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ORIGINAL ARTICLE

# The Toxicology Investigators Consortium 2023 Annual Report

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## Abstract

Since 2010, the American College of Medical Toxicology (ACMT) Toxicology Investigators Consortium (ToxIC) has maintained the ToxIC Core Registry, a national case registry of in-hospital and clinic patient consultations submitted by medical toxicology physicians. Deidentified patient data entered into the registry includes patient demographics, reason for medical toxicology evaluation, exposure agents, clinical signs and symptoms, treatments and antidotes administered, and mortality. This fourteenth annual report provides data from 7392 patients entered into the Core Registry in 2023 by 36 participating sites comprising 61 distinct healthcare facilities, bringing the total case count to 102331 between 2010 and 2023. Ethanol was the most commonly reported exposure agent class (24.4%), followed by opioids (22.7%), non-opioid analgesics (16.7%), and antidepressants (11.7%). For the first time since the registry's initiation, in 2023, ethanol was the leading agent of exposure. There were 98 fatalities (case fatality rate of 1.3%). Additional descriptive analyses in this annual report were conducted to describe the reasons for medical toxicology consultation by age in 2023, and yearly trends for opioid and psychoactive exposures, physostigmine and rivastigmine treatments, and acetaminophen exposures treated with fomepizole.

**Keywords** Poisoning · Overdose · Surveillance · Epidemiology · Medical Toxicology

## Introduction

The Toxicology Investigators Consortium (ToxIC) is a multicenter toxicosurveillance and research network. The ToxIC Core Registry was established in 2010 by the American College of Medical Toxicology (ACMT) as a tool for clinical toxicology research and toxico-surveillance [1, 2].

The ToxIC Core Registry prospectively collects data on patients seen in clinical consultation by medical toxicology physicians in both inpatient and ambulatory settings. The Core Registry began with four sites, and by 2023, ToxIC has grown to 36 participating sites comprising 61 distinct healthcare facilities, enrolling 7392 new cases that year. As of December 31, 2023, 102,331 cases have been entered into the ToxIC Core Registry since its inception. Since 2020, ToxIC has initiated several other multicenter projects such

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as the Fentalog Study which gathers more information on suspected opioid overdose cases, and the Drug Overdose Toxico-Surveillance (DOTS) Reporting Program which enrolls patients presenting with either suspected stimulant or opioid overdoses.

## ToxIC Core Registry – Sub-Registries and Focused Data Collections

The ToxIC Core Registry, a composition of medical toxicology physician consultation cases, has several associated sub-registries and focused data collections that gather detailed data about the patient's exposure or treatment.

The North American Snakebite Registry (NASBR) includes patients presenting with snakebites who have been treated by medical toxicology physicians across the United States (Principal Investigator (PI): Anne-Michelle Ruha, MD, funded by BTG Pharmaceuticals). Celebrating its 10th year, in 2023 the NASBR surpassed 2000 cases with comprehensive data on the circumstances surrounding the snakebite, clinical manifestations, and responses to treatment. In 2023, participating investigators' publications included non-native snake envenomations [3], geographic variations of Mohave rattlesnake envenomation [4], compartment syndrome after snakebite [5], and comparisons between Fab and F(ab')2 antivenom treatment after rattlesnake bite [6].

The Novel Opioid and Stimulant Exposures (NOSE) project was initiated in 2021 through a grant from the American Academy of Addiction Psychiatry (AAAP). This focused data collection within the Core Registry aims to identify cases involving exposures to novel substances, particularly opioids and stimulants (PI: Meghan Spyres, MD, funded by SAMHSA 1H79TI085588). Quarterly reports, are disseminated through the Opioid Response Network (ORN) to highlight real-time case clusters or unique exposures. ToxIC NOSE briefs released in 2023 included topics on kratom exposures, organ donation after overdose death, hypoglycemia related to illicit opioid use, and bupropion stimulant toxicity. These reports can be accessed at www.acmt.net/nose/.

Two additional ongoing sub-registries include the Natural Toxins Registry: Mushrooms and Plants, and the Extracorporeal Therapies Registry, which continued to grow in 2023. The Natural Toxins Registry consists of focused questions related to mushroom and plant exposures, including mushroom/plant related clinical effects, contextual information surrounding the exposure, and detailed information on toxin removal treatment received (if applicable). The Extracorporeal Therapies Registry focuses on specific extracorporeal treatment received, relevant laboratory values, reason for extracorporeal treatment, and the patient's response to treatment.

## Other ToxIC Multicenter Projects

Outside of the ToxIC Core Registry and above sub-registries/focused data collections, ToxIC has initiated several multicenter projects that prospectively identify new and emerging substances. These projects are not dependent upon a medical toxicology consultation service and provide opportunities for medical toxicologists to serve as PIs at each participating site.

The ToxIC Fentalog Study is an ongoing, 5-year, national multicenter study investigating suspected opioid-related overdoses (PI: Alex Manini, National Institutes of Health/National Institute on Drug Abuse 5R01DA048009 and Centers for Disease Control and Prevention Supplement R01DA048009-03S1). This study assesses the prevalence of fentanyl and fentanyl analogs (fentalogs), while also investigating the role of fentalogs, novel psychoactive drugs, adulterants, and other substances in the clinical presentation and treatment of opioid overdose. Patients presenting with a suspected opioid overdose to the emergency department (ED) at one of 10 participating sites are eligible if residual waste blood specimens are available. Qualitative toxicology analyses are performed via liquid chromatography quadrupole time-of-flight mass spectroscopy (LC-QTOF-MS) by the Center for Forensic Science Research and Education (CFSRE). From 2020 through 2023, 1804 patients were entered in the ToxIC Fentalog Study. These efforts have resulted in 27 scientific presentations at national meetings and 4 published peer-reviewed manuscripts, including one of the first non-fatal cohorts of patients presenting to the ED with xylazine exposures that was published in 2023 [7].

In 2023, ToxIC welcomed the addition of a new U.S. Food and Drug Administration funded project (75F4012 2D00028/75F40123F19002), the Drug Overdose Toxico-Surveillance (DOTS) Reporting Program. The DOTS Program aims to assess qualitative and quantitative blood toxicology analyses, sociodemographic characteristics, clinical signs and symptoms, interventions provided, and contextual data on opioid and/or stimulant overdoses from patients presenting to 17 participating medical centers across the United States. This project links in-depth, structured patient interviews, chart reviews, and laboratory confirmation to inform potential regulatory efforts and public health messaging. Patients presenting to a participating ED after a suspected opioid and/or stimulant overdose (ages 13 and older) are approached for consent. After obtaining informed consent, a detailed patient interview is conducted which collects information on the overdose event (suspected drug taken, route of administration, pattern of use, and source of the drug), history of substance use and treatment, and sociodemographic characteristics.

Blood is obtained and sent to CFSRE where qualitative analyses via LC-QTOF-MS and quantitative analyses via liquid chromatography tandem quadrupole mass spectrometry are performed. In 2023, 447 patients were enrolled in DOTS across participating sites.

## ToxIC Publications and Presentations

The year 2023 was marked by considerable growth in ToxIC peer-reviewed publications and presentations. Fourteen publications spanning six journals were published in 2023, and 47 scientific presentations were given at national and international meetings. This represents the largest annual number of peer-reviewed publications and abstracts produced by ToxIC investigators to date. These publications and scientific presentations are listed on the ToxIC website: www.ToxICRegistry.org.

## Changes to the ToxIC Core Registry in 2023

In 2023, data collection was expanded to include additional sections on sociodemographic characteristics and the nature/location of the medical toxicology encounter. The registry now collects data on both sex (male/female) and gender (male, female, genderqueer, non-binary, other). Further categories for transgender identification include male-to-female or female-to-male, the age of initial transition, and whether they are currently receiving gender-affirming care and/or have undergone surgery. The registry now gathers data on whether consultations involved drug shortages. For cases with drug shortages, additional data was collected via the Drug Shortage Supplemental Form—which includes a short narrative of the case, details of the drug shortage, changes in pharmacotherapy due to the shortage, and information on whether the drug shortage impacted the patient's care or outcome. Additionally, ToxIC modified the variable for medical toxicology encounter reason this year to indicate if the patient was sent to an inpatient mental health facility.

## Annual Report Objectives

The objective of this annual report is to describe the cases entered into the ToxIC Core Registry in 2023. In addition to a summary of the Core Registry data, descriptive analyses were conducted to describe the reasons for medical toxicology consultation by age in 2023, and the historical yearly trends for opioid and psychoactive exposures, physostigmine and rivastigmine treatments, and acetaminophen exposures treated with fomepizole.

## Methods

Medical toxicology physicians at participating healthcare sites within the ToxIC Core Registry enter deidentified patient information from medical toxicology consultations and evaluations that are performed as part of standard patient care in the hospital, in the clinic, and via telemedicine. The data gathered in the Core Registry is a culmination of information from the patient's electronic medical record (EMR) and their first-hand evaluation of the patient during their consultation utilizing available evidence (e.g., prehospital reports, patient self-report or family report, presence of the product of exposure, clinical presentation, physical examination, ancillary data, and/or laboratory testing results). Similarly, agents of exposure and/or withdrawal, if applicable, are documented by the medical toxicologist utilizing the approach above. Reasons for the medical toxicology encounter may include up to 2 reasons, such as addiction medicine consultation and withdrawal to opioids if applicable. Each patient's race and ethnicity is obtained by self-report or hospital registration documentation within the EMR. Figure 1 contains a brief overview of the Core Registry data collection elements.

Data were collected and managed using REDCap (Research Electronic Data Capture) hosted by Vanderbilt University [8, 9]. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture, 2) audit trails for tracking data manipulation and export procedures, 3) automated export procedures for seamless data downloads to common statistical packages, and 4) procedures for data integration and interoperability with external sources.

All data entry elements in the Core Registry, including associated sub-registries and focused data collections, are reviewed for quality assurance by ToxIC staff. Any inconsistent or incomplete entries are queried back to the entering site for correction or clarification. ToxIC leadership and staff communicate with all sites to review patient accrual, barriers to data entry, quality assurance efforts, and ongoing project opportunities. Additional information regarding ToxIC can be found at www.toxicregistry.org.

All ToxIC projects have been reviewed by a central institutional review board (IRB), the Western Copernicus Group IRB. Each participating site obtains approval from a corresponding local IRB. The data collected by ToxIC is deidentified and fully compliant with the Health Insurance Portability and Accountability Act.

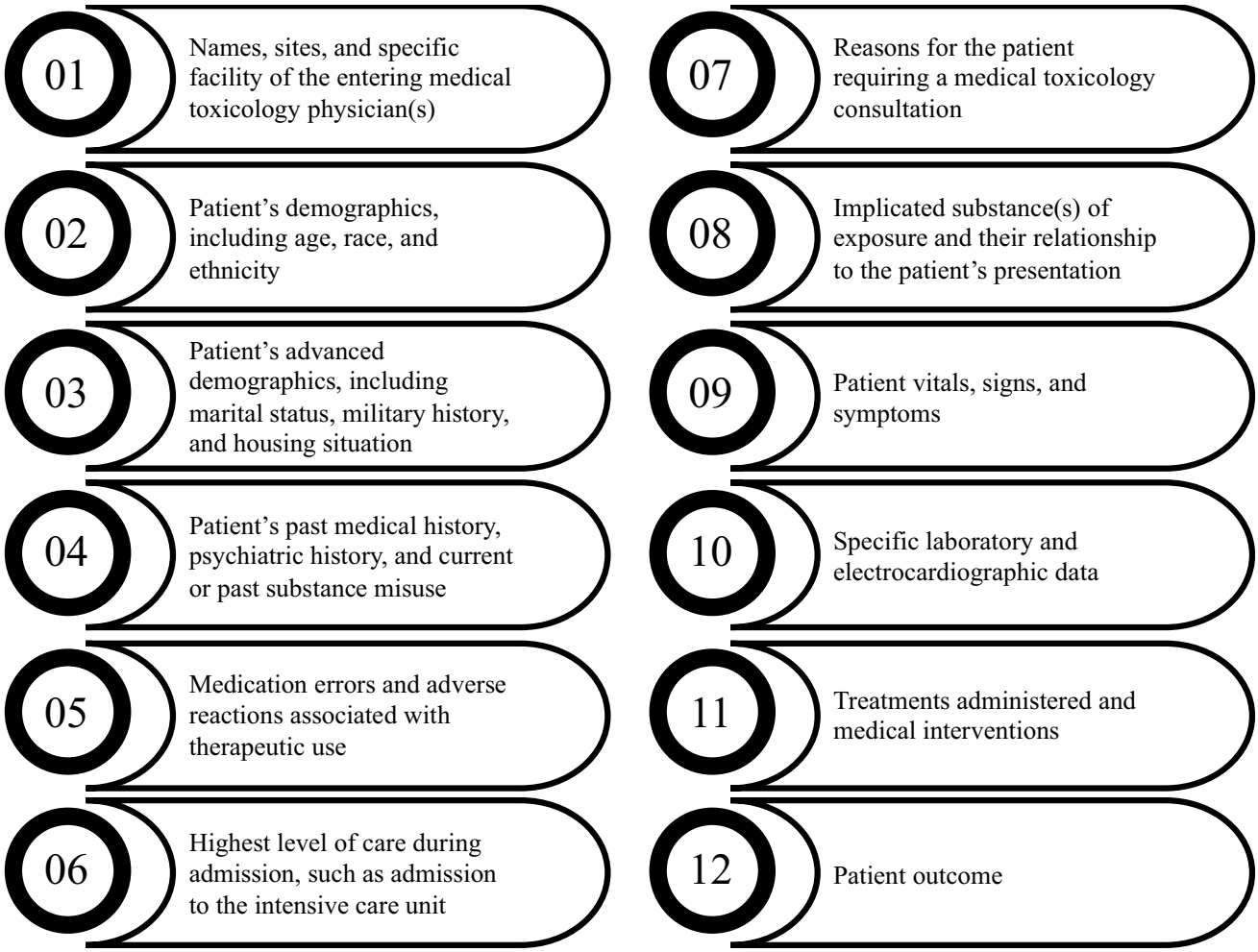


**Fig. 1** Core Registry data collection elements

## Statistical Analysis

ToxIC Core Registry data from January 1, 2023-December 31, 2023 were extracted from REDCap and exported into Microsoft Excel. Descriptive statistics were calculated to obtain relative and absolute frequencies for sociodemographic characteristics, medical toxicology consultation referral source, patient hospitalization course, reasons for encounter, exposure and treatment information, and mortality. Small cell sizes for specific agent exposures were collapsed into "miscellaneous" categories which are detailed in footnotes for relevant tables.

Additional analyses of interest included examining reasons for medical toxicology consultation by age category. Yearly trends (2010–2023) were also assessed for opioid and psychoactive exposures, physostigmine and rivastigmine treatments, and cases exposed to acetaminophen who receive fomepizole.

