Journal of Medical Toxicology
https://doi.org/10.1007/s13181-021-00854-3

ORIGINAL ARTICLE

The Toxicology Investigators Consortium 2020 Annual Report

Meghan B. Spyres[1,2] · Kim Aldy[3,4] · Lynn A Farrugia[5] · A. Min Kang[2,6] · Jennifer S. Love[7] · Sharan L. Campleman[4] · Shao Li[4] · Alexandra Amaducci[8] · Evan Schwarz[9] · Paul M. Wax[3,4] · Jeffery Brent[10] · On behalf of the Toxicology Investigators Consortium Study Group

Received: 24 June 2021 / Revised: 13 July 2021 / Accepted: 19 July 2021

Abstract
The Toxicology Investigators Consortium (ToxIC) Registry was established by the American College of Medical Toxicology in 2010. The registry collects data from participating sites with the agreement that all bedside and telehealth medical toxicology consultation will be entered. This eleventh annual report summarizes the Registry's 2020 data and activity with its additional 6668 cases. Cases were identified for inclusion in this report by a query of the ToxIC database for any case entered from January 1 to December 31, 2020. Detailed data was collected from these cases and aggregated to provide information which included demographics, reason for medical toxicology evaluation, agent and agent class, clinical signs and symptoms, treatments and antidotes administered, mortality, and whether life support was withdrawn. Gender distribution included 50.6% cases in females, 48.4% in males, and 1.0% identifying as transgender. Non-opioid analgesics were the most commonly reported agent class, followed by opioid and antidepressant classes. Acetaminophen was once again the most common agent reported. There were 80 fatalities, comprising 1.2% of all registry cases. Major trends in demographics and exposure characteristics remained similar to past years' reports. Sub-analyses were conducted to describe race and ethnicity demographics and exposures in the registry, telemedicine encounters, and cases related to the COVID-19 pandemic.

Keywords Poisoning · Overdose · Surveillance · Epidemiology · Medical Toxicology

Introduction

The year 2020 marked the beginning of the second decade of the Toxicology Investigators Consortium (ToxIC). It was a year marked by considerable expansion of ToxIC's activities. Our case accrual unabatedly continued, and we welcomed six new sites to the consortium.

Starting in 2020 ToxIC began a partnership with the US Centers for Disease Control and Prevention (CDC) Overdose Data to Action (OD2A) program. Through a data sharing agreement, ToxIC is working with our partners at OD2A to provide data on our experience with opioid and psychoactive substance toxicity. Given the uniqueness of our physician led data collection, ToxIC's patient-oriented database is

Supervising Editor: Mark B. Mycyk, MD

✉ Meghan B. Spyres
mspyres@gmail.com

[1] Department of Emergency Medicine, University of Arizona College of Medicine-Phoenix, Phoenix, AZ, USA

[2] Department of Medical Toxicology, Banner-University Medicial Center Phoenix, 1012 E Willetta Street, Fl 2, Phoenix, AZ 85006, USA

[3] University of Texas Southwestern Medical School, 5323 Harry Hines Boulevard, Dallas, TX 75390, USA

[4] American College of Medical Toxicology, 10645 N Tatum Blvd., Suite 200-111, Phoenix, AZ 85028, USA

[5] Hartford Hospital and University of Connecticut School of Medicine, 80 Seymour Street, Hartford, CT 06102, USA

[6] Departments of Medicine and Child Health, University of Arizona College of Medicine-Phoenix, Phoenix, AZ, USA

[7] Oregon Health & Science University, 3181 SW Sam Jackson Park Rd, Portland, OR 97239, USA

[8] Lehigh Valley Health Network, 2545 Schoenersville Rd, Bethlehem, PA 18017, USA

[9] Department of Emergency Medicine, Washington University School of Medicine, 660 South Euclid, St Louis, MO 63110, USA

[10] University of Colorado School of Medicine, 13001 E 17th Pl, Aurora, CO 80045, USA

Published online: 17 September 2021

supplying a level of detail on adverse drug effects not generally available from alternate drug-toxicity databases. As our partnership with the CDC grows, we expect to collaborate with their overdose prevention efforts through our main Core Registry, our pediatric opioid and marijuana Sub-Registries, and our novel efforts on opioid and stimulant exposures.

In 2020 ToxIC embarked on two prospective multicenter projects in addition to the continuation of its Core Registry. These two projects are not based on bedside medical toxicology consultations and utilize their own unique data collection interface.

The first multicenter project started its initial year of a 5-year NIH-supported prospective clinical study of opioid overdoses presenting to the emergency department (NIH# 1RO1DA037317- 02). Alex Manini, MD, Professor of Emergency Medicine at the Mt Sinai Icahn School of Medicine and a long time ToxIC collaborator, is the Principal Investigator of this project which characterizes the clinical course, patient characteristics, and in-depth toxicologic analysis of fentanyl analogs (or "fentalogs"). In the course of the Fentalog project, ToxIC is assessing the prevalence and role of fentalogs, novel psychoactive drugs, adulterants, and other substances in the clinical presentation and treatment of these patients. In a supplement to this grant, ToxIC is also partnering Mt Sinai on data collection specific to factors related to COVID-19 infections in patients with a history of opioid misuse. This is the first ToxIC project that has included comprehensive toxicological testing, utilizing liquid chromatography quadrupole time-of-flight mass spectrometry to elucidate the presence of psychoactive substances and their metabolites.

In 2020, the COVID-19 pandemic significantly altered human activity in a multitude of ways. The medical and public health communities vibrantly came to life in a way that had not been seen in a century. As these communities rose to the challenge and aggressively took action to deal with the evolving pandemic, ToxIC quickly mobilized. As we continued our data sharing agreement adopted in 2016 with the US Food and Drug Administration (FDA), new therapeutics were rapidly entering clinical practice via Emergency Use Authorizations employed in a time of unprecedented need. Simultaneously, measures taken by the lay community to prevent and combat COVID-19, such as taking hydroxychloroquine and drinking bleach, reached a concerning level. Because of our already existing data sharing agreement with the FDA and the need to expeditiously identify adverse drug events in this rapidly evolving environment, ToxIC and the FDA collaboratively implemented a real-time national toxicosurveillance project searching for adverse drug events associated with COVID-19 prophylaxis or treatment. The so-called FDA ACMT COVID-19 ToxIC (FACT) Pharmacovigilance Project was organized and swiftly pressed into action. Similar to the Fentalog project above, the FACT project is not based on the ToxIC Core Registry or bedside medical toxicology consults, and data is collected through a separate mechanism and database.

In addition to the summary Core Registry data, this year we are presenting additional data on the use of telemedicine by medical toxicologists, as well as taking a closer look at race and ethnicity, and COVID-19 positive cases since the start of the pandemic.

Twelve full ToxIC publications in six separate journals were published in 2020. This is the largest number of journal publications in any year since ToxIC's inception. Sixteen ToxIC abstracts were published from both national and international meetings. These full publications and abstracts are enumerated on the ToxIC website: www.ToxICRegistry.org.

In addition to the above, the following new ToxIC research projects were proposed and initiated by ToxIC investigators in 2020:

1. Effect of activated charcoal administration on clinical outcome
2. A comparison of clinical outcomes following benzodiazepine or Z-drug toxicity
3. A comparison of hydroxyzine and diphenhydramine poisonings
4. The effect or race and ethnicity on access to opioid treatment facilities
5. Organ donation after death from a toxic exposure
6. Fomepizole use in acetaminophen poisoning
7. Epidemiology of pediatric antiepileptic drug poisoning
8. Trends in gastrointestinal decontamination after acute poisoning
9. Trends in toxicity from household cleaners and sanitizing agents
10. Toxicity of chloroquine and hydroxychloroquine

In 2020 ToxIC was supported by the NIH, FDA, CDC, and BTG International. These collaborations have been enriching for ToxIC but more importantly have provided unique networking opportunities for ToxIC investigators.

