* hypoglycemia, *HPT* hepatoxicity, *HT* hypotension, *HTN* hypertension, *HYS* hemolysis, *HYT* hyperthermia, *INT* intestinal ischemia, *MA* metabolic acidosis, *MET* methemoglobinemia, *MI* myocardial injury/ischemia, *NP* neuropathy, *OG* osmole gap, *OTH1* rash, *OTH2* skin blisters, necrosis, *PCT* pancytopenia, *PLT* thrombocytopenia, *PNC* pancreatitis, *PST* paresthesia, *QRS* QRS prolongation, *QTc* QTc prolongation, *RAD* asthma/reactive airway disease, *RBM* rhabdomyolysis, *RD* respiratory depression, *RFX* hyperreflexia/tremor, *SZ* seizures, *TC* tachycardia, *VD* ventricular dysrhythmia, *WBC* leukocytosis, *WKN* weakness/paralysis, *BAL* dimercaprol, *CPR* cardiopulmonary resuscitation, *ECMO* extracorporeal membrane oxygenation, *NAC* n-acetyl cysteine, *$NaHCO_3$* sodium bicarbonate

[a] Age in years unless otherwise stated

[b] Pharmacological and non-pharmacological support as reported by medical toxicologist

Table 36 Most common drugs associated with ADRs

	N (%)[a]
Lithium	14 (4.1)
Valproic acid	13 (3.8)
Haloperidol	10 (2.9)
Bupropion	9 (2.7)
Phenytoin	9 (2.7)
Clonazepam	8 (2.4)
Diphenhydramine	8 (2.4)
Baclofen	7 (2.1)

ADRs adverse drug reactions

[a] Percentages are calculated out of the total number of cases reporting an ADR (*N* = 339)

Alternatively, there may be an inconsistent reporting of deaths in the Registry which could have increased this figure. Since a patient might die at some time after a toxicology consult and the Registry case entry, the consultant would need to actively go back and update the case after a death occurs.

Exposures in Pediatric Patients

As with the Registry overall, analgesics and antidepressants were the most commonly reported agent classes in pediatric patients (Table 8). The anticholinergic/antihistamine class was the next most common in pediatrics, though it was sixth overall in the Registry. The majority of pediatric patients with anticholinergic/antihistamine exposures were in the 13–18 year old age group. Opioids were ranked sixth in agent class frequency for pediatrics with the majority of exposures

Table 37 Antidotal therapy

	N (%)[a]
N-acetylcysteine	820 (28.3)
Naloxone/nalmefene	633 (21.9)
Sodium bicarbonate	343 (11.8)
Thiamine	267 (9.2)
Folate	157 (5.4)
Fomepizole	102 (3.5)
Calcium	74 (2.6)
Physostigmine	66 (2.3)
Glucagon	63 (2.2)
Octreotide	57 (2.0)
Cyproheptadine	36 (1.2)
L-carnitine	34 (1.2)
Vitamin K	34 (1.2)
Atropine	33 (1.1)
Insulin-euglycemic therapy	32 (1.1)
Flumazenil	31 (1.1)
Lipid resuscitation	27 (0.9)
Pyridoxine	24 (0.8)
Fab for digoxin	16 (0.6)
Methylene blue	11 (0.4)
Dantrolene	8 (0.3)
Hydroxocobalamin	8 (0.3)
Bromocriptine	6 (0.2)
2-PAM	4 (0.2)
Coagulation factor replacement	3 (0.1)
Silimarin	2 (0.1)
Anticoagulation reversal	2 (0.1)
Botulinum antitoxin	1 (< 0.1)
Nitrites	1 (< 0.1)
Total	2895 (100)

[a] Percentages are out of the total number of antidotes administered (2895); 2319 registry cases (30.6%) received at least one antidote. Cases may have involved the use of multiple antidotes

involving 13–18 year olds, though they were also the most common agent class in those under age 2.