## Results

In 2023, there were a total of 7392 cases of toxicologic exposures reported to the ToxIC Core Registry from 61 healthcare facilities at 36 participating sites. Two new sites were added in 2023, and both are affiliated with Weill Cornell Medicine in New York. Individual healthcare facilities contributing to cases in 2023 are listed in Table 1.

## Sociodemographic Characteristics

Tables 2, 3, and 4 summarize demographics for gender, age, and race/ethnicity, respectively. In 2023, 47.4% of cases involved female patients, 51.2% were male, and 1.4% of patients identified as transgender (44.1% female-to-male, 26.5% male-to-female, 17.6% non-binary, 8.8% gender nonconforming, and 1.0% genderqueer). One hundred and forty

**Table 1** Participating institutions providing cases to the toxic core registry in 2023

| State or Country | City | Hospitals |
|---|---|---|
| Alabama | Birmingham | Children's of Alabama |
| | | University of Alabama Birmingham Hospital—Highlands |
| | | University of Alabama Birmingham Hospital |
| Arizona | Phoenix | Banner—University Medical Center Phoenix |
| | | Phoenix Children's Hospital |
| Arkansas | Little Rock | Arkansas Children's Hospital |
| California | Loma Linda | Loma Linda University Medical Center |
| | Los Angeles | Ronald Reagan University of California Los Angeles Medical Center |
| | | University of California Los Angeles—Santa Monica Medical Center |
| | Sacramento | University of California Davis Medical Center |
| Colorado | Denver | Children's Hospital Colorado |
| | | Denver Health Medical Center |
| | | Advent Health Porter |
| | | Swedish Medical Center |
| | | University of Colorado Hospital |
| Connecticut | Hartford | Hartford Hospital |
| Florida | Jacksonville | University of Florida Health Jacksonville |
| Georgia | Atlanta | Grady Memorial Hospital |
| Indiana | Indianapolis | Indiana University Health—University Hospital |
| | | Indiana University Health—Methodist Hospital |
| | | Riley Hospital for Children |
| Kansas | Kansas City | University of Kansas Medical Center |
| Kentucky | Lexington | University of Kentucky Albert B. Chandler Hospital |
| | | University of Kentucky Good Samaritan Hospital |
| Massachusetts | Boston | Beth Israel Deaconess Medical Center |
| | | Boston Children's Hospital |
| | Worcester | University of Massachusetts Memorial Medical Center |
| Michigan | Grand Rapids | Corewell Health |
| Mississippi | Jackson | University of Mississippi Medical Center |
| Missouri | Kansas City | Children's Mercy Hospital |
| | St. Louis | Missouri Baptist Medical Center |
| | | Barnes-Jewish Hospital |
| Nebraska | Omaha | University of Nebraska Medical Center |
| New Jersey | Newark | Rutgers New Jersey Medical School—University Hospital |
| New York | New York | New York—Presbyterian Weill Cornell Medical Center* |
| | | New York—Presbyterian Lower Manhattan Hospital* |
| | Syracuse | Upstate University Hospital—Downtown Campus |
| North Carolina | Charlotte | Carolinas Medical Center |
| Oregon | Portland | Oregon Health & Science University Hospital |
| Pennsylvania | Bethlehem | Lehigh Valley Hospital—Cedar Crest |
| | | Lehigh Valley Hospital—Muhlenberg |
| | Philadelphia | Einstein Medical Center Elkins Park |
| | | Einstein Medical Center Montgomery |
| | | Jefferson Einstein Philadelphia Hospital |
| | Pittsburgh | University of Pittsburgh Medical Center Shadyside |
| | York | York Hospital |
| Texas | Dallas | Children's Medical Center Dallas |
| | | Parkland Memorial Hospital |
| | | William P. Clements Jr University Hospital |
| | Houston | HCA Houston Kingwood |
| Virginia | Charlottesville | University of Virginia Medical Center |

**Table 1** (continued)

| State or Country | City | Hospitals |
|---|---|---|
| Canada | Calgary | Alberta Children's Hospital |
| | | Foothills Medical Centre |
| | | Peter Lougheed Centre |
| | | Rockyview General Hospital |
| | | South Health Campus |
| England | London | Guy's and St Thomas' NHS Foundation Trust |
| | | St Thomas' Hospital |
| Israel | Haifa | Carmel Medical Center |
| | | Rambam Health Care Campus |
| Thailand | Bangkok | Vajira Hospital |

*New participating ToxIC sites in 2023

**Table 2** Patient gender and pregnancy status

| | *N (%)* |
|---|---|
| Female | 3507 (47.4) |
| Male | 3783 (51.2) |
| Transgender | 102 (1.4) |
| Female to male | 45 (44.1)[a] |
| Gender non-conforming | 9 (8.8)[a] |
| Genderqueer | 1 (1.0)[a] |
| Male to female | 27 (26.5)[a] |
| Non-binary | 18 (17.6)[a] |
| Other | 1 (1.0)[a] |
| Missing | 1 (1.0)[a] |
| Total | 7392 (100) |
| Pregnant | 140 (4.0)[b] |

[a]Percentages based on total number of transgender cases (N = 102)

[b]Percentage based on number of cases in female patients (N = 3507)

**Table 3** Patient age category

| | *N (%)* |
|---|---|
| Less than 2 years old | 215 (2.9) |
| 2–6 years old | 348 (4.7) |
| 7–12 years old | 214 (2.9) |
| 13–18 years old | 1272 (17.2) |
| 19–65 years old | 4679 (63.3) |
| 66–89 years old | 648 (8.8) |
| Over 89 years old | 10 (0.1) |
| Age unknown | 6 (0.1) |
| Total | 7392 (100) |

patients (4.0%) were pregnant. The majority of patients were adults aged 19–65 (63.3%), followed by adolescents aged 13–18 (17.2%). Children (12 years of age and younger) made up 10.5%, and 8.9% of cases involved older adults (over 65 years of age).

**Table 4** Patient race/ethnicity

| | *N (%)* |
|---|---|
| Non-Hispanic White | 4661 (63.1) |
| Black/African American | 1053 (14.2) |
| Hispanic | 1011 (13.7) |
| Asian | 183 (2.5) |
| American Indian/Alaskan Native | 129 (1.7) |
| Mixed, not otherwise specified | 79 (1.1) |
| Native Hawaiian/Pacific Islander | 15 (0.2) |
| Race unknown | 261 (3.5) |
| Total | 7392 (100) |

The predominant race/ethnicity was Non-Hispanic White (63.1%), followed by Black/African American (14.2%), Hispanic (13.7%), and Asian (2.5%). Cases where race/ethnicity was cited as unknown/uncertain constituted a smaller percentage compared to previous years (3.5%).

Patient marital status, military service, and housing situation are collected for patients over 12 years of age (Table 5). The majority of patients were single (66.5%), followed by married or with a long-term partner (21.6%), and divorced or separated (9.2%). Among those with known military service status (n = 2997), the majority (97.9%) reported no prior military service. Of the 2.1% who reported prior military service, 85.5% were retired or had former military service. Among the 94.7% with documented housing status, secure housing was reported in 92.0% of cases (home or stable living situation). Those who were classified as undomiciled or unhoused comprised 5.8%.

**Table 5** Patient marital status, military service, and housing situation

| | *N (%)* |
|---|---|
| Marital Status | |
| Unknown | 761 (11.5)[a] |
| Total reported marital status | 5854 (88.5)[a] |
| Single | 3892 (66.5)[b] |
| Married or long-term partner | 1264 (21.6)[b] |
| Divorced or separated | 541 (9.2)[b] |
| Widowed | 157 (2.7)[b] |
| Military Service | |
| Unknown | 3618 (54.7)[a] |
| Total reported military service | 2997 (45.3)[a] |
| No, previous military service | 2935 (97.9)[c] |
| Yes, previous military service | 62 (2.1)[c] |
| Former/retired | 53 (85.5)[d] |
| Current (including reserves) | 2 (3.2)[d] |
| Unknown if former/current | 7 (11.3)[d] |
| Housing Status | |
| Unknown | 392 (5.3)[e] |
| Total reported housing status | 7000 (94.7)[e] |
| Secured housing (home or stable living situation) | 6445 (92.0)[f] |
| Undomiciled (homelessness, unsecured housing) | 406 (5.8)[f] |
| Non-criminal supervised care (foster, group home, nursing home) | 56 (0.8)[f] |
| Rehabilitation or psychiatric facility | 32 (0.5)[f] |
| Correctional related facility (jail, prison, incarceration) | 55 (0.8)[f] |
| Other | 6 (0.1)[f] |

[a]Percentages based on patients age > 12 years old (N = 6615)

[b]Percentages based on total cases reporting marital status (N = 5854)

[c]Percentages based on total cases reporting military service (N = 2997)

[d]Percentages based on total cases reporting yes, previous military service (N = 62)

[e]Percentages based on total reported cases (N = 7392)

[f] Percentages based on total cases reporting housing status (N = 7000)

## Source of Medical Toxicology Referral, Location of Patient During Hospitalization, and Reasons for Encounter

Table 6 outlines the medical toxicology consultation referral source for both inpatient and outpatient encounters. The majority (53.9%) of inpatient cases originated from ED referrals, followed by referrals from an admitting service (29.1%). Consultations originating from referrals through the poison center (0.7%) or primary care/outpatient physician providers (0.1%) were infrequent. For outpatient encounters, primary care and other outpatient physicians were the primary referral sources (65.8%), followed by self-referrals (18.4%), and employer/independent medical evaluations (12.7%).

Table 7 provides an overview of the patient's locations during hospitalization. The majority of patients spent time in the ED (79.6%), followed by the hospital floor (58.6%), and critical care unit (29.4%). A small number of patients were placed in the observation unit during their hospitalization (3.2%). Patients may have moved through more than one hospital location during their stay. Inpatient mental health facility placement occurred in 18.3% of patients.

Telemedicine referrals, as outlined in Table 8, were predominantly from the ED (50.0%) and an admitting service (37.0%), with lesser numbers from requests by other hospital services such as other consulting physicians (10.2%) and primary care providers or other outpatient treating physicians (1.9%). Telemedicine consultations were facilitated through video (50.9%), chart review only (30.9%), and over-the-phone interactions with patients (17.6%).

Table 9 and 10 delineate reasons for medical toxicology encounters and the specifics of the intentional pharmaceutical exposures, respectively. Consistent with previous years, intentional pharmaceutical exposures remained the most common reason for medical toxicology consultations (28.1%) within the Core Registry. However, the proportion of intentional pharmaceutical exposures observed in 2023

**Table 6** Case Referral Sources by Inpatient/ Outpatient Status

| | *N (%)* |
|---|---|
| Emergency Department (ED) or an Inpatient Unit[a] | |
| ED | 3897 (53.9) |
| Admitting service | 2104 (29.1) |
| Request from another hospital service (not ED) | 723 (10.0) |
| Outside hospital transfer | 434 (6.0) |
| Poison Center | 51 (0.7) |
| Self-referral | 18 (0.2) |
| Primary care provider or other outpatient treating physician | 5 (0.1) |
| Employer/Independent medical evaluation | 2 (0.0) |
| Total | 7234 (100) |
| Outpatient Clinic/Office Consultation[b] | |
| Primary care provider or other outpatient physician | 104 (65.8) |
| Self-referral | 29 (18.4) |
| Employer/Independent medical evaluation | 20 (12.7) |
| Poison Center | 3 (1.9) |
| Admitting service | 1 (0.6) |
| ED | 1 (0.6) |
| Total | 158 (100) |

[a]Percentages based on total number of cases (N = 7234) seen by a medical toxicologist as an inpatient

[b]Percentages based on total number of cases (N = 158) seen by a medical toxicologist as an outpatient, including clinic visits or office consultations

**Table 7** Locations of patient during hospitalization and inpatient mental health placement

| | *N (%)*[a] |
|---|---|
| ED | 5761 (79.6) |
| Hospital floor | 4239 (58.6) |
| Critical care unit | 2127 (29.4) |
| Observation unit | 234 (3.2) |
| Inpatient mental health facility[b] | 1326 (18.3) |

[a]Percentages based on total number of cases (N = 7234) seen by a medical toxicologist as an inpatient. Case numbers may include more than one hospital location

[b]Inpatient mental health facility includes facility at participating hospital or transfer to an outside facility

marked the lowest recorded since the Core Registry's establishment in 2010 [10–22].

In 2023, ethanol withdrawal (13.7%) and ethanol misuse (12.4%) were the second and third most prevalent reason or medical toxicology encounter, respectively, aligning with trends observed in 2022 [10]. Among intentional pharmaceutical exposures (n = 2488), the majority of cases involved self-harm attempts (n = 1844, 74.1%), predominantly suicide attempts (n = 1617, 87.7%) (Table 10). Misuse accounted for 13.8% of intentional pharmaceutical exposures.

Table 11 provides the detailed encounter reason for medical toxicology consultations stratified by age cohort. Intentional pharmaceutical and non-pharmaceutical exposures in a self-harm attempt (70.3%) were the most frequent consultation reason for patients between 13–18 years old being seen by a medical toxicologist. Pediatric patients between 0–12 years old were most often evaluated by a medical toxicologist for unintentional pharmaceutical and non-pharmaceutical exposures (63.1%). Adult patients between 19–65 years old were most often presenting to the hospital for intentional pharmaceutical or non-pharmaceutical exposures (37.2%), and most frequently the intention of the exposure was self-harm (19.2%) followed by misuse (11.9%). The next most frequent reason for patients 19–65 years old was ethanol related (24.7%). Conversely, in patients 66 years and older, ethanol misuse and withdrawal were the most common reason (29.6%), followed by intentional pharmaceutical and non-pharmaceutical exposures (24.7%).

Table 12 outlines addiction medicine consultations reported by medical toxicology physicians in 2023. Analogous to previous years, the majority of consultations pertained to opioid agonist therapy (70.5%), followed by counseling and support (11.5%), and pain management (10.7%).