Methods

ToxIC was started on January 1, 2010, as a Case Registry [1]. That Core Registry continues today and prospectively enrolls patients presenting to participating sites. All sites agree to enter all inpatients or outpatients presenting to their site on whom a formal medical toxicology consultation was completed. ToxIC staff periodically meet with all sites to review patient accrual, obstacles to achieving full compliance with patient entry, quality assurance efforts, and ongoing project opportunities. Deidentified case information is entered into an online data collection form using the REDCap (Research

Electronic Data Capture) platform. REDCap is a secure, web-based software platform designed as an electronic data capture tool for research studies hosted at the Vanderbilt University Health Core. REDCap provides (1) an intuitive interface for validated data capture, (2) trail audits 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.

In 2020, the Core Registry collected data in the following areas:

1. Names, sites, and specific facility of the entering medical toxicologist(s)
2. Specific focused data collections on areas of contemporary interest
3. Medication errors and adverse reactions associated with therapeutic use
4. Patient demographics
5. HIV status
6. Specific aspects of the patient's medical history
7. The source of the patient referral
8. The reasons for the patient requiring a medical toxicology consultation
9. The implicated substance(s) and their relationship, if any, to the patient's presentation
10. Patient signs and symptoms
11. Specific laboratory and electrocardiographic data
12. Treatments administered
13. Outcome

ToxIC's data collection in 2020 included the addition of teletoxicology and COVID-19 status (defined as a positive SARS-CoV-2 test). A full enumeration of all fields collected in the Core Registry is provided in the supplemental materials.

In addition to the Core Registry data collected on every bedside medical toxicology consultation, there are five detailed Sub-Registries that are completed on relevant patients. These are:

1. North American Snakebite Registry
2. Pediatric Marijuana and Opioid Registry
3. Extracorporeal Therapies Registry
4. Lipid Emulsion Therapy Registry
5. Natural Toxins Registry: Mushrooms and Plants

ToxIC has been reviewed by the Western Institutional Review Board (IRB) and operates in pursuant to the approval of the participating site IRBs. All data collected by ToxIC is deidentified and is compliant with the Health Insurance Portability and Accountability Act. All cases entered into the Core Registry, Sub-Registries, FACT Pharmacovigilance Project, and the Fentalog project are reviewed for quality assurance by the ToxIC staff. Any inconsistent or incomplete entries are queried back to the entering medical toxicologist for correction or clarification.

Additional information regarding ToxIC can be found at https://www.toxicregistry.org.

Results

In 2020 there were a total of 6668 individual cases of toxicologic exposures reported to the ToxIC Registry from 37 sites comprised of 58 separate health care facilities. This is a decrease in total cases compared with 2019 [2]. Individual facilities contributing cases in 2020 are listed in Table 1.

Demographics

Tables 2 and 3 summarize selective demographics for age and gender and race and ethnicity, respectively. Gender breakdown was similar to recent years [2–5]. In 2020, 50.6% of cases involved female patients, and 1% involved transgender or gender non-conforming patients (37 female-to-male, 17 male-to-female, 8 gender non-conforming). Sixty-nine patients (1%) were pregnant. Age distribution was similar to recent years. Adults age 19–65 made up approximately half of the cases (55.5%) followed by adolescents age 13–18 (24.6%). Children ($\leq$ 12 years of age) made up 9.5%; 5.9% of cases involved older adults (> 65 years of age).

The most commonly reported race was Caucasian (62.6%), followed by Black/African (15.1%) and Asian (2.3%). Hispanic ethnicity was reported in 12.4% of cases; however 15.7% of cases reported ethnicity as unknown/uncertain. Race and ethnicity are self-reported by patients, or in cases in which a patient is unable to report, it may be determined by the examining medical toxicologist to the best of their ability or abstracted from the medical record.

Table 4 details the referral source of inpatient and outpatient medical toxicology encounters. The majority (53.5%) of inpatient cases were generated by the emergency department, and very few cases were referred from poison centers (0.2%) or outpatient physicians (0.2%). Outpatient encounters were primarily referred by primary care and other outpatient physicians (68.7%), followed by self-referrals (11.0%). These trends were similar to recent years.

Tables 5 and 6 describe the reason for the toxicology encounter and the details of intentional pharmaceutical exposures, respectively. Consistent with recent years, intentional pharmaceutical exposures were by far the most common reason for medical toxicology encounters (43.8%). Addiction medicine consult was a new reason for encounter in 2018 and has increased in frequency each year (2.7% to 6.6% to 7.1%) [2, 3]. Within the intentional pharmaceutical exposures,

Table 1 Participating institutions providing cases to ToxIC in 2020

State or country	City	Hospitals
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*	Keck Medical Center of University of Southern California
		Ronald Reagan University of California Los Angeles Medical Center
		University of California Los Angeles Olive View
		University of Southern California Verdugo Hills
	Sacramento	University of California Davis Medical Center
	San Diego	Scripps Mercy Hospital
		University of California San Diego - Hillcrest
Colorado	Denver	Colorado Children's Hospital
		Denver Health Medical Center
		Porter and Littleton Hospital
		Swedish Medical Center
		University of Colorado Hospital
Connecticut	Hartford	Hartford Hospital
Georgia	Atlanta	Children's Healthcare of Atlanta Egleston
		Emory University Hospital
		Grady Memorial Hospital
Illinois	Chicago	University of Illinois at Chicago - Rush-Cook
	Evanston	Evanston North Shore University Health System
Indiana	Indianapolis	IU - Eskenazi Hospital
		IU - Indiana University Hospital
		IU - Methodist Hospital - Indianapolis
		IU - Riley Hospital for Children
Kansas	Kansas City*	University of Kansas Medical Center
Kentucky	Lexington	University of Kentucky Chandler Medical Center
Massachusetts	Boston	Boston Children's Hospital
	Worcester	University of Massachusetts Memorial Medical Center
Michigan	Grand Rapids	Spectrum Health Hospitals
Mississippi	Jackson	University of Mississippi Medical Center
Missouri	Kansas City	Children's Mercy Hospitals and Clinics
	St. Louis	Washington University School of Medicine in St Louis
Nebraska	Omaha	University of Nebraska Medical Center

Table 1 (continued)

State or country	City	Hospitals
New Jersey	Newark	Rutgers/New Jersey Medical School
New Mexico	Albuquerque	University of New Mexico
New York	Rochester	Strong Memorial Hospital
	Syracuse	Upstate Medical University - Downtown Campus
North Carolina	Charlotte	Carolinas Medical Center
Oregon	Portland	Doernbecher Children's Hospital
		Oregon Health & Science University Hospital
Pennsylvania	Bethlehem	Lehigh Valley Hospital Cedar Crest
		Lehigh Valley Hospital Muhlenberg
	York*	York Hospital
Tennessee	Nashville*	Vanderbilt Children's Hospital
		Vanderbilt University Hospital
Texas	Beaumont*	Christus St. Elizabeth Hospital
	Dallas	Children's Medical Center Dallas
		Parkland Memorial Hospital
		William P. Clements University Hospital
Wisconsin	Milwaukee	Children's Hospital of Wisconsin
		Froedtert Memorial Lutheran Hospital
Canada	Calgary	Alberta Children's Hospital
		Foothills Medical Centre
	Toronto	Hospital for Sick Children
Israel	Haifa	Rambam Health Care Campus
Thailand	Bangkok	Vajira Hospital

*New participating ToxIC sites in 2020

Table 2 ToxIC case demographics—gender and age

		N (%)
Male		3227 (48.4)
Female		3377 (50.6)
Transgender		64 (0.96)
	Male to female	17 (26.6)
	Female to male	37 (57.8)
	Gender non-conforming	8 (12.5)
Total		**6668**
Pregnant		69 (1.0)
Age (years)		
< 2		250 (3.7)
2–6		386 (5.8)
7–12		275 (4.1)
13–18		1639 (24.6)
19–65		3704 (55.5)
66–89		376 (5.6)
> 89		10 (0.1)
Unknown		28 (0.4)
Total		**6668 (100)**

the majority of cases were again an attempt at self-harm (73.9%), primarily suicide attempts (87.5%).