The most commonly reported pediatric agent classes in ToxIC are notable in that they are dissimilar to those reported by the National Poison Data System (NPDS) [9]. The NPDS describes the most common agent class exposures reported in children less than or equal to 5 years old. When the same subset of patients in the ToxIC database is compared, there are differences in the frequency of agent classes reported. Whereas the NPDS reported the most common pediatric exposures as involving cosmetic and household cleaning products, these were infrequently reported in the ToxIC database. Household products were ranked 15th in frequency in ToxIC, making up just 2.5% of pediatric exposures. The other non-pharmaceutical class made up only 0.3% of pediatric

Table 38 Antivenom therapy

	N (%)[a]
Crotalidae polyvalent immune fab (ovine)	173 (92.0)
Other snake antivenom	7 (3.7)
Scorpion antivenom	3 (1.6)
Spider antivenom	2 (1.1)
Not recorded	3 (1.6)
Total	188 (100)

[a] Percentages are out of the total number of antivenom treatments administered ($N = 188$)

exposures. The leading agent class in children ≤ 5 years old in the ToxIC database was cardiovascular agents (15.6%), though this agent class made up only 2.1% of the exposures in the NPDS [9]. Opioids (8.4%) and sympathomimetics (7.7%) were the next most frequently reported agents classes in the ToxIC database. The NPDS reported foreign bodies/toys/miscellaneous as the fourth most common agent class (6.5%), compared to being one of the least commonly reported agent classes in ToxIC (0.3%).

Of note, the most recent NPDS data available are from 2016, though the agent classes reported are consistent with prior NPDS reports and would not be expected to significantly change in 2017 [10, 11]. Additionally, there are some differences in the categorization of agents into agent classes between the NPDS and ToxIC, though the general trends are still clear. These differences in agent class reporting between the NPDS and ToxIC support the idea that the ToxIC database represents a unique population of patients, with an inclination

Table 39 Supportive care—pharmacological

	N (%)[a]
Benzodiazepines	1756 (49.1)
Opioids	511 (14.3)
Vasopressors	302 (8.4)
Antipsychotics	250 (7.0)
Neuromuscular blockers	197 (5.5)
Anticonvulsants	146 (4.1)
Glucose (concentration > 5%)	137 (3.8)
Antihypertensives	83 (2.3)
Albuterol (or other bronchodilator)	62 (1.7)
Corticosteroids	56 (1.6)
Antiarrhythmics	41 (1.1)
Beta blockers	24 (0.7)
Vasodilators	9 (0.3)
Total	3574 (100)

[a] Percentages are out of the total number of treatments administered (3574); 2501 registry cases (33.0%) received at least one form of pharmacological treatment. Cases may have involved the use of multiple forms of treatment

Table 40 Supportive care—non-pharmacological

	N (%)[a]
IV fluid resuscitation	2912 (72.3)
Intubation/ventilatory management	919 (22.9)
CPR	74 (1.8)
Transfusion	36 (0.9)
Therapeutic hypothermia	18 (0.4)
Hyperbaric oxygen	15 (0.4)
ECMO	14 (0.3)
Cardioversion	11 (0.3)
Pacemaker	9 (0.2)
Organ transplantation	3 (0.1)
Aortic balloon pump	1 (0.02)
Total	4012 (100)

[a] Percentages are out of the total number of treatments administered (4012); 3141 registry cases (41.5%) received at least one form of non-pharmacological treatment. Cases may have involved the use of multiple forms of treatment. CPR Cardiopulmonary resuscitation, ECMO extra-corporeal membrane oxygenation

towards more severe exposures. This is likely due to that fact that the cases entered are ones in which a patient presented for care and were evaluated by a medical toxicologist. Additionally, the differences between agent class frequencies in the two databases may speak to the important role of poison control centers in reducing the overuse of healthcare settings for non-life threatening exposures that can be safely managed at home.