**Table 8** Telemedicine encounters

| | *N (%)*[a] |
|---|---|
| Source of Telemedicine Referral | |
| ED | 162 (50.0) |
| Admitting service | 120 (37.0) |
| Request from another hospital service (not ED) | 33 (10.2) |
| Primary care provider or other outpatient treating physician | 6 (1.9) |
| Self-referral | 3 (0.9) |
| Nature of Telemedicine Consultation | |
| Patient encounter via video/internet | 165 (50.9) |
| Chart review only | 100 (30.9) |
| Patient encounter over the phone | 57 (17.6) |
| Missing | 2 (0.6) |
| Reason for Telemedicine Encounter | |
| Attempt at self-harm[b] | 86 (26.5) |
| Withdrawal – Ethanol | 64 (19.7) |
| Misuse[b] | 37 (11.4) |
| Addiction medicine consult[c] | 32 (9.9) |
| Unintentional pharmaceutical and/or nonpharmaceutical exposures | 29 (9.0) |
| Withdrawal – opioids | 22 (6.8) |
| Therapeutic use or intent[b] | 12 (3.7) |
| Unknown | 10 (3.1) |
| Environmental evaluation | 9 (2.8) |
| Interpretation of laboratory data | 8 (2.5) |
| Envenomations | 5 (1.5) |
| Miscellaneous[d] | 10 (3.1) |

[a]Percentages based on total cases indicating a telemedicine consultation (N = 324)

[b]Includes intentional pharmaceutical and/or intentional nonpharmaceutical exposures

[c]Includes opioid agonist therapy, opioid antagonist therapy, pain management, and alcohol dependency pharmacotherapy

[d]Includes occupational evaluation, organ system dysfunction, withdrawal – sedative, withdrawal – other, and malicious criminal

## Agent Classes

Toxicologic exposure by agent class reported to the Core Registry are described in Table 13. Among the 7392 cases entered into the Core Registry in 2023, 6712 involved at least one agent of exposure. Single agents were implicated in 4944 (73.7%) cases. Table 14 describes the top 10 single agent exposure classes reported in 2023. Ethanol was the most commonly reported single agent exposure (26.3%), followed by opioids (17.4%), non-opioid analgesics (11.1%), and envenomations (8.0%). Among all agent classes (irrespective of single or multiple agent exposures), ethanol was the most common exposure reported for the first time in the Core Registry's history (24.4%). Following ethanol, the opioid class ranked as the second most commonly reported (22.7%), followed by non-opioid analgesics (16.7%) and antidepressant (11.7%) classes.

## Ethanol and Toxic Alcohols

Data describing ethanol and other toxic alcohol exposures are presented in Table 15. In 2023, ethanol was the most frequently reported agent overall and as a single agent, a shift from prior years where opioids were the most frequently reported agent overall [10–22]. Isopropyl alcohol accounted for the highest proportion of non-ethanol toxic alcohol exposures (42.7%), followed by ethylene glycol (26.8%) and methanol (7.3%). Miscellaneous alcohols, constituting 17.1% of non-ethanol toxic alcohol exposures,

**Table 9** Reason for medical toxicology encounter

| | *N (%)*[a] |
|---|---|
| Intentional exposure—pharmaceutical | 2488 (28.1) |
| Withdrawal—ethanol | 1208 (13.7) |
| Ethanol misuse | 1098 (12.4) |
| Intentional exposure—non-pharmaceutical | 741 (8.4) |
| Withdrawal—opioid | 648 (7.3) |
| Addiction medicine consultation | 539 (6.1) |
| Unintentional exposure—pharmaceutical | 480 (5.4) |
| Unintentional exposure—non-pharmaceutical | 377 (4.3) |
| Organ system dysfunction | 376 (4.2) |
| Envenomation—snake | 374 (4.2) |
| Interpretation of toxicology lab data | 177 (2.0) |
| Environmental evaluation | 131 (1.5) |
| Withdrawal—sedative/hypnotic | 82 (0.9) |
| Envenomation—spider | 40 (0.5) |
| Withdrawal—cocaine/amphetamine | 35 (0.4) |
| Occupational evaluation | 24 (0.3) |
| Malicious/criminal | 15 (0.2) |
| Withdrawal—other | 9 (0.1) |
| Envenomation—scorpion | 4 (0.0) |
| Envenomation—other | 3 (0.0) |
| Marine /fish poisoning | 2 (0.0) |
| Total | 8851 (100) |

[a]Percentages based on total number of reasons for toxicology encounter (N = 8851); 1459 Core Registry cases (19.7%) reported a second reason for encounter. Case entries may include more than one reason for a medical toxicology encounter

**Table 10** Detailed reason for encounter—intentional pharmaceutical exposure[a]

| | *N (%)* |
|---|---|
| Reason for Intentional Pharmaceutical Exposure Subgroup[b] | |
| Attempt at self-harm | 1844 (74.1) |
| Misuse | 344 (13.8) |
| Therapeutic use | 168 (6.8) |
| Unknown | 132 (5.3) |
| Attempt at Self-harm—Suicidal Intent Subclassification[c] | |
| Suicidal intent | 1617 (87.7) |
| Suicidal intent unknown | 162 (8.8) |
| No suicidal intent | 60 (3.2) |
| Missing | 5 (0.3) |

[a]Six cases listed more than one reason for encounter due to intentional pharmaceutical exposure

[b]Percentage based on number of cases reporting intentional pharmaceutical exposure (N = 2488)

[c]Percentage based on number of cases indicating attempt at self-harm (N = 1844)

included agents such as diethylene glycol, acetone, and various glycol ethers.

## Opioids

Details of opioid exposure agents are outlined in Table 16. For the second consecutive year, fentanyl exposures were more prevalent than all other opioids combined, comprising 62.9% of all opioid exposures in 2023. The subsequent most frequently reported opioids were oxycodone (7.4%), methadone (6.5%), buprenorphine (5.5%), and heroin (4.5%).

## Non-Opioid Analgesics

For the 14th consecutive year, acetaminophen has remained the most common non-opioid analgesic reported to the Core Registry, accounting for 66.0% of this category in 2023 (Table 17) [10–22]. Following acetaminophen, the next most commonly reported non-opioid analgesics were ibuprofen (11.3%), acetylsalicylic acid (8.0%) and gabapentin (7.0%). Though acetylsalicylic acid and aspirin were previously classified as separate agents in the Core Registry, they have been combined for the 2023 report. Salicylic acid (1.5%) remains a distinct category. However, due to low case volumes, methylsalicylate has been combined with other agents in the miscellaneous category, which includes unspecified NSAIDs, celecoxib, ketorolac, phenazopyridine, and others.

## Antidepressants

The frequencies of antidepressant exposures, detailed in Table 18, are further subcategorized by antidepressant class. Selective serotonin reuptake inhibitors comprise the most common antidepressant class (43.5%), followed by other antidepressants (38.3%), which included bupropion (22.2%), trazodone (12.2%), and mirtazapine (3.3%), among others. Bupropion was the single most common antidepressant agent reported overall (22.2%), while sertraline was the second most common (17.2%). Tricyclic antidepressants (TCAs) represented only 8.9% of all antidepressant exposures. Tianeptine was included in the TCA category under the "miscellaneous" subcategory due to the low number of cases reported in 2023.

**Table 11** Primary reason for medical toxicology encounter by age[a]

| | 0–12 years | 13–18 years | 19–65 years | Over 66 years | Unknown | Total % from subcategory | Total % of all 2023 cases |
|---|---|---|---|---|---|---|---|
| | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *%* |
| Intentional (Pharmaceutical and Non-pharmaceutical) | | | | | | | |
| Attempt at self-harm | 64 (8.2) | 894 (70.3) | 897 (19.2) | 60 (9.1) | 1 (16.7) | 1916 (61.3) | 25.9 |
| Misuse | 16 (2.1) | 173 (13.6) | 558 (11.9) | 46 (7.0) | 1 (16.7) | 794 (25.4) | 10.7 |
| Therapeutic use or intent | 9 (1.2) | 20 (1.6) | 104 (2.2) | 47 (7.1) | 0 (0.0) | 180 (5.8) | 2.4 |
| Drug Concealment | 0 (0.0) | 1 (0.1) | 28 (0.6) | 0 (0.0) | 0 (0.0) | 29 (0.9) | 0.4 |
| Unknown/Missing | 13 (1.7) | 32 (2.5) | 153 (3.3) | 10 (1.5) | 0 (0.0) | 208 (6.6) | 2.8 |
| Subtotal | 102 (13.1) | 1120 (88.1) | 1740 (37.2) | 163 (24.7) | 2 (33.3) | 3127 (100.0) | 42.2 |
| Unintentional (Pharmaceutical and Non-pharmaceutical) | | | | | | | |
| Subtotal | 491 (63.1) | 30 (2.3) | 226 (4.8) | 87 (13.2) | 2 (33.3) | 836 (100.0) | 11.3 |
| Ethanol Related | | | | | | | |
| Ethanol misuse | 0 (0.0) | 9 (0.7) | 430 (9.2) | 100 (15.2) | 1 (16.7) | 540 (39.7) | 7.3 |
| Withdrawal—Ethanol | 0 (0.0) | 1 (0.1) | 724 (15.5) | 95 (14.4) | 0 (0.0) | 820 (60.3) | 11.1 |
| Subtotal | 0 (0.0) | 10 (0.8) | 1154 (24.7) | 195 (29.6) | 1 (16.7) | 1360 (100.0) | 18.4 |
| Withdrawal | | | | | | | |
| Withdrawal—Cocaine/amphetamines | 0 (0.0) | 0 (0.0) | 16 (0.3) | 0 (0.0) | 0 (0.0) | 16 (2.8) | 0.2 |
| Withdrawal—Opioids | 3 (0.4) | 9 (0.7) | 474 (10.1) | 17 (2.6) | 0 (0.0) | 503 (87.5) | 6.8 |
| Withdrawal—Other | 0 (0.0) | 0 (0.0) | 7 (0.2) | 1 (0.2) | 0 (0.0) | 8 (1.4) | 0.1 |
| Withdrawal—Sedative hypnotics | 1 (0.1) | 1 (0.1) | 38 (0.8) | 8 (1.2) | 0 (0.0) | 48 (8.3) | 0.7 |
| Subtotal | 4 (0.5) | 10 (0.8) | 535 (11.4) | 26 (4.0) | 0 (0.0) | 575 (100.0) | 7.8 |
| Addiction medicine | | | | | | | |
| Subtotal | 2 (0.3) | 2 (0.2) | 393 (8.4) | 37 (5.6) | 0 (0.0) | 434 (100.0) | 5.9 |
| Envenomation | | | | | | | |
| Envenomation—Other | 2 (0.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (16.7) | 3 (0.7) | 0.1 |
| Envenomation—Scorpion | 1 (0.1) | 0 (0.0) | 2 (0.0) | 1 (0.2) | 0 (0.0) | 4 (1.0) | 0.1 |
| Envenomation—Snake | 94 (12.1) | 44 (3.4) | 196 (4.2) | 39 (5.9) | 0 (0.0) | 373 (89.0) | 5.0 |
| Envenomation—Spider | 19 (2.4) | 9 (0.7) | 9 (0.2) | 2 (0.3) | 0 (0.0) | 39 (9.3) | 0.5 |
| Subtotal | 116 (14.9) | 53 (4.1) | 207 (4.4) | 42 (6.4) | 1 (16.7) | 419 (100.0) | 5.7 |
| Other | | | | | | | |
| Environmental evaluation | 10 (1.3) | 9 (0.7) | 83 (1.8) | 23 (3.5) | 0 (0.0) | 125 (19.5) | 1.7 |
| Interpretation of toxicology lab data | 22 (2.8) | 7 (0.6) | 88 (1.9) | 29 (4.4) | 0 (0.0) | 146 (22.8) | 2.0 |
| Malicious/criminal | 2 (0.3) | 2 (0.2) | 7 (0.2) | 0 (0.0) | 0 (0.0) | 11 (1.7) | 0.1 |
| Occupation evaluation | 0 (0.0) | 1 (0.1) | 20 (0.4) | 1 (0.2) | 0 (0.0) | 22 (3.4) | 0.3 |
| Organ System dysfunction | 29 (3.7) | 28 (2.2) | 225 (4.8) | 55 (8.4) | 0 (0.0) | 337 (52.6) | 4.6 |
| Subtotal | 63 (8.1) | 47 (3.7) | 423 (9.1) | 108 (16.5) | 0 (0.0) | 641 (100.0) | 8.7 |
| Total | 778 (100.0) | 1272 (100.0) | 4678 (100.0) | 658 (100.0) | 6 (100.0) | 7392 | 100.0 |

[a]Percentages based on primary reasons for toxicology encounter only (N = 7392); 1459 Core Registry cases (19.7%) reported a second reason for encounter, and secondary encounter reasons are not displayed in this table

## Sympathomimetic Agents

The frequency of sympathomimetic agent exposures is depicted in Table 19. Methamphetamine retained its position as the most prevalent sympathomimetic exposure (44.0%), with cocaine following closely behind (30.7%) [10–13]. Amphetamine (9.3%) and dextroamphetamine (3.8%) were the third and fourth most common agents in this class.

**Table 12** Addiction medicine consultations

| | *N (%)*[a] |
|---|---|
| Opioid agonist therapy | 380 (70.5) |
| Counseling and support only | 62 (11.5) |
| Pain management | 58 (10.7) |
| Alcohol dependence pharmacotherapy | 30 (5.6) |
| Opioid antagonist therapy | 8 (1.5) |
| Missing | 1 (0.2) |
| Total | 539 (100) |

[a]Percentage based on total number indicating addiction medicine consultations (N = 539)

## Opioid and Psychoactive Exposures by Year

Figure 2 illustrates the percentage of opioid and psychoactive exposures among all cases reported to the Core Registry from 2010 to 2023. Medical toxicologists have seen a higher percentage of patients with opioid exposures compared to psychoactive exposures consistently across 2010–2023. Psychoactive exposures have doubled from 2.2% in 2010 to 4.3% in 2023. The percentage of opioid exposures among all cases in the Core Registry have gradually increased from 13.7% in 2010 to 19.3% in 2023.

## Clinical Signs and Symptoms

### Toxidromes

One or more toxidromes were documented in 23.4% of cases in the Core Registry in 2023 (Table 20). Opioid toxidromes were the most frequently reported (9.7%) followed by sedative-hypnotic (3.9%), anticholinergic (3.9%), and sympathomimetic (2.7%) toxidromes.

## Major Vital Sign Abnormalities

Major vital sign abnormalities were reported in 17.9% of Core Registry cases (Table 21). Tachycardia (10.9%) was the most frequently reported abnormality, followed by hypotension (5.3%), hypertension (3.9%), and bradycardia (3.2%).