Tables 7 and 8 describe the top three primary reasons for encounter by race and ethnicity, respectively. Distribution of reasons for encounter was largely similar across races and ethnicities, with intentional pharmaceutical exposures being the most common reason for encounter across all groups. Of note, however snake envenomation was a top three encounter reason among Native American/Alaska Native (8.2%) and Asian (17.4%) race groups, but not among other race groups. Addiction medicine consultation was the primary reason for the encounter in 5.9% of non-Hispanic patients, but only 3.4% of Hispanic patients.

Table 3 ToxIC case demographics—race and Hispanic ethnicity

	N (%)
Race	
Caucasian	4174 (62.6)
Black/African	1007 (15.1)
Asian	245 (2.3)
American Indian/Alaska Native	73 (1.1)
Native Hawaiian or Pacific Islander	7 (0.1)
Mixed	109 (1.6)
Other	13 (0.2)
Unknown	1129 (16.9)
Missing	1 (0.01)
Total	6668
Hispanic Ethnicity[a]	
Hispanic	828 (12.4)
Non-Hispanic	4793 (71.9)
Unknown	1047 (15.7)
Total	6668

[a] Hispanic ethnicity as indicated exclusive of race

Agent classes

Agent class contributions to the Core Registry are described in Table 9. In 2020, of the 6668 cases entered into the ToxIC Registry, 5987 included specific agents of exposure. Four thousand two hundred sixty-two (71.2%) cases involved single agents. Consistent with recent years, the non-opioid analgesic class was the most common (15.5%) class of drugs reported. Again in 2020, the opioid class was the second most common agent class reported (12.7%) [2] followed by the antidepressant (10.4%) and ethanol (8.4%) classes.

Tables 10 and 11 detail the top five agent classes broken down by race and ethnicity, respectively. The primary substance responsible for most encounters varied across racial groups: ethanol for Native Americans/Alaska Natives (13.7%); analgesics for Asians (10.3%), Caucasians (14.4%), and mixed-race patients (21.1%); opioids for Blacks (17.0%); and toxic alcohols for Pacific Islanders/Native Hawaiians (28.6%). Primary substances associated with both Hispanic and non-Hispanic patient encounters were similar.

Analgesics

Table 12 presents the non-opioid analgesics, the largest class in the Core Registry. Acetaminophen was again the most commonly reported agent (64.6%), reaching its claim as the highest reported drug of exposure every year since ToxIC was established. It is distantly followed by ibuprofen (12.3%), aspirin (6.7%), and gabapentin (6.5%). Aspirin and acetylsalicylic acid are listed separately in the registry; when combined they compose 11.0% of the non-opioid analgesic class.

Opioids

Table 13 describes the opioid class. Similar to recent years, heroin was again the most common agent in the class (32.1%) [2, 3]. The relative contribution of fentanyl increased again this year, now representing 25.4% of the opioid class (14.6% in 2019), and again was the second most common agent.[2] Oxycodone was the third most common agent reported again this year (13.9%) [2]. Other opioid agents remained fairly stable compared with prior years.

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

	N (%)
Emergency department (ED) or inpatient (IP)[a]	
ED	3482 (53.5)
Admitting service	2199 (33.8)
Request from another hospital service (not ED)	412 (6.3)
Outside hospital transfer	370 (5.7)
Poison center	15 (0.2)
Primary care provider or other outpatient treating physician	11 (0.2)
Employer/independent medical evaluation	10 (0.2)
Self-referral	6 (0.1)
ED/IP total	6505 (100)
Outpatient (OP)/clinic/office consultation[b]	
Primary care provider or other OP physician	112 (68.7)
Self-referral	18 (11.0)
Employer/independent medical evaluation	15 (9.2)
Poison center	11 (6.7)
Request from another hospital service (not ED)	3 (1.8)
ED	2 (1.2)
Admitting service	2 (1.2)
Outside hospital transfer	0 (0.0)
OP total	163 (100)

[a] Percentage based on the total number of cases (*N* = 6505) seen by a medical toxicologist as consultant (ED or IP) or as attending (IP)

[b] Percentage based on the total number of cases (N=163) seen by a medical toxicologist as outpatient, clinic visit, or office consultation.

Table 14 describes breakdown of analgesics by race. In comparing opioid and non-opioid analgesic agents, acetaminophen was associated with the highest percentage of encounters across most racial sub-groups. However, among

Table 5 Reason for medical toxicology encounter

	N (%)
Intentional exposure—pharmaceutical	3288 (43.8)
Intentional exposure—non-pharmaceutical	935 (12.5)
Unintentional exposure—pharmaceutical	546 (7.3)
Addiction medicine consultation	532 (7.1)
Withdrawal—ethanol	399 (5.3)
Unintentional exposure—non-pharmaceutical	336 (4.5)
Organ system dysfunction	269 (3.6)
Envenomation—snake	263 (3.5)
Ethanol abuse	242 (3.2)
Withdrawal—opioid	234 (3.1)
Interpretation of toxicology lab data	164 (2.2)
Environmental evaluation	89 (1.2)
Withdrawal—sedative/hypnotic	51 (0.7)
Occupational evaluation	49 (0.7)
Envenomation—spider	25 (0.3)
Withdrawal—other	19 (0.3)
Envenomation—other	19 (0.3)
Malicious/criminal	19 (0.3)
Withdrawal—cocaine/amphetamine	10 (0.1)
Envenomation—scorpion	7 (0.1)
Marine /fish poisoning	5 (0.1)
Total	7501 (100)

Table 6 Detailed reason for encounter—intentional pharmaceutical exposure[a]

	N (%)[a]
Reason for intentional pharmaceutical exposure subgroup[b]	
Attempt at self-harm	2408 (73.9)
Misuse/abuse	404 (12.4)
Therapeutic use	240 (7.4)
Unknown	207 (6.4)
Total	3259 (100)
Attempt at self-harm- suicidal intent subclassification[c]	
Suicidal intent	2105 (87.5)
Suicidal intent unknown	217 (9.0)
No suicidal intent	84 (3.5)
Total	2406 (100)

[a] Nine cases listed more than one reason for encounter due to intentional pharmaceutical exposure (*N* = 3251)

[b] Percentage of total number indicating reason for encounter due to intentional pharmaceutical exposure

[c] Percentage of number of cases indicating attempt at self-harm

Table 7 Top three primary reasons for encounter by race

	N (%)
Native American/Alaska Native	**73 (1.1)**[a]
Intentional pharmaceutical	31 (42.3)[b]
Intentional non-pharmaceutical	11 (15.1)
Envenomation snake	6 (8.2%)
Unintentional pharmaceutical	6 (8.2%)
Asian	**155 (2.3)**
Intentional pharmaceutical	68 (43.9)
Envenomation snake	27 (17.4)
Unintentional pharmaceutical	13 (8.4)
Black	**1007 (15.1)**
Intentional pharmaceutical	458 (45.5)
Intentional non-pharmaceutical	144 (14.3)
Unintentional pharmaceutical	119 (11.8)
Caucasian	**4174 (62.6)**
Intentional pharmaceutical	1987 (47.6)
Intentional non-pharmaceutical	542 (13)
Unintentional pharmaceutical	287 (6.9)
Pacific Islander/Native Hawaiian	**7 (0.1)**
Intentional pharmaceutical	3 (42.9)
Unintentional non-pharmaceutical	2 (28.6)
Intentional non-pharmaceutical	1 (14.3)
Organ system dysfunction	1 (14.3)
Mixed race	**109 (1.6)**
Intentional pharmaceutical	60 (55.0)
Intentional non-pharmaceutical	19 (17.4)
Unintentional pharmaceutical	13 (11.9)

[a] Percentages in bold based on the number of cases in a given race category in 2020 relative to the total number of Core Registry cases in 2020 ($N = 6668$)

[b] Percentages based on number of cases for a primary encounter type relative to the number of cases in given race category in 2020

Table 8 Top three primary reasons for encounter by ethnicity

	N (%)
Hispanic patients	**828 (12.4)**[a]
Intentional pharmaceutical	406 (49.0)[b]
Intentional non-pharmaceutical	121 (14.6)
Unintentional non-pharmaceutical	63 (7.6)
Non-Hispanic patients	**4793 (71.9)**
Intentional pharmaceutical	2237 (46.7)
Intentional non-pharmaceutical	614 (12.8)
Unintentional pharmaceutical	390 (8.1)

[a] Percentages in bold based on the number of cases in a given ethnicity category in 2020 relative to the total number of Core Registry cases in 2020 ($N = 6668$)

[b] Percentages based on number of cases for a primary encounter type relative to the number of cases in given ethnicity category in 2020

Black and Caucasian patients, opioids were associated with more encounters compared with other individual non-opioid analgesics (17.0% Black patients and 12.7% Caucasian patients).