Pediatric Exposures to Drugs of Abuse

A total of 832 patients from the 2017 ToxIC registry were exposed to drugs of abuse with 123 patients of those being between the ages of 0–18 (14.8%). Pediatric patients exposed to drugs of abuse made up 1.6% of the total Registry. Cases were included after a manual search of pediatric patients for drugs of abuse. Any additional agents in a polypharmacy exposure were also included. The following agents were included: 25I-NBOMe, alprazolam, bupropion, butanoyl-4-fluorofentanyl, caffeine, cannabinoid non-synthetic, cannabinoid synthetic, clonidine, cocaine, delta-9-tetrahydrocannabinol, diphenhydramine, ethanol, fentanyl, fluoxetine, gamma hydroxybutyrate, heroin, hydroxyzine, ketamine, LSD (lysergic acid diethylamide), marijuana, methamphetamine, methylenedioxymethamphetamine, methylnorfentanyl, methylphenidate, molly, N-allyl norfentanyl, nicotine, oxycodone, paliperidone, pharmaceutical THC, phencyclidine, phenylephrine, psychoactive unspecified, quetiapine, sympathomimetic unspecified, tramadol, trazodone, and valproic acid. Those patients presenting for withdrawal were excluded from the data analysis. The majority of the pediatric patients were between the ages of 13–18 (54%) followed by ages 2–6 (22%). Fifty-nine percent identified as Caucasian and non-Hispanic (41%). Pediatric patients were more likely to present due to an intentional exposure of a non-pharmaceutical agent (38.2%). The most commonly reported class of drug was psychoactives (46.3%) followed by sympathomimetics (43.9%). The majority of patients had a single agent exposure (61.8%) as opposed their adult counterparts. There were 2 pediatric deaths related to drugs of abuse. The first was an 11-month-old Caucasian male admitted after an unintentional exposure to cocaine and methamphetamine. The second was a 14-year-old female who received ketamine and propofol. She later developed propofol infusion syndrome and sustained cardiac

Table 41 Chelation therapy

	N (%)[a]
DMSA	12 (38.7)
Deferoxamine	8 (25.8)
Dimercaprol	6 (19.4)
EDTA	5 (16.1)
Total	31 (100)

[a] Percentages are out of the total number of chelation treatments administered (31); 25 registry cases (0.3%) received at least one form of chelation treatment. DMSA dimercaptosuccinic acid, EDTA ethylenediaminetetraacetic acid

Table 42 Decontamination

	N (%)[a]
Activated charcoal	226 (79.6)
External irrigation	23 (8.1)
Whole bowel irrigation	22 (7.7)
Gastric lavage	13 (4.6)
Total	284 (100)

[a] Percentages are out of the total number of treatments administered (334); 264 registry cases (3.5%) received at least one form of decontamination

Table 43 Enhanced elimination

	N (%)[a]
Urinary alkalinization	64 (26.4)
Hemodialysis (toxin removal)	60 (24.8)
Continuous renal replacement therapy	60 (24.8)
Hemodialysis (other indication)	45 (18.6)
Multiple-dose activation charcoal	11 (4.5)
Exchange transfusion	2 (0.8)
Total	242 (100)

[a] Percentages are out of the total number of treatments administered (242); 226 registry cases (3.0%) received at least one form of enhanced elimination

Table 44 Cases involving extracorporeal membrane oxygenation (ECMO): a detailed look from 2013 to 2017

Year	ECMO cases	%[a]	Age range (mean)[b]	Deaths	Toxicological etiology?			Type of exposure				Primary agent category								
					Yes	No	U	IN	UN	U	Other	Analgesic	Opioid	CV	Psych	Symp	Antichol	Sed	Other[c]	U
2013	11	0.12%	2–48 (20.1)	2	8	2	1	5	3	1	2			2	3		2	1	7	1
2014	7	0.08%	2–29 (17.4)	0	4	1	2	4	1	0	2		1	1	2	1		5	4	2
2015	19	0.23%	1–43 (20.1)	6	16	3	0	14	1	1	3	5	2	4	4	3	1	1	6	1
2016	11	0.13%	15–47 (26.6)	3	8	0	3	10	0	1	0	2	3	2	3		2		2	2
2017	14	0.18%	13–51 (24.4)	4	14	0	0	10	2	0	2	3	5	5	3	1		4	6	1
Totals	60		1–51 (22)	15	50	6	6	43	7	3	9	10	11	14	15	5	5	11	25	7