## Clinical Signs and Symptoms – Neurologic

Neurologic signs and symptoms were the most frequently reported clinical features in the Core Registry in 2023, with 42.2% of cases associated with at least one or more neurologic effects (Table 22). Coma/CNS depression (18.9%) was the most commonly encountered neurologic clinical effect

**Table 13** Exposure agent classes reported in medical toxicology consultations

| | *N (%)*[a] |
|---|---|
| Ethanol | 1641 (24.4) |
| Opioid | 1521 (22.7) |
| Analgesic | 1120 (16.7) |
| Antidepressant | 787 (11.7) |
| Sympathomimetic | 658 (9.8) |
| Sedative-hypnotic/muscle relaxant | 524 (7.8) |
| Cardiovascular | 468 (7.0) |
| Anticholinergic/antihistamine | 467 (7.0) |
| Envenomation | 399 (5.9) |
| Psychoactive | 328 (4.9) |
| Antipsychotic | 310 (4.6) |
| Anticonvulsant | 169 (2.5) |
| Diabetic medication | 99 (1.5) |
| Herbal products/dietary supplements | 86 (1.3) |
| Gases/irritants/vapors/dusts | 84 (1.3) |
| Toxic alcohols | 82 (1.2) |
| Cough and cold products | 80 (1.2) |
| Metals | 76 (1.1) |
| Lithium | 69 (1.0) |
| Plants and fungi | 67 (1.0) |
| Caustic | 57 (0.8) |
| Household products | 57 (0.8) |
| Antimicrobials | 50 (0.7) |
| Gastrointestinal | 37 (0.6) |
| Endocrine | 31 (0.5) |
| Hydrocarbon | 30 (0.4) |
| Other pharmaceutical product | 30 (0.4) |
| Anesthetic | 24 (0.4) |
| Other nonpharmaceutical product | 24 (0.4) |
| Chemotherapeutic and immune | 23 (0.3) |
| Unknown class | 21 (0.3) |
| Insecticide | 15 (0.2) |
| Anticoagulant | 14 (0.2) |
| Herbicide | 8 (0.1) |
| Pulmonary | 5 (0.1) |
| Rodenticide | 5 (0.1) |
| Anti-parkinsonism drugs | 4 (0.1) |
| WMD[b]/riot agent/radiological | 3 (0.0) |
| Ingested foreign body | 1 (0.0) |
| Other | 1 (0.0) |
| Chelators | 0 (0.0) |
| Cholinergic | 0 (0.0) |
| Fungicide | 0 (0.0) |
| Marine toxin | 0 (0.0) |
| Photosensitizing agents | 0 (0.0) |
| Total agents | 9475 (100) |

[a]Percentages based on total number of reported agent entries from N = 6712 cases; 4944 Core Registry cases (73.7%) reported [a]single agent

[b]*WMD:* Weapon of Mass Destruction

**Table 14** Top 10 single agent exposure classes

| Rank | Single Agents | *N (%)*[a] |
|---|---|---|
| 1 | Ethanol | 1301 (26.3) |
| 2 | Opioid | 858 (17.4) |
| 3 | Analgesic | 550 (11.1) |
| 4 | Envenomation | 395 (8.0) |
| 5 | Antidepressant | 264 (5.3) |
| 6 | Sympathomimetic | 187 (3.8) |
| 7 | Anticholinergic/antihistamine | 171 (3.5) |
| 8 | Psychoactive | 169 (3.4) |
| 9 | Sedative-hypnotic/muscle relaxant | 155 (3.1) |
| 10 | Cardiovascular | 152 (3.1) |

[a]Percentages based on cases reporting a single agent (N = 4944)

**Table 15** Ethanol and toxic alcohols

| | *N (%)* |
|---|---|
| Ethanol[a] | 1641 (100) |
| Toxic alcohols[b] | |
| Isopropanol | 35 (42.7) |
| Ethylene glycol | 22 (26.8) |
| Methanol | 6 (7.3) |
| Toxic alcohol unspecified | 5 (6.1) |
| Miscellaneous[c] | 14 (17.1) |
| Class total | 82 (100) |

[a]Ethanol is considered a separate agent class

[b]Percentages based on total number of reported toxic alcohol (non-ethanol alcohols and glycols) class entries

[c]Includes acetone, alcohol ethoxylate, butyl ethylene glycol, denatured alcohol non-ethanol, diethylene glycol, methyl ethyl ketone, propylene glycol, and triethylene glycol monobutyl ether

followed by agitation (12.6%), hyperreflexia/myoclonus/clonus/tremor (11.9%), and seizures (6.1%).

## Clinical Signs and Symptoms – Pulmonary and Cardiovascular

Pulmonary (9.2%) and cardiovascular (7.6%) signs and symptoms were also frequently reported in 2023 (Table 23). Respiratory depression (7.6%) and QTc prolongation (5.6%) were the most commonly encountered pulmonary and cardiovascular effects, respectively.

## Clinical Signs and Symptoms – Other Organ Systems

Other signs and symptoms were reported in the Core Registry in 2023 by organ system and included metabolic (7.6%), hematologic (7.4%), renal/musculoskeletal (6.4%), gastrointestinal/hepatic (5.9%) and dermatologic (2.4%) presentations (Table 24). The most frequently reported clinical effects by organ system were metabolic acidosis (4.0%), hemolysis (2.7%), acute kidney injury (4.2%), hepatotoxicity with an ALT 100–1000 IU/L (3.6%) and rash (1.3%), respectively.

**Table 16** Opioids

| | *N (%)*[a] |
|---|---|
| Fentanyl | 957 (62.9) |
| Oxycodone | 113 (7.4) |
| Methadone | 99 (6.5) |
| Buprenorphine | 84 (5.5) |
| Heroin | 68 (4.5) |
| Opioid Unspecified | 65 (4.3) |
| Tramadol | 35 (2.3) |
| Hydrocodone | 28 (1.8) |
| Morphine | 19 (1.2) |
| Naloxone | 18 (1.2) |
| Hydromorphone | 12 (0.8) |
| Naltrexone | 7 (0.5) |
| Miscellaneous[b] | 16 (1.1) |
| Class total | 1521 (100) |

[a]Percentages based on total number of reported opioid class entries

[b]Includes carfentanil, codeine, depropionylfentanyl, dihydrocodeine, loperamide, meperidine, opium, oxymorphone, and samidorphan

**Table 17** Analgesics

| | *N (%)*[a] |
|---|---|
| Acetaminophen | 739 (66.0) |
| Ibuprofen | 126 (11.3) |
| Acetylsalicylic acid | 90 (8.0) |
| Gabapentin | 78 (7.0) |
| Naproxen | 28 (2.5) |
| Salicylic acid | 17 (1.5) |
| Pregabalin | 16 (1.4) |
| Meloxicam | 6 (0.5) |
| Miscellaneous[b] | 20 (1.8) |
| Class total | 1120 (100) |

[a]Percentages based on total number of reported analgesic class entries

[b]Includes acemetacin, celecoxib, diclofenac, ketorolac, metamizole, methylsalicylate, non-steroidal anti-inflammatory (NSAID) unspecified, phenazopyridine, and piroxicam

**Table 18** Antidepressants

| | *N (%)*[a] |
|---|---|
| Selective serotonin reuptake inhibitors (SSRIs) | 342 (43.5) |
| Sertraline | 135 (17.2) |
| Escitalopram | 85 (10.8) |
| Fluoxetine | 72 (9.1) |
| Citalopram | 32 (4.1) |
| Paroxetine | 8 (1.0) |
| Fluvoxamine | 6 (0.8) |
| Miscellaneous[b] | 4 (0.5) |
| Other antidepressants | 302 (38.3) |
| Bupropion | 175 (22.2) |
| Trazodone | 96 (12.2) |
| Mirtazapine | 26 (3.3) |
| Miscellaneous[c] | 5 (0.6) |
| Serotonin-norepinephrine reuptake inhibitors (SNRIs) | 73 (9.3) |
| Venlafaxine | 42 (5.4) |
| Duloxetine | 23 (2.9) |
| Desvenlafaxine | 8 (1.0) |
| Tricyclic Antidepressants (TCAs) | 70 (8.9) |
| Amitriptyline | 42 (5.3) |
| Doxepin | 16 (2.0) |
| Nortriptyline | 6 (0.8) |
| Miscellaneous[d] | 6 (0.8) |
| Class total | 787 (100) |

[a]Percentages based on total number of reported antidepressant class entries

[b]Includes vilazodone

[c]Includes mianserin, phenelzine, and vortioxetine

[d]Includes clomipramine, and tianeptine

**Table 19** Sympathomimetic Agents

| | *N (%)*[a] |
|---|---|
| Methamphetamine | 290 (44.0) |
| Cocaine | 202 (30.7) |
| Amphetamine | 61 (9.3) |
| Dextroamphetamine | 25 (3.8) |
| Methylphenidate | 24 (3.6) |
| Lisdexamfetamine | 12 (1.8) |
| 3,4-Methylenedioxymethamphetamine (MDMA), Ecstasy) | 11 (1.7) |
| Atomoxetine | 7 (1.1) |
| Dexmethylphenidate | 5 (0.8) |
| Phenylephrine | 5 (0.8) |
| Miscellaneous[b] | 16 (2.4) |
| Class total | 658 (100) |

[a]Percentages based on total number of reported sympathomimetic class entries

[b]Includes benzphetamine, clenbuterol, epinephrine, mixed amphetamine salts, phentermine, phenylpropylaminopentane, propylhexedrine, pseudoephedrine, and sympathomimetic unspecified

# Treatment

## Antidotal Therapy

Table 25 describes the reported antidotes administered within the Core Registry in 2023, reflecting a 2.9% increase in antidotal therapy compared with 2022 (38.3% in 2022 vs 41.2% in 2023) [10]. Thiamine (30.4%), folate (26.3%), and N-acetylcysteine (14.1%) continue to rank as the top three most commonly reported antidotal therapies.

## Antivenom Treatment

In 2023, Crotalidae immune fab2 (equine) accounted for 55.0% of reported antivenom administrations, surpassing the 31.9% reported in 2022 (Table 26) [10]. This marks a notable shift from previous years when crotalidae polyvalent immune fab (ovine) was the most commonly administered antivenom, now representing 39.4% of cases in 2023.

## Pharmacologic Supportive Care

Table 27 describes the pharmacologic supportive care treatments reported in 2023, marking a 3.3% increase compared to 2022 (43.0% in 2022 vs 46.3% in 2023) [10]. Benzodiazepines (38.1%) and phenobarbital (14.9%) remain the two most commonly reported, followed by opioids (13.2%).

## Non-Pharmacologic Supportive Care

Intravenous fluid resuscitation (83.4%) and intubation/ventilatory management (14.1%) were the predominant treatments in this category of non-pharmacologic supportive care in 2023, aligning with trends observed in previous years (Table 28) [10–22].

## Chelation Therapy

Chelation therapy was administered to 0.2% of the total Core Registry cases in 2023, with some patients receiving more than one chelating agent (Table 29). Dimercaptosuccinic acid (DMSA) was the most common chelating agent used (53.8%), followed by British Anti-Lewisite (BAL) (23.1%).

## Decontamination Interventions

Decontamination interventions continue to be infrequent, with only 2.1% of cases reported to the Core Registry receiving such interventions in 2023 (Table 30). This frequency has consistently remained at or below 3.7% since 2016 [10–16]. Among the decontamination interventions

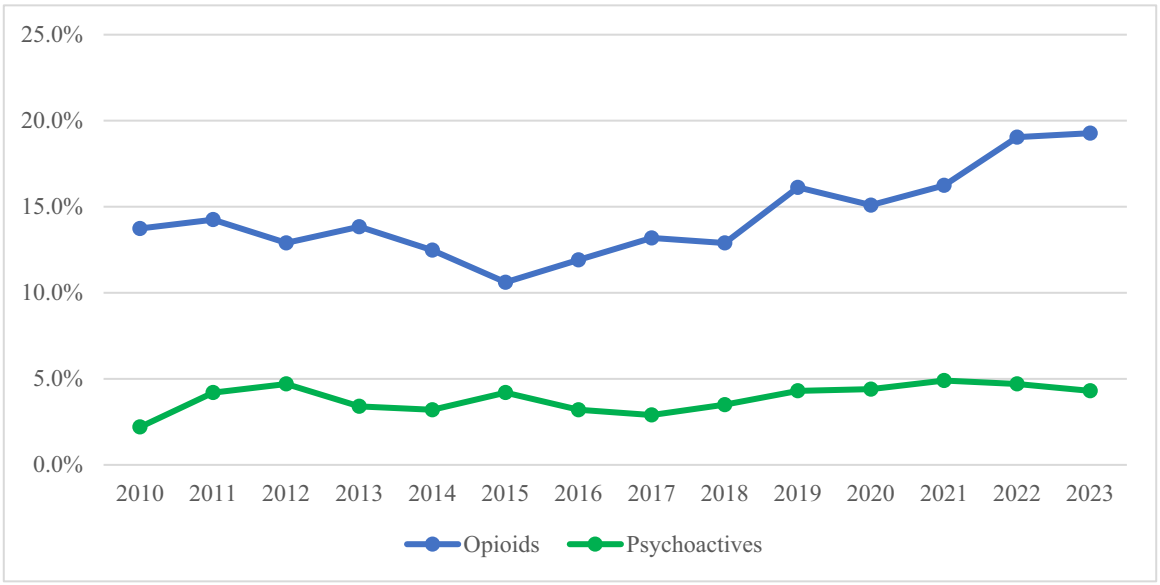


**Fig. 2** Percentage of medical toxicology consults with opioid and psychoactive exposures by year

**Table 20** Toxidromes

| | *N (%)*[a] |
|---|---|
| Cases with signs/symptoms, but no toxidrome reported | 4043 (54.7) |
| Cases with one or more toxidromes reported | 1727 (23.4) |
| Total Reported Toxidromes[b] | 1843 |
| Opioid | 719 (9.7) |
| Sedative-hypnotic | 287 (3.9) |
| Anticholinergic | 287 (3.9) |
| Sympathomimetic | 196 (2.7) |
| Serotonin syndrome | 146 (2.0) |
| Alcoholic ketoacidosis | 113 (1.5) |
| Washout syndrome | 37 (0.5) |
| Sympatholytic | 30 (0.4) |
| Cannabinoid hyperemesis | 10 (0.1) |
| Anticonvulsant hypersensitivity | 6 (0.1) |
| Neuroleptic malignant syndrome | 5 (0.1) |
| Cholinergic | 4 (0.1) |
| Overlap syndromes | 3 (0.0) |

[a]Percentage based on number of cases reporting toxidromes relative to total number of Core Registry cases (N = 7392)

[b]Cases may be associated with more than one toxidrome

utilized, activated charcoal remains the most common (86.4%). Whole bowel irrigation was employed in only 7.4% of cases receiving decontamination. There were 162 instances of decontamination reported in 156 unique patients. Therefore, some individuals received more than one decontamination modality.

## Enhanced Elimination Interventions

Enhanced elimination interventions were performed in 1.4% of cases reported in the Core Registry in 2023 (Table 31). The most frequent mechanism of enhanced elimination was continuous renal replacement therapy (33.3%), followed by hemodialysis performed for non-toxin removal indications (24.6%), hemodialysis for toxin removal (23.0%), and urinary alkalinization (12.7%).

## Addiction Medicine Treatments

Of all treatments administered by medical toxicologists among cases in the Core Registry for 2023, 27.4% were addiction medicine treatments (Table 32). The most commonly administered addiction medicine treatment was acamprosate (21.2%), followed by buprenorphine/naloxone dual formulations (19.2%), buprenorphine without an opioid antagonist (15.0%) and clonidine (11.3%). Nicotine replacement therapy was the least frequently reported addiction medication therapy, accounting for only 2.6%.