Antidepressants

Table 15 describes the antidepressant class. SSRIs (39.5%) and other antidepressants (37.4%) represented the majority of this class. Sertraline (14.5%) was the most common SSRI reported and bupropion (21.6%) was the most common other antidepressant, similar to last year.[2]

Sedative hypnotics

Table 16 presents the sedative hypnotic/muscle relaxant class. Benzodiazepines (primarily alprazolam (25.8%) and clonazepam (12.2%)) and muscle relaxants (primarily baclofen (10.2%) and cyclobenzaprine (7.9%)) were the most common subtypes, similar to recent years. Other sedatives, Z-drugs, and barbiturates were again less common.

Toxic alcohol and ethanol

Table 17 describes data on ethanol and toxic alcohols. Ethanol was considered its own agent class, consistent with prior years and was the fourth most commonly reported agent class (up from fifth in 2019) [2]. The most commonly reported nonethanol alcohols and glycols were ethylene glycol (47.0%) and isopropanol (31.8%). Methanol and miscellaneous alcohols each made up 10.6% of the class.

Sympathomimetics

Table 18 presents the sympathomimetic class. This year, methamphetamine (40.3%) overtook cocaine (23.9%) as the most common agent in this class, followed again by amphetamine (10.1%).

Anticholinergic/antihistamine

Table 19 describes the anticholinergic/antihistamine class. Consistent with recent years, diphenhydramine (58.6%), followed by hydroxyzine (18.1%), remains the most commonly reported agents in this class.

Cardiovascular agents

Table 20 shows data on the cardiovascular class. Consistent with recent years, sympatholytics (32.5%) remain the most common subclass of cardiovascular drugs, followed by beta-blockers (23.5%) and calcium channel blockers (16.5%).

Table 9 Agent classes involved in medical toxicology consultation

	N (%)[a]
Analgesic	1377 (15.5)
Opioid	1128 (12.7)
Antidepressant	923 (10.4)
Ethanol	743 (8.4)
Sedative-hypnotic/muscle relaxant	599 (6.8)
Sympathomimetic	566 (6.4)
Cardiovascular	520 (5.9)
Anticholinergic/antihistamine	514 (5.8)
Antipsychotic	409 (4.6)
Psychoactive	306 (3.5)
Anticonvulsant	252 (2.8)
Envenomation and marine	250 (2.8)
Diabetic medication	129 (1.5)
Lithium	105 (1.2)
Cough and cold products	89 (1.0)
Herbal products/dietary supplements	89 (1.0)
Unknown class	87 (1.0)
Metals	86 (1.0)
Household products	71 (0.8)
Gases/irritants/vapors/dusts	69 (0.8)
Caustic	67 (0.8)
Toxic alcohols	67 (0.8)
Antimicrobials	63 (0.7)
Plants and fungi	49 (0.6)
Hydrocarbon	41 (0.5)
GI	39 (0.4)
Chemotherapeutic and immune	30 (0.3)
Anticoagulant	25 (0.3)
Other pharmaceutical product	25 (0.3)
Endocrine	24 (0.3)
Anesthetic	24 (0.3)
Other nonpharmaceutical product	23 (0.3)
Herbicide	11 (0.1)
Insecticide	11 (0.1)
Rodenticide	9 (0.1)
Pulmonary	9 (0.1)
Ingested foreign body	7 (0.1)
Amphetamine-like hallucinogen	7 (0.1)
WMD/riot agent/radiological	5 (0.1)
Anti-parkinsonism drugs	5 (0.1)
Marine toxin	3 (0.0)
Cholinergic	1 (0.0)
Class total	8857 (100)

[a] Percentages are out of total number of reported agent entries in 2020 from 5987 unique cases; 4262 cases (71.2%) reported single agents

WMD weapons of mass destruction

Table 10 Top five primary agent classes by race[a]

	N (%)
Native American/Alaska Native	**73 (1.1)**[b]
Ethanol	10 (13.7)[c]
Analgesic	9 (12.3)
Envenomation	5 (6.8)
Alcohol—toxic	4 (5.5)
Anticonvulsant	4 (5.5)
Opioid	4 (5.5)
Asian	**155 (2.3)**
Analgesic	16 (10.3)
Antidepressant	9 (5.8)
Ethanol	6 (3.9)
Cardiovascular	6 (3.9)
Envenomation	6 (3.9)
Black	**1007 (15.1)**
Opioids	171 (17.0)
Analgesic	163 (16.2)
Cardiovascular	71 (7.1)
Antidepressant	58 (5.8)
Antipsychotics	50 (5.0)
Caucasian	**4174 (62.6)**
Analgesic	602 (14.4)
Opioids	530 (12.7)
Ethanol	431 (10.3)
Antidepressant	350 (8.4)
Sympathomimetic	214 (5.1)
Pacific Islander/Native Hawaiian	**7 (0.1)**
Toxic Alcohol	2 (28.6)
Analgesic	1 (14.3)
Anticoagulant	1 (14.3)
Antipsychotic	1 (14.3)
Opioid	1 (14.3)
Psychoactive	1 (14.3)
Mixed Race	**109 (1.6)**
Analgesic	23 (21.1)
Sympathomimetic	15 (13.8)
Opioids	11 (10.1)
Cardiovascular	8 (7.3)
Antidepressant	7 (6.4)
Psychoactive	7 (6.4)

[a] Counts include only the primary agent #1 selected for each Core Registry case

[b] Percentages in bold based on the number of cases in a given race category in 2020 relative to the total number of Core Registry cases in 2020 (*N* = 6668)

[c] Percentages based on number of cases for an agent type relative to the number of cases in given race category in 2020

Clonidine (24.0%) and metoprolol (10.0%) were again the most common sympatholytic and beta-blocker agents, respectively. Amlodipine (9.8%) remained the most common calcium channel blocker.

Table 11 Top five primary agent classes by ethnicity[a]

	N (%)
Hispanic patients	**828 (12.4)**[b]
Analgesic	155 (18.7)[c]
Opioids	115 (13.9)
Antidepressant	52 (6.3)
Ethanol	46 (5.6)
Sympathomimetic	46 (5.6)
Non-Hispanic Patients	**4793 (71.9)**
Analgesic	672 (14.0)
Opioids	627 (13.1)
Ethanol	454 (9.5)
Antidepressant	375 (7.8)
Sympathomimetic	255 (5.3)

[a] Counts include only the primary agent #1 selected for each Core Registry case

[b] Percentages in bold based on the number of cases in a given ethnicity category in 2020 relative to the total number of Core Registry cases in 2020 ($N = 6668$)

[c] Percentages based on number of cases for an agent type relative to the number of cases in given ethnicity category in 2020

Antipsychotics

Table 21 details the antipsychotic class. Trends in the antipsychotic class were similar to recent years. The atypicals, led by quetiapine (41.3%) and olanzapine (13.2%), represent the majority of cases reported.