U unknown, *IN* intentional *UN* unintentional, *CV* cardiovascular agents, *Psych* antidepressant agents and antipsychotic agents, *Symp* sympathomimetics, *Antichol* anticholinergics, *Sed* sedative-hypnotics/muscle relaxants

[a] Percentages are out of the total number of ToxIC registry cases for that year ($N = 7577$ for 2017; $N = 8529$ for 2016; $N = 8115$ for 2015; $N = 9094$ for 2014; $N = 8284$ for 2013)

[b] 2 cases had unknown/unlisted age; these were not included in the means

[c] Other category included 4 ethanol, 4 gases/irritants/vapors/dusts, 4 diabetic agents, 3 anticonvulsants, 2 psychoactives, 1 chemotherapeutic/immunological agent, 2 antimicrobial, 1 herbicide, 1 insecticide, 1 herbal products/dietary supplements, 1 gastrointestinal agent, and 1 endocrine agent

arrest. The circumstances surrounding ketamine exposure were not described. When analyzed by gender, there were no significant differences in the reason for exposure, agent used or demographics in the pediatric drug of abuse population.

Cannabis—the Trouble with Edibles

Cannabis is the most commonly used illicit drug in the USA, according to the 2016 National Survey on Drug Use and Health [12]. While cannabis is typically consumed through smoke inhalation, the increase in the legalization of cannabis has made "edibles" (products containing cannabis intended for oral consumption) more accessible as the cannabis market continues to evolve [13]. There is often significant variation in the potency of "edibles," which can contribute to accidental overdose, especially with inexperienced users. Perhaps more troubling is the unintentional ingestion of edibles by young children and adolescents that can result in significant toxicity, including agitation, ataxia, hallucinations, lethargy, myoclonus, respiratory depression, seizures, and tachycardia [14–16].

Since the first edibles cases were reported in the ToxIC Registry in 2012, there has been a substantial increase in the number of cases involving children 0–6 years of age [4]. In 2012, there were no "edibles" cases reported to the ToxIC Registry that involved children 0–6 years of age, compared with 10 cases in 2016 (52.6% of total "edibles" cases) and 8 cases in 2017 (50.0% of total "edibles" cases) [4, 8]. In 2017, among the children 0–6 years of age that had unintentionally consumed a product containing cannabis, CNS depression was reported in five, delirium in three, agitation in one, hallucinations in one, respiratory depression in one, and seizures in one, with no fatalities reported. Certainly, this is a concerning trend, and clinicians should be proactive in educating parents about the dangers that "edibles" pose to young children.

Increase in ToxIC Gabapentinoid (GP) Cases

Gabapentin and pregabalin are substituted derivatives of the neurotransmitter gamma-aminobutyric acid (GABA) labeled in the USA for the treatment of neurologic pain and seizures [17, 18]. Their weak GABA-mimetic features include feelings of relaxation and euphoria reported by some patients and recreational users [17]. As with the benzodiazepines and other addictive GABA-mimetics, withdrawal symptoms can occur and tolerance to the euphoria develops, increasing their addiction potential [17]. This, combined with a global increase in GP prescribing for a variety of on- and off-label uses (e.g., anxiety, insomnia, and recreational drug withdrawal, among others), is thought to help explain the recent spikes in the numbers of GP abuse cases reported to pharmacovigilance databases in Europe [19, 20]. In the USA, although population-level estimates of GP misuse/abuse are not yet

available, GP misuse/abuse appears on the rise as well [21]. A recent analysis of data from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) system, a national prescription drug surveillance system covering all states except Hawaii, reported 407 cases of gabapentin diversion in 41 states from 2002 to 2015 and showed steady annual increases of gabapentin diversion from 2002 to 2015, with a 2015 diversion rate comparable to OxyContin [21]. In 2016, the US National Poison Data System (NPDS) reported 3443 intentional (including misuse/abuse, suicide, and unknown) single agent gabapentin exposures, up from 0 in 2011, the first year it was reported separately [9, 22]. These recent spikes in GP misuse/abuse are mirrored in the numbers of GP cases recorded in ToxIC, up from 54 (1.4% of all ToxIC cases) in 2010 to 201 (2.7% of all ToxIC cases) in 2017. Approximately half the ToxIC 2017 cases were suicide attempts and one-quarter were misuse/abuse cases.