## Treatment Trends for Specific Exposures

Figure 3 outlines physostigmine and rivastigmine use for anticholinergic exposures as a percentage of total anticholinergic exposures in the Core Registry by year. From 2010–2020, physostigmine use ranged between 5.7% to 19.4%. With the physostigmine drug shortage in 2023 [23], rivastigmine

**Table 21** Major Vital Sign Abnormalities

| | *N (%)*[a] |
|---|---|
| Cases with signs/symptoms, but no major vital sign abnormality | 4246 (57.4) |
| Cases with one or more major vital sign abnormality | 1324 (17.9) |
| Total Reported Major Vital Sign Abnormalities[b] | 1905 |
| Tachycardia (HR[c] > 140 beats per minute) | 803 (10.9) |
| Hypotension (systolic BP[d] < 80 mmHg) | 391 (5.3) |
| Hypertension (systolic BP[d] > 200 mmHg and/or diastolic BP[d] > 120 mmHg) | 288 (3.9) |
| Bradycardia (HR[c] < 50 beats per minute) | 237 (3.2) |
| Bradypnea (RR[e] < 10 breaths per minute) | 159 (2.2) |
| Hyperthermia (temperature > 105° F) | 27 (0.4) |

[a]Percentage based on number of cases reporting major vital sign abnormalities relative to the total number of Core Registry cases (N = 7392)

[b]Cases may be associated with more than one major vital sign abnormality

[c]*HR:* heart rate

[d]*BP:* blood pressure

[e]*RR:* respiratory rate

**Table 22** Clinical signs and symptoms – neurologic

| | *N (%)*[a] |
|---|---|
| Cases with signs/symptoms, but no neurologic effects | 2448 (33.1) |
| Cases with one or more neurologic effects | 3122 (42.2) |
| Total Reported Neurologic Clinical Effects[b] | 4528 |
| Coma/CNS depression | 1399 (18.9) |
| Agitation | 935 (12.6) |
| Hyperreflexia/Myoclonus/Clonus/Tremor | 883 (11.9) |
| Seizures | 452 (6.1) |
| Delirium/Toxic psychosis | 426 (5.8) |
| Hallucinations | 282 (3.8) |
| Weakness/Paralysis | 57 (0.8) |
| Numbness/Paresthesia | 53 (0.7) |
| EPS/Dystonia/Rigidity | 34 (0.5) |
| Peripheral neuropathy (objective) | 7 (0.1) |

[a]Percentage based on number of cases reporting neurologic effects relative to total number of Core Registry cases (N = 7392)

[b]Cases may be associated with more than one neurologic effect

**Table 23** Clinical signs – pulmonary and cardiovascular

| | *N (%)*[a] |
|---|---|
| Pulmonary | |
| Cases with signs/symptoms, but no pulmonary effects | 5090 (68.9) |
| Cases with one or more pulmonary effects | 680 (9.2) |
| Total Reported Pulmonary Effects[b] | 723 |
| Respiratory depression | 562 (7.6) |
| Aspiration pneumonitis | 89 (1.2) |
| Acute lung injury/ARDS[c] | 49 (0.7) |
| Asthma/Reactive airway disease | 23 (0.3) |
| Cardiovascular | |
| Cases with signs/symptoms, but no cardiovascular effects | 5207 (70.4) |
| Cases with one or more cardiovascular effects | 563 (7.6) |
| Total Reported Cardiovascular Effects[b] | 638 |
| Prolonged QTc (≥ 500 ms) | 413 (5.6) |
| Prolonged QRS (≥ 120 ms) | 104 (1.4) |
| Myocardial injury or infarction | 55 (0.7) |
| Ventricular dysrhythmia | 51 (0.7) |
| AV Block (> 1st degree) | 15 (0.2) |

[a]Percentage based on number of cases reporting pulmonary or cardiovascular effects relative to total number of Core Registry cases (N = 7392)

[b]Cases may be associated with more than one pulmonary or cardiovascular effect

[c]*ARDS*: Acute respiratory distress syndrome

treatment for anticholinergic toxicity made a debut reaching use in 3.6% of cases presenting with anticholinergic exposure.

Figure 4 presents the percentage of acetaminophen exposure cases that were treated with a fomepizole adjunct regimen. Fomepizole has been increasingly used by medical toxicology physicians in acetaminophen toxicity, ranging from the lowest reported use of 0.1% of acetaminophen exposure cases in 2012 to a peak of 9.1% in 2023.

## Fatalities

In 2023, there were 98 reported fatalities, comprising 1.3% of Core Registry cases, a 1.6% decrease from the

**Table 24** Clinical signs – other organ systems

| | *N (%)*[a] |
|---|---|
| Metabolic | |
| Cases with signs/symptoms, but no metabolic effects | 5208 (70.5) |
| Cases with one or more metabolic effects | 562 (7.6) |
| Total Reported Metabolic Clinical Effects[b] | 689 |
| Metabolic acidosis (pH < 7.2) | 297 (4.0) |
| Elevated anion gap (> 20) | 264 (3.6) |
| Hypoglycemia (glucose < 50 mg/dL) | 100 (1.4) |
| Elevated osmole gap (> 20) | 28 (0.4) |
| Hematologic | |
| Cases with signs/symptoms, but no hematologic effects | 5221 (70.6) |
| Cases with one or more hematologic effects | 549 (7.4) |
| Total Reported Hematologic Clinical Effects[b] | 568 |
| Hemolysis (Hgb[c] < 10 g/dL) | 200 (2.7) |
| Coagulopathy (PT[d] > 15 s) | 176 (2.4) |
| Thrombocytopenia (platelets < 100 K/μL) | 162 (2.2) |
| Leukocytosis (WBC[e] > 20 K/μL) | 115 (1.6) |
| Methemoglobinemia (MetHgb ≥ 2%) | 18 (0.2) |
| Pancytopenia | 9 (0.1) |
| Renal/Musculoskeletal | |
| Cases with signs/symptoms, but no renal/musculoskeletal effects | 5296 (71.6) |
| Cases with one or more renal/musculoskeletal effects | 474 (6.4) |
| Total Reported Renal/Musculoskeletal Clinical Effects[b] | 541 |
| Acute kidney injury (creatinine > 2.0 mg/dL) | 310 (4.2) |
| Rhabdomyolysis (CPK[f] > 1000 IU/L) | 231 (3.1) |
| Gastrointestinal/Hepatic | |
| Cases with signs/symptoms, but no gastrointestinal/hepatic effects | 5334 (72.2) |
| Cases with one or more gastrointestinal/hepatic effects | 436 (5.9) |
| Total Reported Gastrointestinal/Hepatic Clinical Effects[b] | 549 |
| Hepatotoxicity (ALT[g] 100—1000 IU/L) | 268 (3.6) |
| Hepatotoxicity (AST[h] ≥ 1000 IU/L) | 137 (1.9) |
| Hepatotoxicity (ALT[g] ≥ 1000 IU/L) | 83 (1.1) |
| Gastrointestinal bleeding | 26 (0.4) |
| Pancreatitis | 20 (0.3) |
| Corrosive injury | 13 (0.2) |
| Intestinal ischemia | 2 (0.0) |
| Dermatologic | |
| Cases with signs/symptoms, but no dermatologic effects | 5590 (75.6) |
| Cases with one or more dermatologic effects | 180 (2.4) |
| Total Reported Dermatologic Clinical Effects[b] | 216 |
| Rash | 98 (1.3) |
| Blister/Bullae | 68 (0.9) |
| Necrosis | 28 (0.4) |
| Angioedema | 22 (0.3) |

[a]Percentage based on number of cases reporting other organ system effects relative to total number of Core Registry cases (N = 7392)

[b]Cases may be associated with more than category effect

[c]*Hgb:* hemoglobin

[d]*PT:* prothrombin time

[e]*WBC:* white blood cells

[f]*CPK*: creatine phosphokinase

[g]*ALT*: alanine transaminase

[h]*AST:* aspartate aminotransferase

**Table 25** Antidotal therapy

| | *N (%)*[a] |
|---|---|
| Thiamine | 1517 (30.4) |
| Folate | 1312 (26.3) |
| *N*-acetylcysteine | 704 (14.1) |
| Naloxone | 515 (10.3) |
| Sodium bicarbonate | 213 (4.3) |
| Glucagon | 208 (4.2) |
| Fomepizole | 144 (2.9) |
| Calcium | 73 (1.5) |
| Flumazenil | 59 (1.2) |
| Methylene blue | 28 (0.6) |
| Octreotide | 28 (0.6) |
| Insulin-euglycemic therapy | 23 (0.5) |
| Vitamin K | 22 (0.4) |
| Atropine | 21 (0.4) |
| Cyproheptadine | 21 (0.4) |
| Rivastigmine | 20 (0.4) |
| Lipid resuscitation therapy | 15 (0.3) |
| Pyridoxine | 14 (0.3) |
| Carnitine | 12 (0.2) |
| Hydroxocobalamin | 12 (0.2) |
| Fab for digoxin | 8 (0.2) |
| Physostigmine | 8 (0.2) |
| Dantrolene | 3 (0.1) |
| Bromocriptine | 2 (0.0) |
| Thiosulfate | 2 (0.0) |
| Anticoagulation reversal agent | 1 (0.0) |
| Botulinum antitoxin | 1 (0.0) |
| Ethanol | 1 (0.0) |
| Factor replacement | 1 (0.0) |
| Protamine | 1 (0.0) |
| 2-PAM | 1 (0.0) |
| Total | 4990 (100) |

[a]Percentages based on total number of antidote treatments administered (N = 4990); 3044 Core Registry cases (41.2%) received at least one antidote. Cases may have involved the use of multiple antidotes

**Table 26** Antivenom treatment

| | *N (%)*[a] |
|---|---|
| Crotalidae immune $fab_2$ (equine) | 149 (55.0) |
| Crotalidae polyvalent immune fab (ovine) | 107 (39.4) |
| Other snake antivenom | 10 (3.7) |
| Scorpion antivenom | 4 (1.5) |
| Spider antivenom | 1 (0.4) |
| Total | 271 (100) |

[a]Percentages based on total number of antivenom treatments administered (N = 271); 254 Core Registry cases (3.4%) received at least one antivenom treatment. Cases may have involved the use of multiple antivenom treatments

**Table 27** Supportive care – pharmacologic

| | *N (%)*[a] |
|---|---|
| Benzodiazepines | 2236 (38.1) |
| Phenobarbital | 877 (14.9) |
| Opioids | 774 (13.2) |
| Propofol | 368 (6.2) |
| Antipsychotics | 292 (5.0) |
| Vasopressors | 282 (4.8) |
| Dexmedetomidine | 235 (4.0) |
| Albuterol and other bronchodilators | 219 (3.7) |
| Anticonvulsants | 157 (2.7) |
| Glucose > 5% | 109 (1.9) |
| Neuromuscular blockers | 92 (1.6) |
| Ketamine | 83 (1.4) |
| Steroids | 49 (0.8) |
| Antihypertensives | 39 (0.7) |
| Beta-blockers | 33 (0.6) |
| Antiarrhythmics | 16 (0.3) |
| Vasodilators | 6 (0.1) |
| Total | 5867 (100) |

[a]Percentages based on total number of pharmacologic interventions (N = 5867); 3425 Core Registry cases (46.3%) received at least one pharmacologic intervention. Cases may have involved the use of multiple interventions

118 fatalities reported in 2022 and 1.4% reduction from the 120 fatalities reported in 2021 [10, 11]. Single agent exposures were implicated in 61 cases (Table 33), while 23 cases involved multiple agents (Table 34). There were 14 fatalities reported to the Core Registry with unknown toxicological exposure (Table 35). There were 42 fatality cases in which life support was withdrawn, representing 42.9% of all fatality cases in 2023. Brain death was declared in 22 (52.4%) of these cases.

Ethanol emerged as the most commonly implicated agent in single agent fatalities, with 10 reported cases (10.2% of all fatalities). The opioid class was involved in 10 single agent fatalities and 2 multiple agent fatalities (12.2% of all fatalities), with fentanyl as the opioid agent most frequently reported in 9 cases (9.2% of all fatalities). Acetaminophen remains a common agent associated with fatalities reported to the Core Registry, involved in 8 single agent and 8 multiple agent deaths (16.3% of all fatalities).

Among all fatalities, 16 pediatric deaths (age 0–18 years) were reported to the Core Registry (16.3%). Notably, a single agent marijuana related death was reported in a 3-year-old whose clinical signs and symptoms included coma/CNS depression, respiratory depression, and hypotension. Delta-8

**Table 28** Supportive care – nonpharmacologic

| | *N (%)*[a] |
|---|---|
| IV fluid resuscitation | 3694 (83.4) |
| Intubation/ventilatory management | 625 (14.1) |
| CPR[b] | 42 (1.0) |
| Transfusion | 21(0.5) |
| ECMO[c] | 15 (0.3) |
| Hyperbaric oxygen | 14 (0.3) |
| Cardioversion | 8 (0.2) |
| Pacemaker | 4 (0.1) |
| Therapeutic hypothermia | 4 (0.1) |
| Balloon pump | 2 (0.0) |
| **Total** | **4429 (100)** |

[a]Percentages based on total number of treatments administered (N = 4429); 3841 Core Registry cases (52.0%) received at least one nonpharmacologic treatment. Cases may have involved the use of multiple forms of treatment

[b]*CPR:* Cardiopulmonary resuscitation

[c]*ECMO:* extracorporeal membrane oxygenation

**Table 29** Chelation therapy

| | *N (%)*[a] |
|---|---|
| DMSA[b] | 14 (53.8) |
| BAL[c] | 6 (23.1) |
| Deferoxamine | 3 (11.5) |
| EDTA[d] | 3 (11.5) |
| Total | 26 (100) |

[a]Percentages based on total number of chelation treatments administered (N = 26); 18 Core Registry cases (0.2%) received at least one chelation treatment

[b]*DMSA:* dimercaptosuccinic acid

[c]*BAL:* British anti-Lewisite (dimercaprol)

[d]*EDTA:* Ethylenediaminetetraacetic acid

**Table 30** Decontamination Interventions

| | *N (%)*[a] |
|---|---|
| Activated charcoal | 140 (86.4) |
| Whole bowel irrigation | 12 (7.4) |
| Irrigation | 9 (5.6) |
| Gastric lavage | 1 (0.6) |
| Total | 162 (100) |

[a]Percentages based on total number of decontamination interventions (N = 162); 156 Core Registry cases (2.1%) received at least one decontamination intervention. Cases may have involved the use of multiple interventions

**Table 31** Enhanced elimination

| | *N (%)*[a] |
|---|---|
| Continuous renal replacement therapy | 42 (33.3) |
| Hemodialysis with other indication | 31 (24.6) |
| Hemodialysis for toxin removal | 29 (23.0) |
| Urinary alkalinization | 16 (12.7) |
| Multiple-dose activation charcoal | 6 (4.8) |
| Exchange transfusion | 2 (1.6) |
| Total | 126 (100) |

[a]Percentages based on total number of treatments administered (N = 126); 100 Core Registry cases (1.4%) received at least one enhanced elimination intervention. Cases may have involved the use of multiple interventions

tetrahydrocannabinol was associated with one multiple agent fatality, along with ethanol and an unspecified pharmaceutical. This patient's clinical findings were CNS depression, respiratory depression, bradycardia, hypertension, QRS prolongation, and seizures.