Table 12 Analgesics

	N (%)
Acetaminophen	890 (64)
Ibuprofen	169 (12)
Aspirin	92 (6.7)
Gabapentin	90 (6.5)
Acetylsalicylic acid	59 (4.3)
Naproxen	41 (3.0)
Pregabalin	14 (1.0)
Salicylic acid	6 (0.4)
Meloxicam	5 (0.4)
Miscellaneous[a]	11 (0.8)
Class total	**1377 (100)**

[a] Includes analgesic unspecified, diclofenac, indomethacin, ketorolac, metamizole (dipyrone), nabumetone, phenazopyridine, salsalate, ziconotide

Table 13 Opioids

	N (%)
Heroin	362 (32.1)
Fentanyl	286 (25.4)
Oxycodone	157 (13.9)
Buprenorphine	72 (6.4)
Methadone	49 (4.3)
Tramadol	45 (4.0)
Opioid Unspecified	37 (3.3)
Hydrocodone	34 (3.0)
Morphine	30 (2.7)
Hydromorphone	16 (1.4)
Codeine	14 (1.2)
Naloxone	14 (1.2)
Miscellaneous[a]	12 (1.1)
Class total	**1128 (100)**

[a] Includes bucinnazine (AP 237, 1-butyryl-4-cinnamylpiperazine), loperamide, naltrexone, tapentadol

Anticonvulsants, mood stabilizers, and lithium

Table 22 presents data on anticonvulsants, mood stabilizers, and lithium. Consistent with past years, lithium was considered as its own agent class and made up just over 1% of reported agents in the Core Registry [2, 3]. Among anticonvulsants and mood stabilizers, lamotrigine (29.4%) and valproic acid (19.4%) were the most commonly reported agents followed by oxcarbazepine (10.7%) and phenytoin (9.5%).

Psychoactives

Table 23 presents data on the psychoactive class including the amphetamine-like hallucinogen methylenedioxymethamphetamine (Molly). Marijuana was again the most common agent in this class (25.5%) followed closely by tetrahydrocannabinol (20.3%). Synthetic cannabinoid cases continued to fall again this year (5.6% in 2020 vs 9.4% in 2019 and 12.3% in 2018) [2–4]. When combined, all non-synthetic cannabinoid product exposures represented 65.7% of the psychoactive class. Molly exposures remained low, with 7 cases reported.

Envenomations and marine poisonings

Table 24 shows data on envenomations and marine poisonings. Snake envenomations represented by Crotalus (35.6%), Agkistrodon (34.4%), and snake unspecified (17.0) were the top three exposures reported to this class. Agkistrodon envenomations showed an increase this year from 16.9% in

Table 14 Comparison of opioid and non-opioid analgesic frequencies by race[a]

	N (%)
Native American/Alaska Native	**73 (1.1)**[b]
Acetaminophen	7 (9.6)[c]
Opioid	4 (5.5)
Salicylates	1 (1.4)
Ibuprofen	1 (1.4)
Asian	**155 (2.3)**
Acetaminophen	12 (7.7)
Opioid	4 (2.6)
Salicylates	2 (1.3)
Ibuprofen	2 (1.3)
Black	**1007 (15.1)**
Opioids	171 (17.0)
Acetaminophen	129 (12.8)
Salicylates	14 (1.4)
NSAIDs	12 (1.2)
Gabapentin/Pregabalin	8 (0.8)
Caucasian	**4174 (62.6)**
Opioids	530 (12.7)
Acetaminophen	451 (10.8)
Salicylates	71 (1.7)
NSAIDs	56 (1,3)
Gabapentin/Pregabalin	22 (0.5)
Pacific Islander/Native Hawaiian	**7 (0.1)**
Acetaminophen	1 (14.2)
Opioid	1 (14.2)
Mixed Race	**109 (1.6)**
Acetaminophen	17 (15.6)
Opioids	11 (10.1)
Salicylates	5 (4.6)
Ibuprofen	1 (0.9)

[a] Counts include only cases for which an opioid or non-opioid analgesic was selected as primary agent #1

[b] Percentages in bold based on the number of cases in a given race category in 2020 relative to the total number of Core Registry cases in 2020 ($N = 6668$)

[c] Percentages based on number of cases for an agent type relative to the number of cases in given race category in 2020

2019, nearly approaching that of Crotalus envenomations. Again in 2020, Loxosceles exposures were the fourth most common exposure in this class (5.1%) [2–4].

Diabetic agents

Table 25 presents the diabetic medication agent class. Metformin was the most common agent at 39.4% of the agent class, followed by insulin (22.5%) and glipizide (21.7%).

Table 15 Antidepressants

	N (%)
Selective serotonin reuptake inhibitors (SSRIs)	**365 (39.5)**
Sertraline	134 (14.5)
Escitalopram	87 (9.4)
Fluoxetine	86 (9.3)
Citalopram	45 (4.9)
Paroxetine	10 (1.1)
Vilazodone	3 (0.3)
Other antidepressants	**345 (37.4)**
Bupropion	199 (21.6)
Trazodone	118 (12.8)
Mirtazapine	20 (2.2)
Miscellaneous[a]	5 (0.5)
Antidepressant unspecified	3 (0.3)
Tricyclic antidepressants (TCAs)	**95 (10.3)**
Amitriptyline	66 (7.2)
Doxepin	11 (1.2)
Nortriptyline	9 (1.0)
Miscellaneous[b]	9 (1.0)
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	**116 (12.6)**
Venlafaxine	67 (7.3)
Duloxetine	44 (4.8)
Miscellaneous[c]	5 (0.5)
Monoamine oxidase inhibitor (MAOIs)	**2 (0.2)**
Phenelzine	2 (0.2)
Class total	923 (100)

[a] Includes vortioxetine, tianeptine, sibutramine

[b] Includes imipramine, clomipramine, desipramine, noxiptiline

[c] Includes desvenlafaxine, levomilnacipran

Metals

Table 26 presents the metal class. Lithium is its own agent class and is reported with the anticonvulsants and mood stabilizers. Trends were similar to recent years with lead (37.6%) and iron (28.2%) composing the majority of reported cases [2–4]. Mercury and arsenic were reported each in 6 (7.1%) cases.

Herbal products and dietary supplements

Table 27 details herbal products and dietary supplements. Caffeine (38.2%) and melatonin again made up the majority of this class [2, 3]. Infrequently reported miscellaneous agents made up 38.2% of the agent class.

Household agents

Table 28 describes household agents reported to the Core Registry. Cleaning solutions and disinfectants (28.2%),

Table 16 Sedative-hypnotic/muscle relaxants by type

	N (%)
Benzodiazepine	**357 (59.7)**
Alprazolam	154 (25.8)
Clonazepam	73 (12.2)
Lorazepam	54 (9.0)
Benzodiazepine unspecified	32 (5.4)
Diazepam	26 (4.3)
Temazepam	8 (1.3)
Midazolam	5 (0.8)
Miscellaneous[a]	5 (0.8)
Muscle relaxant	**156 (26.1)**
Baclofen	61 (10.2)
Cyclobenzaprine	47 (7.9)
Tizanidine	35 (5.9)
Methocarbamol	5 (0.8)
Carisoprodol	5 (0.8)
Metaxalone	3 (0.5)
Other sedatives	**35 (5.9)**
Buspirone	16 (2.7)
Sed-hypnotic/muscle relaxant unspecified	10 (1.7)
Miscellaneous[b]	9 (1.5)
Non-benzodiazepine agonists ("Z" drugs)	**34 (5.7)**
Zolpidem	33 (5.5)
Eszopiclone	1 (0.2)
Barbiturates	**15 (2.5)**
Phenobarbital	5 (0.8)
Butalbital	5 (0.8)
Miscellaneous[c]	5 (0.8)
Paralytic	**1 (0.2)**
Vecuronium	1 (0.2)
Class total	**598 (100)**

[a] Includes chlordiazepoxide and bromazepam

[b] Includes propofol, phenibut (beta-phenyl-gamma-aminobutyric acid), meprobamate, flumazenil, etizolam, and acamprosate

[c] Includes butabarbital, pentobarbital, and barbituate unspecified

laundry detergent pods (19.7%), and sodium hypochlorite ≤ 6% (12.7%) were the most commonly reported agents in this class.

Gases, irritants, vapors, and dusts

Table 29 presents data for the gases, irritants, vapors, and dusts class. Carbon monoxide again represented the large majority of this class (63.8%).

Cough and cold preparations

Table 30 details data on cough and cold preparations reported to the Core Registry. Dextromethorphan was again the most commonly reported agent, making up 77.5% of the class.