Some speculate that off-label prescriptions are increasing as physicians attempt to provide non-opioid pain relief to their patients, despite the lack of efficacy and long-term safety data for common off-label pain indications [23, 24]. There are also published case reports of GP abuse by patients with substance use disorders (SUDs), especially prescription opioid misusers and heroin users, and of patients attempting to potentiate the effects of methadone or buprenorphine or to get high from the buprenorphine/gabapentin combination [9, 24, 25]. A recent systematic review concluded that those most at risk of GP addiction were patients with current or past SUDs, particularly opioid and multi-drug users, and that the risk of overdose lethality increases with multiple agent exposures, particularly those involving opioids and sedatives [17]. Potential mechanisms include pharmacodynamic (i.e., additive respiratory depression of opioids and gabapentin) and pharmacokinetic (i.e., increased gabapentin absorption in the upper small intestine after slowed motility from opioid ingestion) factors [26]. In the GP misuse/abuse cases in ToxIC, coma/CNS (central nervous system) depression affects approximately half or more of both the single and multiple agent cases, regardless of coingestant category, and respiratory depression is seen in approximately one-third or more of the multiple agent cases. Overall, the ToxIC data illustrate the range of potentially severe medical outcomes associated with GP misuse/abuse and provide complimentary insight on its burden on US healthcare facilities.

Limitations

The ToxIC Registry is a unique database that is able to provide an informed reported relationship between exposures and clinical outcomes due to its involvement of actively practicing medical toxicologists. There are, however, some limitations within the Registry. One of these is a possible bias towards more severe case presentations since cases are only entered if they are evaluated at the bedside by a medical toxicologist. Cases in which the patient did not present for care or in which a medical toxicology consult was not called would not have been reported. Therefore, the Registry likely represents a different population from other agencies such as Poison Control Centers. There may also be a bias in the types of cases reported based on regional variations in drug use and abuse and toxicological exposures. The scope of the ToxIC Registry includes medical toxicologists from multiple, diverse locations, but the entire country is not fully or equally represented. Larger, academic medical centers may be more likely to have practicing medical toxicologists and be more likely to be members of the Consortium. Therefore, some areas of the USA and more rural populations may be underrepresented.

Additionally, there may be a reporting bias towards more complicated or more interesting cases at the level of the individuals reporting cases to the Registry. We attempt to limit this as much as possible by way of a written agreement with all participating sites requiring that all cases that are seen be entered into the Registry. Data regarding substances of exposure, or species of envenomation, relies heavily on patient self-report which is limited by willingness to disclose as well as lack of knowledge about substances involved. This may be particularly true of illicit drugs, making the subset of patients with analytical confirmation of fentanyl analogue exposure particularly valuable. Lastly, improving data quality remains an issue for the registry. While member sites are instructed to complete all applicable data fields in each case, there are still a number of cases with likely incomplete data. This is best demonstrated the fatality cases where no notable signs/symptoms or treatments were reported. Efforts remain underway to improve reporting of data, in particular demographic and fatality data.

Conclusions

The ToxIC Registry continues to be the only database of its kind, poised to collect data on toxicological exposures that have each been evaluated by a bedside medical toxicologist. While limited to the scope of those participating medical toxicologists, this also enhances the ability of the Registry to correlate exposures to clinical findings. Quality improvement efforts have improved the consistent reporting of information, and these efforts continue to be a major focus of the Registry going forward. The most commonly reported exposures, types of encounters, toxidromes, and clinical signs and symptoms overall remain consistent and represent the current practice of participating medical toxicologists. While nearly three-quarters of cases required treatment intervention, fatalities were uncommon.

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