For the second time since the Core Registry started in 2010, and for the second consecutive year, a fatality was reported following snakebite envenomation. The 41-year-old patient sustained a captive unspecified snake bite in the Southeastern United States. The clinical findings reported after the envenomation were coma/CNS depression, respiratory depression, hypotension, and ventricular dysrhythmia. The patient was treated with a total of 12 vials of antivenom and received vasopressors for persistent hypotension. On hospital day 5, the patient was found to have an anoxic brain injury on MRI. The patient had a prolonged hospital course of 24 days.

## Comparison of the 2023 Annual Report to Previous Annual Reports

For the first time in the ToxIC Core Registry, ethanol was identified as the leading agent exposure (24.4%) in 2023. Ethanol withdrawal was the second highest reason for encounter in 2023, steadily rising from the 10th reason for encounter in 2016 to the 5th in 2020 [12–16]. Ethanol was also involved in a considerable number of single agent and multiple agent fatalities (17.3% of all fatalities). Ethanol exposures have shown a rising trend in incidence, accounting for 10.7% of reported cases in 2021 and 14.9% of cases in 2022 [10, 11].

For the third consecutive year, fentanyl exposures were more prevalent than all other opioids combined, comprising 62.9% of all opioid exposures in 2023 (an increase from 40.1% in 2021 and 53.9% in 2022) [10, 11]. Conversely, the frequency of reported heroin exposures reported has

**Table 32** Addiction medicine treatments

| | *N (%)*[a] |
|---|---|
| Acamprosate | 688 (21.2) |
| Buprenorphine/naloxone dual formulations (e.g. Suboxone) | 623 (19.2) |
| Buprenorphine without an opioid antagonist (e.g. Subutex) | 490 (15.0) |
| Clonidine | 366 (11.3) |
| Disulfiram | 310 (9.5) |
| Methadone | 300 (9.2) |
| Naloxone overdose prevention kit or prescription | 267 (8.2) |
| Naltrexone | 119 (3.7) |
| Nicotine replacement therapy (patch, gum, etc.) | 85 (2.6) |
| Other specify—Outpatient substance use services/recovery care | 3 (0.1) |
| Total | 3251 (100) |

[a]Percentages based on total number of treatments administered (N = 3251); 2026 Core Registry cases (27.4%) received at least one addiction medicine treatment. Cases may have involved the use of multiple addiction medicine treatments

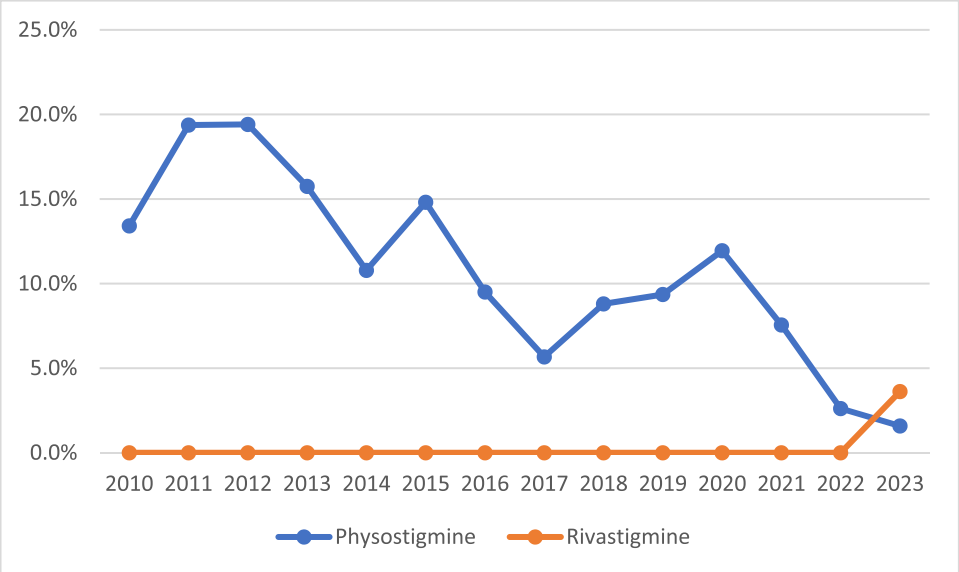


**Fig. 3** Percentage of medical toxicology consults with anticholinergic exposures receiving physostigmine or rivastigmine treatment by year

steadily declined over the past 5 years [10–13]. While heroin accounted for 32.1% of opioid exposures in 2020, it represented only 20.6% in 2021, 9.4% in 2022, and 4.5% in 2023 [10–12].

Acetaminophen has maintained its status as the most common non-opioid analgesic reported to the Core Registry for the 14th consecutive year, constituting 66.0% of this category in 2023 [10–22]. Similarly, consistent with the pattern observed over the previous four years, methamphetamine remained the most prevalent sympathomimetic exposure at 44.0% [10–13].

Consistent with recent years, intentional pharmaceutical exposures were the leading reason for medical toxicology encounters (28.1%). However, the proportion of intentional pharmaceutical exposures observed in 2023 marked the lowest recorded since the registry's inception in 2010 [10–22]. Intentional pharmaceutical exposures made up 52.4% of cases in both 2018 and 2019, declining to 43.8% in 2020 and 32.0% in 2022 [10, 12–14].

In 2023, there were 98 fatalities reported to the Core Registry (1.3% of all cases). This is a slight relative decrease from the 118 fatalities reported in 2022 (1.6%) and 120 fatalities reported in 2021 (1.4%) [10, 11]. For the first time in the ToxIC Core Registry, ethanol was the most common agent class reported in single agent fatalities (10.2% of all fatalities). The frequency of pediatric deaths (age 0–18 years) reported to the Core Registry has increased since 2021 (10.6% in 2021, 13.6% in 2022, and 16.3% in 2023). For the second time since the Core Registry started in 2010, and for the second consecutive year, a fatality was reported following a captive unknown type of snake envenomation in the Southeastern United States.

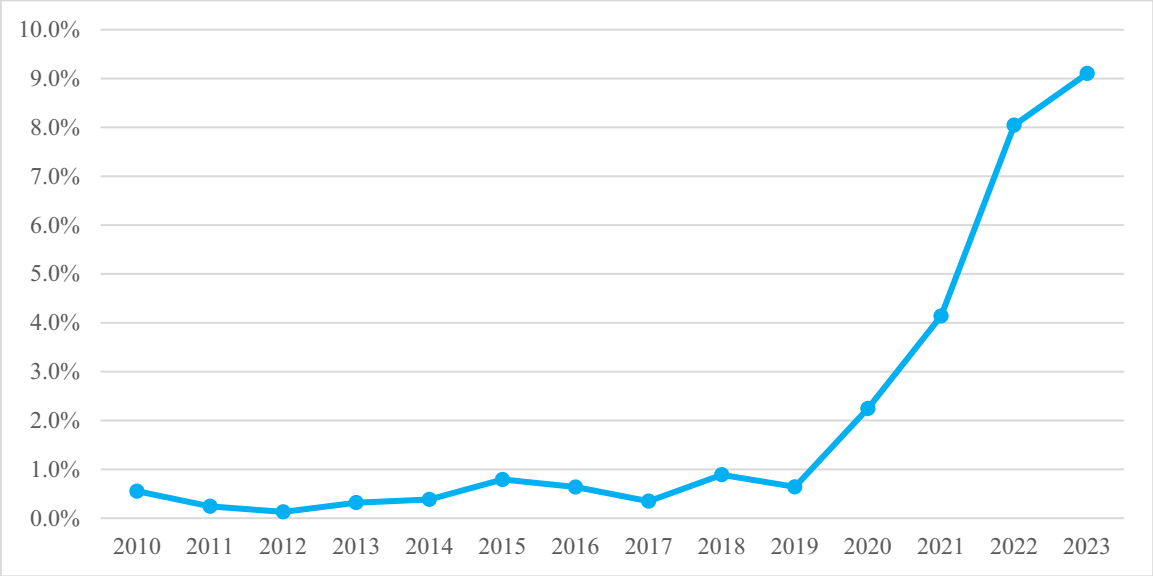


**Fig. 4** Percentage of medical toxicology consults with acetaminophen exposures receiving fomepizole treatment by year

## Discussion

In addition to the flagship Core Registry, ToxIC has led other multicenter projects that aim to conduct surveillance on opioid and stimulant overdoses and to identify new and emerging substances [2]. The Fentalog Study started in 2020 and gathers detailed information from chart reviews and qualitative blood toxicology tests from patients presenting with a suspected opioid overdose to an emergency department at one of 10 participating sites around the country. The ToxIC Fentalog Study has become a key non-fatal overdose data source featured by the Centers for Disease Control and Prevention through a dedicated dashboard on their website [24]. The DOTS Reporting Program was implemented in 2023 at 17 sites within the United States and enrolls patients ages 13 and older presenting with either suspected stimulant or opioid overdose. By the end of 2023, DOTS had 447 enrolled patients with detailed interviews, chart reviews, and laboratory confirmation that can be used to assess the overdose event, including responses to treatment. These projects are a testament to ToxIC's mission to provide opportunities for medical toxicologists to participate in and lead medical toxicology research projects [2].

This report describes the fourteenth year of data collection for the ToxIC Core Registry. Core Registry case numbers increased slightly this year (7206 cases in 2022 vs 7392 in 2023) [10]. The Core Registry continues to grow, adding a new site from New York with 2 participating hospitals this year. Since the Consortium's inception in 2010, the ToxIC Core Registry has amassed over 100,000 entered cases [2].

For the first time in the Core Registry, ethanol was designated as the leading agent of exposure (24.4%) and the most commonly reported agent associated with single agent fatalities (10.2% of all fatalities). Ethanol related reasons for the medical toxicology encounter involved ethanol withdrawal in 13.7% of cases and ethanol misuse in 12.4%. Ethanol exposures have shown a rising trend in incidence over the past few years, accounting for 10.7% of reported cases in 2021 and 14.9% of cases in 2022 [10, 11]. This rise echoes publications that found a stark increase in alcohol sales by 20% and alcohol related deaths by 25% associated with the COVID-19 pandemic [25, 26]. However, more analyses are needed to determine whether the Core Registry cases align with the national trends of alcohol-related morbidity and mortality, in addition to assessing differences in race/ethnicity, age, sex, and gender.

For the third consecutive year, fentanyl was the predominant opioid subclass reported to the Core Registry (62.9% of opioid exposures) and was associated with the 2nd highest number of single agent fatalities. Heroin has decreased from 32.1% of opioid exposures in 2020 to 4.5% in 2023 [12]. This replacement of fentanyl with heroin in drug overdose deaths has also been reported in a recently released National Center for Health Statistics Data Brief which demonstrated that while deaths associated with synthetic opioids rose 4.1% between 2021 and 2022, heroin associated deaths dropped 35.7% during the same time period [27].

Consistent with recent years, intentional pharmaceutical exposures were the most common reason for medical toxicology encounters (28.1%). However, the proportion of intentional pharmaceutical exposures observed in 2023

**Table 33** 2023 Fatalities reported in ToxIC core registry with known toxicological exposure[a]: single agent

| Age / Gender[b] | Race/Ethnicity | Agents Involved | Clinical Findings[c] | Life Support Withdrawn | Brain Death Confirmed | Treatment[d] |
|---|---|---|---|---|---|---|
| 88 M | Black/African | Acemetacin | AG, AKI, BC, CNS, HPT, HT, MA | No | | Benzodiazepines, continuous renal replacement therapy, fomepizole, glucose > 5%, intubation, IV fluid resuscitation, NAC, $NaHCO_3$, NMB, propofol, vasopressors (epinephrine, norepinephrine, phenylephrine, vasopressin) |
| 13 F | Hispanic | Acetaminophen | None | Unknown | | NAC |
| 27 F | Asian | Acetaminophen | HPT | Unknown | | NAC |
| 31 F | Non-Hispanic White | Acetaminophen | AG, AKI, CNS, CPT, HPT, HYS, MA, OG, PLT, QTC, TC, WBC | Yes | Yes | Calcium, continuous renal replacement therapy, folate, glucose > 5%, intubation, IV fluid resuscitation, NAC, $NaHCO_3$, propofol, thiamine, transfusion, vasopressors (norepinephrine, vasopressin), vitamin K |
| 55 M | Black/African | Acetaminophen | AG, AKI, ALI, CA, CNS, CPT, HPT, HT, HYS, MA, WBC | No | | Calcium, continuous renal replacement therapy, CPR, fomepizole, intubation, IV fluid resuscitation, NAC, $NaHCO_3$, opioids, steroids |
| 61 F | Hispanic | Acetaminophen | CA, CNS | Yes | Yes | CPR, intubation, IV fluid resuscitation, NAC, vasopressors (norepinephrine) |
| 61 F | Non-Hispanic White | Acetaminophen | AG, HGY, HPT, MA, TC | No | | Folate, IV fluid resuscitation, NAC, thiamine |
| 70 F | Non-Hispanic White | Acetaminophen | AG, CNS, GIB, HGY, HPT, HT, MA, QRS | Yes | No | Dexmedetomidine, fomepizole, glucose > 5%, hemodialysis for toxin removal, NAC, vasopressors (norepinephrine, phenylephrine, vasopressin), vitamin K |
| 73 F | Non-Hispanic White | Acetaminophen | CNS, HPT, HT, MA, WBC | Yes | Unknown | Continuous renal replacement therapy, fomepizole, NAC |
| 14 F | Non-Hispanic White | Amitriptyline | CA, CNS, QRS | Yes | Yes | CPR, intubation, IV fluid resuscitation, $NaHCO_3$ |
| 30 M | Non-Hispanic White | Carbon monoxide | CNS, RD, SZ | Yes | Yes | Benzodiazepines, hyperbaric oxygen, intubation, naloxone, propofol |
| 53 M | Non-Hispanic White | Carbon monoxide | AK, AKI, CNS, MA, RBM, WBC | Unknown | | Intubation, IV fluid resuscitation |
| 52 M | Black/African | Cocaine | CNS, TC | Yes | Yes | None |
| 24 M | Non-Hispanic White | Cyanide | AG, AP, CNS, HPT, HT, MA, MI, RD, TC, WBC | Yes | Yes | Hydroxocobalamin, intubation, IV fluid resuscitation, thiosulfate |
| 76 M | Unknown | Cyclobenzaprine | CNS, DLM, QRS, RFX | No | | None |
| 14 F | Non-Hispanic White | Dextromethorphan | CNS, QTC, TC | No | | IV fluid resuscitation |
| 69 F | Non-Hispanic White | Dextromethorphan | MA, RD | Unknown | | Continuous renal replacement therapy, fomepizole, intubation, IV fluid resuscitation, NAC, opioids, vasopressors (norepinephrine, vasopressin) |
| 17 M | Asian | Digoxin | None | Yes | Yes | None |
| 77 M | Non-Hispanic White | Digoxin | CNS, HTN, RD, TC | Unknown | | Digoxin immune fab, intubation, IV fluid resuscitation, thiamine, vasopressors (vasopressin) |
| 78 F | Unknown | Digoxin | None | Unknown | | None |