Table 17 Ethanol and toxic alcohols

	N (%)
Ethanol[a]	**743 (100)**
Nonethanol alcohols and glycols	
Ethylene glycol	31 (47.0)
Isopropanol	21 (31.8)
Methanol	7 (10.6)
Miscellaneous[b]	7 (10.6)
Class total	**66 (100)**

[a] Ethanol is considered a separate agent class

[b] Includes diethylene glycol, denatured alcohol, ethylene glycol monohexyl ether, glycolic acid, toxic alcohol unspecified, and triethylene glycol mono butyl ether

Caustics

Table 31 presents the caustic agent class. Sodium hydroxide was the most common agent reported in this class (17.9%) followed by sodium hypochlorite concentration unknown (14.9%).

Antimicrobials

Table 32 presents data on antimicrobial agents. Antibiotics were the most common subclass (57.2%), with amoxicillin representing 15.9% and miscellaneous antibiotics representing 41.3% of this class. Antivirals and other antimicrobials were less common.

Table 18 Sympathomimetic agents

	N (%)
Methamphetamine	228 (40.3)
Cocaine	135 (23.9)
Amphetamine	57 (10.1)
Methylphenidate	40 (7.1)
Lisdexamfetamine	31 (5.5)
Dextroamphetamine	22 (3.9)
MDMA (Methylenedioxy-N-methamphetamine,Ecstasy)	12 (2.1)
Sympathomimetic unspecified	9 (1.6)
Dexmethylphenidate	9 (1.6)
Phenylephrine	5 (0.9)
Miscellaneous[a]	18 (3.2)
Class total	**566 (100)**

[a] Includes phentermine, atomoxetine, mixed amphetamine salts, clenbuterol, cathinone, norepinephrine, pseudoephedrine, and epinephrine

Table 19 Anticholinergics and antihistamines

	N (%)
Diphenhydramine	301 (58.6)
Hydroxyzine	93 (18.1)
Doxylamine	22 (4.3)
Benztropine	15 (2.9)
Chlorpheniramine	13 (2.5)
Promethazine	11 (2.1)
Loratadine	9 (1.8)
Pyrilamine	8 (1.6)
Cyproheptadine	6 (1.2)
Dicyclomine	6 (1.2)
Anticholinergic unspecified	5 (1.0)
Cetirizine	5 (1.0)
Miscellaneous[a]	20 (3.9)
Class total	**514 (100)**

[a] Includes, oxybutynin, chlorcyclizine, fexofenadine, hyoscyamine, meclizine, scopolamine, antihistamine unspecified, dimenhydrinate, trihexyphenidyl

Plants and fungi

Table S1 describes plant and fungi exposures reported to the Core Registry. In 2020 mold was again the most common single exposure (26.5%) followed by *Mitragyna speciosa* (kratom) (16.3%). Infrequent miscellaneous agents, however, made up the majority of this class (57.1%).

Hydrocarbons

Table S2 presents the hydrocarbon agent class. The largest single contributor to the class was toluene (14.6%), however, infrequent miscellaneous agents represented the majority (73.2%) of the class.

Gastrointestinal agents

Table S3 presents gastrointestinal agents. Ondansetron (25.6%), omeprazole (12.8%), famotidine (12.8%) and pantoprazole (10.3%) were the most commonly reported agents.

Insecticides, herbicides, rodenticides, and fungicides

Table S4 presents the pesticide (insecticide, herbicide, rodenticide and fungicide) class. There were 13 herbicides reported (41.9%), with glyphosate being the most common. There were 11 (35.5%) insecticides and 9 (29.0%) rodenticides. No fungicides were reported.

Table 20 Cardiovascular agents by type

	N (%)
Alpha-2 Agonist	**169 (32.5)**
Clonidine	125 (24.0)
Guanfacine	42 (8.1)
Dexmedetomidine	2 (0.4)
Beta Blockers	**122 (23.5)**
Metoprolol	52 (10.0)
Propranolol	36 (6.9)
Carvedilol	19 (3.7)
Atenolol	8 (1.5)
Miscellaneous[a]	7 (1.3)
Calcium Channel Blocker	**86 (16.5)**
Amlodipine	51 (9.8)
Diltiazem	13 (2.5)
Verapamil	11 (2.1)
Nifedipine	10 (1.9)
Nicardipine	1 (0.2)
Other antihypertensives and vasodilators	**39 (7.5)**
Prazosin	19 (3.7)
Hydralazine	8 (1.5)
Miscellaneous[b]	12 (2.3)
ACEI/ARB	**37 (7.1)**
Lisinopril	22 (4.2)
Losartan	10 (1.9)
Miscellaneous[c]	5 (1)
Diuretics	**23 (4.4)**
Hydrochlorothiazide	10 (1.9)
Spironolactone	5 (1.0)
Furosemide	5 (1.0)
Miscellaneous[d]	3 (0.6)
Cardiac Glycosides	**21 (4.0)**
Digoxin	20 (3.8)
Digitoxin	1 (0.2)
Antidysrhythmics and other CV Agents	14 (2.7)
Amiodarone	5 (1.0)
Miscellaneous[e]	9 (1.7)
Antihyperlipidemic	**9 (1.7)**
Miscellaneous[f]	9 (1.7)
Class total	**520 (100)**

[a] Includes labetalol, nadolol, and levobunolol

[b] Includes minoxidil, doxazosin, isobutyl nitrite, sacubitril, nitroprusside, isosorbide, and antihypertensive unspecified

[c] Includes valsartan, olmesartan, enalapril, and benazepril

[d] Includes torsemide and chlorthalidone

[e] Includes sotalol, flecainide, dofetilide, ranolazine, and dronedarone

[f] Includes atorvastatin, rosuvastatin, pravastatin, and fenofibrate

Chemotherapeutic and immunological agents

Table S5 describes chemotherapeutic and immunological agents. Methotrexate (23.3%), hydroxychloroquine (13.3%), and colchicine (13.3%) were the three most commonly reported agents.

Anticoagulants

Table S6 details anticoagulant class exposures. Warfarin (36.0%) was again the most common agent reported.

Table 21 Antipsychotics

	N (%)
Quetiapine	169 (41.3)
Olanzapine	54 (13.2)
Risperidone	52 (12.7)
Aripiprazole	45 (11.0)
Ziprasidone	20 (4.9)
Haloperidol	17 (4.2)
Lurasidone	12 (2.9)
Clozapine	9 (2.2)
Brexpiprazole	8 (2.0)
Chlorpromazine	7 (1.7)
Paliperidone	6 (1.5)
Miscellaneous[a]	10 (2.4)
Class total	**409 (100)**

[a] Includes prochlorperazine, fluphenazine, thioridazine, antipsychotic unspecified, pimpozide, cariprazine, perphenazine, and droperidol

Anesthetics

Table S7 describes the anesthetic class exposures reported in 2020. Lidocaine and benzonatate (each 29.2%) were the most commonly reported agents.

Other pharmaceuticals

Table S8 presents the other pharmaceutical products agent class. The majority of the class (72.0%) was made up of infrequently reported miscellaneous agents. Sumatriptan was the most commonly reported single agent (16.0%).

Table 22 Anticonvulsants and mood stabilizers

	N (%)
Lithium[a]	105 (100)
Lamotrigine	74 (29.4)
Valproic acid	49 (19.4)
Oxcarbazepine	27 (10.7)
Phenytoin	24 (9.5)
Topiramate	20 (7.9)
Carbamazepine	19 (7.5)
Divalproex	14 (5.6)
Levetiracetam	11 (4.4)
Miscellaneous[b]	14 (5.6)
Class total	**252 (100)**

[a] Lithium is considered a separate agent class

[b] Includes anticonvulsant unspecified, clobazam, eslicarbazepine, felbamate, lacosamide, tiagabine, and zonisamide

Table 23 Psychoactives

	N (%)
Molly - Amphetamine-like hallucinogen[a]	7 (100)
Marijuana	78 (25.5)
Tetrahydrocannabinol	62 (20.3)
Cannabinoid nonsynthetic	28 (9.2)
Delta-9-tetrahydrocannabinol	21 (6.9)
LSD[b]	19 (6.2)
Cannabinoid synthetic	17 (5.6)
Gamma hydroxybutyrate	15 (4.9)
Phencyclidine	13 (4.2)
Nicotine	12 (3.9)
Cannabidiol	7 (2.3)
Hallucinogenic amphetamines	6 (2.0)
Miscellaneous[c]	17 (5.6)
Class total	**306 (100)**

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

[b] *LSD* lysergic acid diethylamide

[c] Includes methylenedioxymethamphetamine, psychoactive unspecified, pharmaceutical THC, hallucinogen unspecified, gamma butyrolactone, disulfram, 1,4 butanediol

Endocrine

Table S9 describes the 24 endocrine agents reported. Levothyroxine represented nearly half of the reported agents (45.8%).