**Table 33** (continued)

| Age / Gender[b] | Race/Ethnicity | Agents Involved | Clinical Findings[c] | Life Support Withdrawn | Brain Death Confirmed | Treatment[d] |
|---|---|---|---|---|---|---|
| 80 F | Non-Hispanic White | Diltiazem | AP, CNS, RD, TC, VD | Yes | Yes | Calcium, glucagon, HIE, intubation, IV fluid resuscitation |
| 11 mo M | Black/African | Doxepin | AG, AKI, CNS, HT, MA, MI, RD, SZ, TC | Yes | Yes | Anticonvulsants, benzodiazepines, intubation, IV fluid resuscitation, NMB, opioids, phenobarbital, vasopressors (epinephrine, norepinephrine, vasopressin) |
| 34 F | Non-Hispanic White | Ethanol | AG, AGT, CNS, CPT, DLM, HPT, HYS, RFX | No | | Benzodiazepines, folate, intubation, IV fluid resuscitation, $NaHCO_3$, thiamine |
| 35 M | Asian | Ethanol | CPT, GIB, HYS, MI, PLT, RFX | Yes | No | Benzodiazepines, folate, thiamine |
| 47 F | Non-Hispanic White | Ethanol | AG, AKI, CNS, CPT, GII, HGY, HPT, HT, HYS, MA, PLT, QTC, RD, WBC | Yes | No | Benzodiazepines, calcium, continuous renal replacement therapy, folate, fomepizole, glucose > 5%, intubation, IV fluid resuscitation, leucovorin, NAC, $NaHCO_3$, NMB, opioids, propofol, pyridoxine, steroids, thiamine, transfusion, vasopressors (angiotensin, epinephrine, norepinephrine, phenylephrine, vasopressin) |
| 47 M | Non-Hispanic White | Ethanol | QTC, RFX | No | | Benzodiazepines, folate, intubation, IV fluid resuscitation, naloxone, phenobarbital, thiamine |
| 54 M | Non-Hispanic White | Ethanol | AG, AKI, CPT, HT, QTC, TC | Unknown | | Benzodiazepines, folate, glucagon, IV fluid resuscitation, naloxone, opioids, thiamine |
| 60 M | Non-Hispanic White | Ethanol | CPT, HYS, RFX | Unknown | | Benzodiazepines, folate, IV fluid resuscitation, $NaHCO_3$, thiamine |
| 63 M | Unknown | Ethanol | AG, AKI, CPT, HYS, PCT, PLT, RBM | No | | Benzodiazepines, dexmedetomidine, folate, IV fluid resuscitation, phenobarbital, thiamine, vasopressors (dopamine, epinephrine, norepinephrine, phenylephrine) |
| 64 M | Black/African | Ethanol | AG, AGT, AKI, AVB, BC, BP, CA, CNS, DLM, HAL, HT, HYS, OG, RFX, SZ | No | | Benzodiazepines, CPR, folate, fomepizole, intubation, IV fluid resuscitation, NMB, opioids, phenobarbital, propofol, steroids, thiamine |
| 72 M | Hispanic | Ethanol | HAL | Unknown | | Anticonvulsants, benzodiazepines, bronchodilators, folate, glucagon, IV fluid resuscitation, $NaHCO_3$, thiamine |
| 84 M | Non-Hispanic White | Ethanol | None | Unknown | | Benzodiazepines, folate, IV fluid resuscitation, opioids, propofol, thiamine |
| 15 M | Hispanic | Fentanyl | ALI, CA, CNS, OT, VD | No | | Benzodiazepines, CPR, dexmedetomidine, intubation, IV fluid resuscitation, NAC, opioids, propofol |
| 28 M | Non-Hispanic White | Fentanyl | CA, CNS, HTN, OT, QRS, QTC, RD, TC | Unknown | | CPR, intubation, IV fluid resuscitation, $NaHCO_3$, opioids, phenobarbital, propofol |
| 34 F | Non-Hispanic White | Fentanyl | ALI, BL, DLM, HAL, QTC, TC, WBC, WS | Yes | No | Methadone |
| 35 M | Non-Hispanic White | Fentanyl | OT, RD | Unknown | | None |

**Table 33** (continued)

| Age / Gender[b] | Race/Ethnicity | Agents Involved | Clinical Findings[c] | Life Support Withdrawn | Brain Death Confirmed | Treatment[d] |
|---|---|---|---|---|---|---|
| 36 M | Hispanic | Fentanyl | CA, CNS, OT, RD | No | | CPR, intubation, IV fluid resuscitation, naloxone |
| 44 F | Black/African | Fentanyl | HYS, RS | No | | Antihypertensives, methadone, opioids |
| 56 F | Black/African | Fentanyl | BP, CNS, HPT, OT, RD, VD | Yes | Yes | Antiarrhythmics, cardioversion, intubation, IV fluid resuscitation, naloxone, propofol, vasopressors (norepinephrine) |
| 62 F | Non-Hispanic White | Fentanyl | OT | Unknown | | IV fluid resuscitation, methadone, naloxone |
| 13 M | Hispanic | Fluoxetine | CNS, DLM, HYT, RBM, RD, SS, SZ, TC | Yes | Yes | Anticonvulsants, hemodialysis, IV fluid resuscitation, propofol |
| 46 M | Hispanic | Ibuprofen | AKI | Yes | No | Bronchodilators, intubation, IV fluid resuscitation, vasopressors (epinephrine, norepinephrine) |
| 61 F | Non-Hispanic White | Ibuprofen | HPT, MA, TC | No | | Benzodiazepines, folate, IV fluid resuscitation, NAC, thiamine |
| 3 F | Mixed NOS | Marijuana | CNS, HT, RD | No | | IV fluid resuscitation |
| 58 F | Black/African | Metformin | AG, AKI, HPT, MA, OG | No | | Calcium, fomepizole, glucose > 5%, hemodialysis, IV fluid resuscitation, $NaHCO_3$ |
| 61 M | Non-Hispanic White | Metformin | AG, AKI, CNS, HPT, HT, MA, QTC | Yes | Yes | Continuous renal replacement therapy, glucose > 5%, HIE, intubation, IV fluid resuscitation, NAC, thiamine, vasopressors (angiotensin, epinephrine, norepinephrine, phenylephrine, vasopressin) |
| 66 F | Non-Hispanic White | Metformin | AG, AKI, CNS, CPT, HGY, HT, MA, PLT, WBC | Yes | Unknown | Glucose > 5%, intubation, IV fluid resuscitation, vasopressors (norepinephrine) |
| 70 F | Non-Hispanic White | Metformin | AG, AKI, CA, CNS, HT, MA, QRS | Yes | Yes | Continuous renal replacement therapy, CPR, intubation, IV fluid resuscitation, methylene blue, $NaHCO_3$, vasopressors (epinephrine, norepinephrine, phenylephrine, vasopressin) |
| 2 mo F | Unknown | Nitroprusside | None | Yes | Unknown | None |
| 50 F | Non-Hispanic White | Opioid unspecified | AG, CNS, HPT, MA, SS, TC | Yes | Yes | Benzodiazepines |
| 1 mo F | Hispanic | Oxycodone | ALI, BP, CA, OT | No | | Anticonvulsants, CPR, IV fluid resuscitation, naloxone, steroids |
| 32 F | Hispanic | Phentermine | BC, HGY, HT, RD | Unknown | | Glucose > 5%, intubation, IV fluid resuscitation, thiamine, vasopressors (dobutamine, epinephrine, norepinephrine) |
| 60 M | Non-Hispanic White | Pregabalin | AGT, RFX, TC, VD | No | | Benzodiazepines |
| 74 F | Non-Hispanic White | Propafenone | AG, CNS, GIB, HT, MA, QRS, QTC, TC, VD | Yes | Unknown | $NaHCO_3$ |
| 17 F | Hispanic | Propranolol | BC, CNS, HGY, HPT, HT, MA, MI, PLT, VD | No | | Benzodiazepines, glucagon, glucose > 5%, intubation, IV fluid resuscitation, steroids, vasopressors (epinephrine, norepinephrine) |

**Table 33** (continued)

| Age / Gender[b] | Race/Ethnicity | Agents Involved | Clinical Findings[c] | Life Support Withdrawn | Brain Death Confirmed | Treatment[d] |
|---|---|---|---|---|---|---|
| 80 M | Non-Hispanic White | Sertraline | QRS, QTC | No | | IV fluid resuscitation |
| 41 M | Non-Hispanic White | Snake unspecified | CNS, HT, RD, VD | Unknown | | Fab antivenom, IV fluid resuscitation, therapeutic hypothermia, vasopressors (norepinephrine, phenylephrine) |
| 19 F | Black/African | Sodium nitrate | CNS, HT, MGH, RD, VD | Yes | No | Calcium, methylene blue, $NaHCO_3$, transfusion |
| 79 F | Non-Hispanic White | Sodium thiosulfate | AG, MA, RS | Yes | No | None |
| 45 F | Non-Hispanic White | Unknown agent | AKI, HPT, MA | Yes | No | Fomepizole, hemodialysis for toxin removal, IV fluid resuscitation, NAC |
| 67 F | Black/African | Venetoclax | AKI, CNS, CPT, GIB, HGY, HPT, HT, PLT, TC | No | | None |

[a]Based on response from Medical Toxicologist "Did the patient have a toxicological exposure?" equals Yes with known agent(s)

[b]Age in years unless otherwise stated. mo: months, M: male, F: female

[c]AG: anion gap, AGT: agitation, AK: alcoholic ketoacidosis, AKI: acute kidney injury, ALI: acute lung injury/ARDS, AP: aspiration pneumonitis, AVB: AV block, BC: bradycardia, BL: blisters/bullae, BP: bradypnea, CA: cardiac arrest, CNS: coma/CNS depression, CPT: coagulopathy, DLM: delirium, GIB: GI bleeding, GII: intestinal ischemia, HAL: hallucination, HGY: hypoglycemia, HPT: hepatoxicity, HT: hypotension, HTN: hypertension, HYS: hemolysis, HYT: hyperthermia, MA: metabolic acidosis, MHG: methemoglobinemia, MI: myocardial injury/ischemia, NM: numbness/paresthesias, OG: osmolar gap, OT: opioid toxidrome, PCT: pancytopenia, PLT: thrombocytopenia, PNC: pancreatitis, QRS: QRS prolongation, QTC: QTc prolongation, RBM: rhabdomyolysis, RD: respiratory depression, RFX: hyperreflexia/clonus/tremor, RS: rash, SHS: sedative-hypnotic syndrome, SS: serotonin syndrome, SYS: sympathomimetic syndrome, SZ: seizures, TC: tachycardia, VD: ventricular dysrhythmia, WBC: leukocytosis, WS: washout syndrome

[d]Pharmacological and Non-pharmacological support as reported by Medical Toxicologist; CPR: cardiopulmonary resuscitation, HIE: high dose insulin euglycemic therapy, NAC: n-acetyl cysteine, $NaHCO_3$: sodium bicarbonate, NMB: neuromuscular blockers

**Table 34** 2023 Fatalities reported in ToxIC Core Registry with known toxicological exposure[a]: Multiple agents

| Age / Gender[b] | Race/Ethnicity | Agents Involved | Clinical Findings[c] | Life Support Withdrawn | Brain Death Confirmed | Treatment[d] |
|---|---|---|---|---|---|---|
| 59 M | Non-Hispanic White | Acetaminophen, bupropion | AG, AKI, CA, CNS, CPT, HPT, HT, MA, PLT, RD, TC | No | | Continuous renal replacement therapy, CPR, intubation, IV fluid resuscitation, NAC, propofol, vasopressors (angiotensin, epinephrine, norepinephrine, phenylephrine, vasopressin) |
| 34 F | Non-Hispanic White | Acetaminophen, ethanol | AKI, HPT | Yes | Unknown | Fomepizole, IV fluid resuscitation, NAC |
| 59 F | Non-Hispanic White | Acetaminophen, ethanol | AG, AKI, HPT, HT, MA, OG, PLT, PNC, WBC | Yes | No | Continuous renal replacement therapy, fomepizole, intubation, NAC, transfusion, vasopressors (epinephrine, norepinephrine) |
| 16 F | Black/African | Acetaminophen, ethanol, ibuprofen | AGT, AKI, CNS, DLM, HGY, HPT, HT, RD | Yes | Yes | Benzodiazepines, fomepizole, glucagon, intubation, IV fluid resuscitation, NAC, $NaHCO_3$ |
| 37 M | Black/African | Acetaminophen, ibuprofen | CA | Yes | No | Antiarrhythmics, benzodiazepines, CPR, intubation, IV fluid resuscitation, NAC, vasopressors (epinephrine) |
| 66 F | Hispanic | Acetaminophen, ibuprofen | None | Unknown | | Fomepizole, IV fluid resuscitation, NAC, $NaHCO_3$, vasopressors (epinephrine) |
| 41 F | Hispanic | Acetaminophen, naproxen | AGT, HT, MA, PLT, TC | Unknown | | Intubation, IV fluid resuscitation, NAC, vasopressors (norepinephrine) |
| 19 F | Non-Hispanic White | Acetaminophen, sertraline, spironolactone | CNS | No | | NAC |
| 42 F | Asian | Amitriptyline, sertraline | HYT, TC | Yes | Unknown | None |
| 59 M | Black/African | Amlodipine, ibuprofen, lorazepam | AKI, CNS, HT, QTC, RD | Yes | Yes | Benzodiazepines, continuous renal replacement therapy, HIE, intubation, IV fluid resuscitation, vasopressors (epinephrine, norepinephrine) |
| 63 M | Non-Hispanic White | Baclofen, melatonin, pregabalin, quetiapine, sertraline | AKI, CPT, HYS, RD, TC | Unknown | | Antipsychotics, bronchodilators, folate, glucagon, IV fluid resuscitation, naloxone |
| 23 M | Hispanic | Benzodiazepine unspecified, cocaine, fentanyl | HTN, MA, RD, SYS, TC | Yes | Yes | Benzodiazepines, intubation, IV fluid resuscitation, naloxone, opioids, propofol |
| 13 F | Hispanic | Benzonatate, cough & cold unspecified | CA, CNS, HT, MA, TC, VD | No | | CPR |
| 13 T | Non-Hispanic White | Bismuth subsalicylate, diphenhydramine | CA, CNS, HT, MA, QRS, QTC, RBM, RD, SZ, TC | Yes | Yes | Anticonvulsants, CPR, $NaHCO_3$, naloxone, vasopressors (epinephrine, vasopressin) |
| 48 M | Non-Hispanic White | Carbon monoxide, cyanide | AG, ALI, CA, CNS, HPT, HT, MA, QTC, TC, WBC | Yes | Yes | Calcium, CPR, hydroxocobalamin, intubation, IV fluid resuscitation, $NaHCO_3$, vasopressors (epinephrine, norepinephrine, vasopressin) |