Table 24 Envenomations

	N (%)
Crotalus (Rattlesnake)	90 (35.6)
Agkistrodon (Copperhead, Cottonmouth/Water moccasin)	87 (34.4)
Snake unspecified	43 (17.0)
Loxosceles (Recluse spiders)	13 (5.1)
Miscellaneous[a]	20 (7.9)
Class total	**253 (100)**

[a] Includes Centruroides (var Scorpion incl Bark), Latrodectus (Widow spiders), Palytoxin, Vipera palaestinae, spider unspecified, Pyrrharctia isabella (isabella tiger moth), Scolopendra (var Centipede incl Giant Desert, Giant Sonoran, Texas red headed), envenomation unspecified, scorpion unspecified, Cigueterra poisoning, animal bite unspecified, and Hymenoptera (Bees, Wasps, Ants)

Table 25 Diabetic medications

	N (%)
Metformin	51 (39.5)
Insulin	29 (22.5)
Glipizide	28 (21.7)
Glyburide	5 (3.9)
Miscellaneous[a]	16 (12.4)
Class total	**129 (100)**

[a] Includes dulaglutide, empagliflozin, gliclazide, glimepiride, linagliptin, liraglutide, pioglitazone, sitagliptin, sulfonylurea unspecified.

Other non-pharmaceuticals

Table S10 describes the other non-pharmaceutical class. Water (13.0%), silicone (13.0%), and lactic acid (13.0%) were the three most common agents reported.

Pulmonary agents

Table S11 describes reported pulmonary agents. Montelukast was the most common agent reported (66.7%).

Foreign bodies

Table S12 details the foreign object ingestions reported to the Core Registry. Batteries were the most common objects (42.9%).

Anti-Parkinsonism agents

Table S13 presents the anti-parkinsonism agent class, containing 5 entries. Reported agents included pramipexole, ropinirole, levodopa/carbidopa, and rasagiline.

Table 26 Metals

	N (%)
Lead	32 (37.6)
Iron	24 (28.2)
Mercury	6 (7.1)
Arsenic	6 (7.1)
Miscellaneous[a]	17 (20)
Class Total	85 (100)

[a] Includes cobalt, chromium, copper, cadmium, cilver, platinum, manganese, magnesium, cesium, and beryllium

Table 27 Herbal products and dietary supplements

	N (%)
Caffeine	34 (38.2)
Melatonin	21 (23.6)
Miscellaneous[a]	34 (38.2)
Class total	**89 (100)**

[a] Includes aloin (aloe vera extract or outer leaves), biotin, black cohosh, dietary supplement unspecified, eucalyptus oil, guarana, herbal (dietary) multibotanical, L-carnitine, methylxanthine, multiple vitamin, potassium, prenatal vitamin, saw palmetto, sodium chloride, vitamin B complex (undefined), vitamin B3 (niacin), vitamin B6 (pyridoxine), vitamin C (ascorbic acid), vitamin D, vitamin E (tocopherol), yerba mate green tea extract, yohimbine, and zinc

Weapons of mass destruction

Botulinum toxin (5 cases) was the only agent reported in the class of weapons of mass destruction, described in Table S14.

Cholinergics

Table S15 describes the single cholinergic/parasympathetic agent reported, cholinergic/parasympathetic unspecified.

Clinical signs and symptoms

The categories of clinical signs and symptoms describe a diverse range of abnormal clinical findings. Predefined criteria must be met for each category in order for a sign or symptom to be reported as present. For example, tachycardia is defined as a heart rate greater than 140 beats per minute. Additionally, each case may report more than one abnormality within a

Table 28 Household products

	N (%)
Cleaning solutions and disinfectants	20 (28.2)
Laundry detergent pod	14 (19.7)
Sodium hypochlorite ≤ 6%	9 (12.7)
Hand sanitizer unspecified	6 (8.5)
Miscellaneous[a]	22 (31.0)
Class total	**71 (100)**

[a] Includes ammonia ≤ 10%, aromatic or essential oils (carrier/solvent base unspecified), diaper rash ointment, dishwasher detergent, dishwasher detergent pod, drain cleaner (irritant), hair product, household product unspecified, mequinol (4-methoxyphenol), moisturizer/lotion, oven cleaner, soaps and detergents, windshield washer fluid

Table 29 Gases, irritants, vapors, and dusts

	N (%)
Carbon monoxide	44 (63.8)
Chlorine	7 (10.1)
Miscellaneous[a]	18 (26.1)
Class Total	**69 (100)**

[a] Includes cyandide, bromide, chloramine, vaping NOS, acetonitrile, copper cyanide, cyclohexyl nitrate, duster (canned air), gases/vapors/irritants/dusts unspecified, nitrogen oxides, petroleum vapors, smoke, volatile organic compounds (VOCs) unspecified

group or across groups. For example, a single case entry may have multiple vital sign abnormalities or may have both a vital sign abnormality and a neurologic abnormality. The percentages for these categories and their individual signs and symptoms are calculated relative to the total number of Core Registry cases ($N = 6668$). It is therefore possible for the total to be more than 100%.

Toxidromes

Table 33 reports the 1844 toxidromes reported to the Core Registry in 2020. Consistent with recent years, the sedative-hypnotic toxidrome was the most common (8.3%). This year the opioid toxidrome (3.7%) overtook serotonin syndrome (3.0%) as the third most common toxidrome reported.

Major vital sign abnormalities

Table 34 presents the 1738 vital sign abnormalities reported to the Core Registry in 2020. Trends were nearly identical to recent years. Tachycardia (11.2%), hypotension (6.2%), and bradycardia (3.4%) were the most common vital sign abnormalities reported.

Clinical signs and symptoms—neurologic

Table 35 describes the 5111 neurologic clinical signs and symptoms reported to the Core Registry in 2020. Coma/CNS depression (27.6%), agitation (16.4%), hyperreflexia/myoclonus/clonus/tremor (10.6%) and delirium/toxic psychosis (10.0%) were the most commonly reported signs, similar to last year [2].

Table. 30 Cough and cold

	N (%)
Dextromethorphan	69 (77.5)
Guaifenesin	12 (13.5)
Cough and cold unspecified	7 (7.9)
Camphor	1 (1.1)
Class total	**89 (100)**

Table 31 Caustics

	N (%)
Sodium hydroxide	12 (17.9)
Sodium hypochlorite (concentration unknown)	10 (14.9)
Cleaning agent	8 (11.9)
Caustic unspecified	6 (9.0)
Sodium hypochlorite > 6%	6 (9.0)
Miscellaneous[a]	39 (41.5)
Class total	**67 (100)**

[a] Includes acetic acid, ammonium chloride nonpharmaceutical, ammonium nitrate, boric acid (hydroborate), cement, drain cleaner, formaldehyde, hydrochloric acid, hydrogen peroxide > 10%, hydroxy undecanoic acid, lithium hydroxide, peroxyacetic acid (peracetic acid), phosphoric acid, potassium hydroxide, and sulfuric acid

Clinical signs and symptoms—cardiovascular and pulmonary

Table 36 presents the 553 cardiovascular and 745 pulmonary clinical signs reported to the Core Registry in 2020. QTc prolongation (5.1%) and respiratory depression (7.8%) remained the most common signs in their respective categories again this year [2, 3].