**Table 34** (continued)

| Age / Gender[b] | Race/Ethnicity | Agents Involved | Clinical Findings[c] | Life Support Withdrawn | Brain Death Confirmed | Treatment[d] |
|---|---|---|---|---|---|---|
| 14 F | Hispanic | Carbon monoxide, cyanide, smoke | AG, ALI, BL, BP, CA, CNS, MA, MI, PLT, RD, TC, WBC | Yes | Yes | Bronchodilators, CPR, ECMO, hydroxocobalamin, intubation, IV fluid resuscitation, $NaHCO_3$, NMB, opioids, propofol, thiosulfate, vasopressors (norepinephrine, milrinone) |
| 13 M | Non-Hispanic White | Citalopram, valacyclovir | CNS, HT, QRS, SS, SZ, TC, VD | No | | $NaHCO_3$ |
| 43 M | Non-Hispanic White | Cocaine, ethanol, heroin | CNS, NM, SZ | No | | Activated charcoal, benzodiazepines, IV fluid resuscitation, naloxone |
| 17 M | Black/African | Delta-8-tetrahydrocannabinol, ethanol, pharmaceutical unspecified | BC, CNS, HTN, QRS, RD, SZ | No | | IV fluid resuscitation, naloxone |
| 34 M | Non-Hispanic White | Dextroamphetamine, duster (canned air), ethanol | AG, ALI, CA, CNS, MA, RD, SZ, TC, VD, WBC | No | | Balloon pump, calcium, CPR, defibrillation, ECMO, intubation, IV fluid resuscitation, $NaHCO_3$, vasopressors (epinephrine, norepinephrine, phenylephrine, vasopressin) |
| 65 M | Non-Hispanic White | Diquat, glyphosate | MA, QTC | Unknown | | Benzodiazepines, glucagon, IV fluid resuscitation, $NaHCO_3$ |
| 19 F | Hispanic | Ethanol, marijuana, mirtazepine | CNS, HT, SS | No | | IV fluid resuscitation |
| 14 F | Black/African | Guanfacine, opioid unspecified, sertraline, topiramate | BC, CA, CNS, HTN, MA, OT, RD, SHS, VD | Yes | Yes | Anticonvulsants, CPR, intubation, IV fluid resuscitation, naloxone, vasopressors (epinephrine, norepinephrine) |

[a]Based on response from Medical Toxicologist "Did the patient have a toxicological exposure?" equals Yes with known agent(s)

[b]Age in years unless otherwise stated. M: male, F: female, T: transgender

[c]AG: anion gap, AGT: agitation, AKI: acute kidney injury, ALI: acute lung injury/ARDS, BC: bradycardia, BL: blisters/bullae, BP: bradypnea, CA: cardiac arrest, CNS: coma/CNS depression, CPT: coagulopathy, DLM: delirium, HGY: hypoglycemia, HPT: hepatoxicity, HT: hypotension, HTN: hypertension, HYS: hemolysis, HYT: hyperthermia, MA: metabolic acidosis, MI: myocardial injury/ischemia, NM: numbness/paresthesias, OG: osmolar gap, OT: opioid toxidrome, PLT: thrombocytopenia, PNC: pancreatitis, QRS: QRS prolongation, QTC: QTc prolongation, RBM: rhabdomyolysis, RD: respiratory depression, SHS: sedative-hypnotic syndrome, SS: serotonin syndrome, SYS: sympathomimetic syndrome, SZ: seizures, TC: tachycardia, VD: ventricular dysrhythmia, WBC: leukocytosis

[d]Pharmacological and Non-pharmacological support as reported by Medical Toxicologist; CPR: cardiopulmonary resuscitation, ECMO: extra-corporeal membrane oxygenation, HIE: high dose insulin euglycemic therapy, NAC: n-acetyl cysteine, $NaHCO_3$: sodium bicarbonate, NMB: neuromuscular blockers

**Table 35** 2023 Fatalities reported in ToxIC Core Registry with unknown toxicological exposure[a]

| Age / Gender[b] | Race/Ethnicity | Clinical Findings[c] | Life Support Withdrawn | Brain Death Confirmed | Treatment[d] |
|---|---|---|---|---|---|
| 9 M | Non-Hispanic White | AKI, CA, CNS, MA, RD | Unknown | | CPR |
| 31 M | Non-Hispanic White | AG, AKI, BP, CA, CNS, HPT, HT, MA, OT, RD, TC, VD | No | | CPR, naloxone, vasopressors (norepinephrine) |
| 43 F | Non-Hispanic White | AG, CNS, HT, MA, RD, SZ | Yes | Yes | Benzodiazepines, hydroxocobalamin, intubation, IV fluid resuscitation, propofol, vasopressors (epinephrine, norepinephrine, vasopressin) |
| 46 M | Black/African | None | Unknown | | None |
| 50 M | Non-Hispanic White | AG, CNS, MA | Yes | No | None |
| 55 F | Hispanic | None | Unknown | | None |
| 57 F | Non-Hispanic White | AKI, BC, CA, CNS, HT, MA, RBM | Yes | No | Antipsychotics, benzodiazepines, calcium, CPR, intubation, IV fluid resuscitation, ketamine, lipid therapy, $NaHCO_3$, NMB, opioids, pacemaker, vasopressors (dobutamine, epinephrine, norepinephrine, vasopressin) |
| 61 M | American Indian/Alaska Native | AGT, CNS, HT, MA, PLT, RD, SZ | Unknown | | Fomepizole, IV fluid resuscitation, NAC |
| 62 M | Non-Hispanic White | AG, HTN, MA, RD, TC | Unknown | | None |
| 64 M | Non-Hispanic White | AG, CNS, HPT, MA, RBM | No | | Fomepizole, hemodialysis, intubation, IV fluid resuscitation, $NaHCO_3$, vasopressors (epinephrine, norepinephrine, phenylephrine, vasopressin) |
| 65 M | Non-Hispanic White | AGT, DLM | Yes | Unknown | None |
| 66 M | Non-Hispanic White | CNS, RD | No | | Bronchodilators, buprenorphine/naloxone, folate, glucagon, intubation, IV fluid resuscitation, nicotine replacement therapy, thiamine |
| 68 F | Non-Hispanic White | None | Unknown | | None |
| 73 F | Non-Hispanic White | AG, AKI, CNS, HPT, HT, MA, WBC | Yes | No | Benzodiazepines, calcium, continuous renal replacement therapy, fomepizole, hemodialysis, intubation, IV fluid resuscitation, $NaHCO_3$, opioids, thiamine, urinary alkalinization, vasopressors (norepinephrine, phenylephrine, vasopressin) |

[a]Based on response from Medical Toxicologist "Did the patient have a toxicological exposure?" equals No or Unknown

[b]Age in years unless otherwise stated. M: male, F: female

[c]AG: anion gap, AGT: agitation, AKI: acute kidney injury, BC: bradycardia, BP: bradypnea, CA: cardiac arrest, CNS: coma/CNS depression, DLM: delirium, HPT: hepatoxicity, HT: hypotension, HTN: hypertension, MA: metabolic acidosis, OT: opioid toxidrome, PLT: thrombocytopenia, RBM: rhabdomyolysis, RD: respiratory depression, SZ: seizures, TC: tachycardia, VD: ventricular dysrhythmia, WBC: leukocytosis

[d]Pharmacological and Non-pharmacological support as reported by Medical Toxicologist; CPR: cardiopulmonary resuscitation, NAC: n-acetyl cysteine, $NaHCO_3$: sodium bicarbonate, NMB: neuromuscular blockers

marked the lowest recorded since the registry's inception in 2010 [10–22]. Intentional pharmaceutical exposures made up 52.4% of cases in both 2018 and 2019, decreasing to 43.8% in 2020 and 32.0% in 2022 [10, 12–14]. Though the intentional pharmaceutical exposures category in the Core Registry has several subcategories, including self-harm, the

decrease is consistent with reports from the National Institute on Drug Abuse in 2022 that intentional drug overdose deaths have declined overall though are increasing in the 15–24 year age group [28]. Similarly, participating sites within the Core Registry are primarily based at adult hospitals, leading to a paucity of adolescent patients with intentional pharmaceutical exposures that may be transported to a pediatric hospital where medical toxicology physicians are less prevalent. Furthermore, this variation may reflect differences in identifying intentional overdoses that are related to site-specific characteristics.

Opioid and psychoactive exposures reported to the Core Registry were assessed for yearly trends between 2010 and 2023. Not surprisingly, medical toxicology physicians have more commonly seen patients for opioid exposures than psychoactive exposures. The percentage of Core Registry cases with opioid exposures have increased between 2010 to 2023 (13.7% to 19.3%, respectively). However, psychoactive exposures, which include cannabis and ketamine, have almost doubled between 2010 and 2023 (2.2% to 4.3%, respectively). This may be partially attributable to the legalization of cannabis in some states, but also the prevalence of delta-8 tetrahydrocannabinol that is sold in commercial settings and online [29]. These yearly patterns may also be attributed to site-specific variations above and beyond the regional differences in legalization and drug use policies.

Since the addiction medicine treatment section was added to the Core Registry in 2018, medical toxicology physicians have noted increasing patterns of treatment with opioid agonist medications (i.e. methadone and buprenorphine formulations) from 1.8% of cases in 2018 to 19.1% of cases in 2023 [14]. Of note, acamprosate use increased from 1.9% of addiction medicine treatments used in 2022 to 21.2% of those receiving addiction medicine treatment in 2023, highlighting a stark shift in medical toxicology physician reporting of this medication within the Core Registry [10].

Production for the antidote physostigmine was ceased by the manufacturer in the United States in February 2023. Medical toxicology physicians sought an alternative to this drug shortage through the use of rivastigmine, a drug historically indicated for dementia from Alzheimer's disease [30]. In the Core Registry, the use of physostigmine declined from 11.9% in 2020 to 1.6% of anticholinergic exposure cases in 2023, and the use of rivastigmine for anticholinergic toxicity debuted in 2023 reaching 3.6%. This pivot to a new treatment for anticholinergic exposed patients highlights the resourcefulness of medical toxicology physicians around the country in dealing with important antidote shortages [23]. As this shortage unfolds, regimens of rivastigmine will warrant investigation for effectiveness and safety.

Fomepizole, previously developed as an antidote for toxic alcohol poisoning, has been more recently described by medical toxicology physicians as an adjunct for acetaminophen toxicity [31, 32]. The use of fomepizole has exponentially increased between 2019 to 2023 from use in 0.6% of acetaminophen exposure cases to 9.1%. Interestingly, of the 8 fatalities associated with single agent exposures to acetaminophen, 3 were treated with fomepizole in addition to n-acetyl cysteine (NAC). As fomepizole use continues to evolve in medical toxicology practice, its impact on clinical outcomes will be assessed.

In 2023, the Core Registry included several additional variables collected on patients seen by medical toxicology physicians. Transgender variable subcategories were expanded with a new transgender transition variable. For the first time in the Core Registry, information about whether a drug shortage was involved in the case was included. This year, ToxIC also modified the medical toxicology encounter reason variable to indicate whether the patient was dispositioned to an inpatient mental health facility. These recently added variables in 2023 strengthen the Core Registry data to increase our understanding of risk and protective factors associated with poisonings, treatment, and outcomes.

## Limitations

The ToxIC Core Registry serves as a prospective database of cases in which bedside consultation is performed by medical toxicologists, facilitating an informed understanding of the relationship between toxicologic exposures and clinical outcomes. Although the Core Registry is not population-based, it represents a wide geographic distribution of cases evaluated by medical toxicology physicians. These data can be used in conjunction with data from other registries and epidemiological studies to provide a comprehensive understanding of poisoning trends, novel exposures, and their public health implications. However, the Core Registry has its limitations. One limitation is a possible bias towards inclusion of more severe case presentations, as only cases undergoing subspecialty bedside consultation are included. Instances where a medical toxicology consultation was not requested are not included and may represent a group with less severe illness. Thus, the Core Registry likely represents a more complex population compared to other data sources such as Poison Control Centers. However the benefit of the Core Registry is that each patient is evaluated by a medical toxicology physician, and thus the detailed data entered is based on a first-hand report culminating from expert knowledge of toxicological exposures and presentations. Regional variations in drug use, misuse, and other toxic exposures may lead to a disproportionate number of certain cases at some sites. While the Core Registry encompasses sites from diverse locations, nationwide representation is not uniform. Larger tertiary academic medical institutions with more medical toxicologists may be overrepresented, while more

rural populations may be underrepresented. Moreover, there may be a reporting bias towards more interesting or complicated cases at individual sites, although efforts are made to mitigate this bias through written agreements mandating the inclusion of all consecutive cases. Sites may also have variations with reporting the highest level of care with regards to observational units and floor admissions. Data regarding substances of exposure or species of envenomation heavily rely on patient self-report, which may be limited by disclosure willingness and knowledge gaps about specific substances. This limitation is likely most significant with regard to illicit drug exposures as drug screens or more comprehensive drug testing is not uniformly reported. Lastly, the Core Registry continually strives to improve data quality. Despite mandatory requirements within the database for completing all applicable data fields, there continues to be ongoing challenges to obtaining fully completed data, particularly with regards to race/ethnicity, marital status, military service, and housing situation variables.

## Conclusions

The ToxIC program began as a multi-center consortium with the Core Registry, which is based on medical toxicology consultations, and continues to evolve and grow with projects based in the emergency department that are outside of the original paradigm of medical toxicology consultations [2]. This is the first year that ethanol was the leading agent of exposure since the Core Registry's inception. Additionally, for the third consecutive year, fentanyl was the leading opioid exposure reported. Yearly trends showed physostigmine declining and rivastigmine increasing for cases in the Core Registry, and fomepizole has become increasingly more prevalent in cases with acetaminophen exposure. ToxIC's Core Registry and other focused data collections continue to collect important clinical and public health information. The Core Registry remains at the helm, with 2023 being the monumental year where it surpassed 100,000 cases entered by medical toxicology physicians since inception.

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**Data Availability** This data has not been previously presented.

## Declarations

**Conflict of Interest** [AH, AA, SC, SL, MS, HS, JKR, AF, RC, PW, JB, KA]: These authors have no conflicts of interest to report.

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