Table 32 Antimicrobials

	N (%)
Antibiotics	**36 (57.2)**
Amoxicillin	10 (15.9)
Miscellaneous[a]	26 (41.3)
Antivirals	**18 (28.5)**
Tenofovir	5 (7.9)
Miscellaneous[b]	13 (20.6)
Other Antimicrobials	**9 (14.3)**
Miscellaneous[c]	9 (14.3)
Class total	**62 (100)**

[a] Includes ciprofloxacin, clavulanic acid, clindamycin, dapsone, doxycycline, levofloxacin, linezolid, metronidazole, minocycline, penicillin, piperacillin, rifampin, rifaximin, tazobactam, vancomycin.

[b] Includes acyclovir, amantadine, bictegravir, darunavir, emtricitabine, ritonavir, valacyclovir.

[c] Includes antimicrobial unspecified, benzalkonium chloride, itraconazole, piperazine citrate, quinine.

Table 33 Toxidromes[a]

	N (%)[a]
Sedative-hypnotic	556 (8.3)
Anticholinergic	375 (5.6)
Sympathomimetic	295 (4.4)
Opioid	249 (3.7)
Serotonin syndrome	197 (3.0)
Alcoholic ketoacidosis	89 (1.3)
Sympatholytic	39 (0.6)
Washout syndrome	16 (0.2)
Cannabinoid hyperemesis	8 (0.1)
NMS[b]	7 (0.1)
Overlap syndromes	6 (0.1)
Cholinergic	5 (0.1)
Anticonvulsant hypersensitivity	2 (< 0.1)
Class total	**1844 (27.7)**

[a] Percentage based on the number cases reporting specific toxidrome relative to total number of Registry cases in 2020 (*N*=6668)

[b] *NMS* neuroleptic malignant syndrome

Table 35 Clinical signs and symptoms—neurologic

	N (%)[a]
Coma/CNS depression	1842 (27.6)
Agitation	1094 (16.4)
Hyperflexia/Myoclonus/Clonus/Tremor	704 (10.6)
Delirium/Toxic Psychosis	668 (10.0)
Seizures	355 (5.3)
Hallucinations	256 (3.8)
Weakness/Paralysis	61 (0.9)
EPS/Dystonia/Rigidity	58 (0.9)
Numbness/Paresthesia	56 (0.8)
Peripheral Neuropathy (objective)	17 (0.3)
Class total	**5111 (76.6%)**

[a] Percentages are based on the total number of cases reported to the Registry in 2020 (*N* = 6668); 3590 Registry cases (53.8%) reported at least one neurologic clinical effect. Cases may have reported multiple effects

Clinical signs—other organ systems

Table 37 presents the other organ system clinical signs which include metabolic, renal and musculoskeletal, hematological, gastrointestinal and hepatic, and dermatological. Metabolic abnormalities were again the most frequently reported (10.4%), and among these an elevated anion gap (4.0%) and metabolic acidosis (4.0%) were the most common [2, 3]. Renal and musculoskeletal abnormalities were the next most commonly reported (7.4%), with acute kidney injury (4.3%) being the most common sign in this subgroup. Hepatotoxicity was the most common gastrointestinal and hepatic abnormality (2.8%). Coagulopathy was the most commonly reported hematological abnormality (1.6%). Dermatological abnormalities were less frequently reported (3.4%), with rash being the most common (1.6%).

Fatalities

There were 81 fatalities in 2020, comprising 1.2% of Core Registry cases. Single-agent exposures were implicated in 34 cases (Table 38), 26 cases involved multiple agents (Table 39), and in 21 cases it was unknown if there was a toxicologic exposure (Table 40).

There were 12 fatalities (14.8%) involving opioids, an decrease from 2019 and 2018 in which opioids were reported in 19.8% and 34.0% of Core Registry deaths, respectively [2, 3]. Fentanyl was reported in 2 deaths (2.5%) this year compared with 5.5% in 2019 and 9.4% in 2018 [2, 3]; 3 deaths (3.7%) were reported as single opioid ingestions in 2020.

Table 34 Major vital sign abnormalities

	N (%)[a]
Tachycardia (HR > 140)	744 (11.2)
Hypotension (systolic BP < 80 mmHg)	411 (6.2)
Bradycardia (HR < 50)	229 (3.4)
Bradypnea (RR< 10)	166 (2.5)
Hypertension (systolic BP > 200 mmHg and/or diastolic BP > 120 mmHg)	147 (2.2)
Hyperthermia (temp > 105° F)	41 (0.6)
Class total	**1738 (26.1)**

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

[a] Percentage based on the number of cases relative to the total number of Registry cases in 2020 (*N* = 6668). There were 1407 unique cases (21.1% of all Registry cases) reporting at least one major vital sign abnormality. Cases may be associated with more than one major vital sign abnormality

Table 36 Clinical signs—cardiovascular and pulmonary

	N (%)[a]
Cardiovascular	
Prolonged QTc (≥ 500 ms)	339 (5.1)
Prolonged QRS (≥ 120 ms)	85 (1.3)
Myocardial injury or infarction	70 (1.0)
Ventricular dysrhythmia	45 (0.7)
AV Block (> 1st degree)	14 (0.2)
Class total	553 (8.3)
Pulmonary	
Respiratory depression	517 (7.8)
Aspiration pneumonitis	107 (1.6)
Acute lung injury/ARDS[b]	92 (1.4)
Asthma/Reactive airway disease	29 (0.4)
Class Total	**745 (11.2)**

[a] Percentage based on number cases reporting signs or symptoms relative to total number of Registry cases in 2020 (*N* = 6668). There were 1147 unique cases (17.02% of all Registry cases) that reported at least one cardiac or pulmonary clinical effect. Cases may be associated with more than one sign or symptom

[b] *ARDS* acute respiratory distress syndrome

Table 37 Clinical signs—other organ systems

	N (%)[a]
Metabolic	
Elevated anion gap (> 20)	269 (4.0)
Metabolic acidosis (pH < 7.2)	268 (4.0)
Hypoglycemia (glucose < 50 mg/dL)	105 (1.6)
Elevated osmole gap (> 20)	50 (0.7)
Total	**692 (10.4)[b]**
Renal/musculoskeletal	
Acute kidney injury (creatinine > 2.0 mg/dL)	289 (4.3)
Rhabdomyolysis (CPK > 1000 IU/L)	207 (3.1)
Total	**496 (7.4)[b]**
Gastrointestinal/Hepatic	
Hepatotoxicity (AST ≥ 1000 IU/L)	187 (2.8)
Hepatotoxicity (ALT 100–1000 IU/L)	60 (0.9)
Hepatotoxicity (ALT ≥ 1000 IU/L)	56 (0.8)
Gastrointestinal bleeding	42 (0.6)
Pancreatitis	34 (0.5)
Corrosive injury	28 (0.4)
Intestinal ischemia	5 (0.1)
Total	**412 (6.2)[b]**
Hematological	
Coagulopathy (PT > 15 s)	110 (1.6)
Leukocytosis (WBC > 20 K/μL)	91 (1.4)
Thrombocytopenia (platelets < 100 K/μL)	83 (1.2)
Hemolysis (Hgb < 10 g/dL)	63 (0.9)
Methemoglobinemia (MetHgb ≥ 2%)	17 (0.3)
Pancytopenia	8 (0.1)
Total	**372 (5.6)[b]**
Dermatological	
Rash	107 (1.6)
Blister/Bullae	64 (1.0)
Angioedema	28 (0.4)
Necrosis	26 (0.4)
Total	**225 (3.4)[b]**

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

[a] Percentage equals the number of cases reporting specific clinical signs compared to the total number of Registry cases in 2020 (*N* = 6668)

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

Acetaminophen was the most common agent involved in both single and multiple agent fatalities; there were 11 fatalities (13.6%) involving acetaminophen, 5 as a single agent. A single death was reported after laundry pod exposure in a > 89-year-old that sustained a corrosive gastrointestinal injury. A single agent pancrelipase death in a 7-year-old after medication administering error due to the wrong medication (either wrong route or dilution technique) was reported. A single agent lactulose death in a 2-year-old also due to a medication dosing error after receiving 75 g chronically was reported with respiratory depression, CNS depression, seizures, hypernatremia, and hyperglycemia. A single agent paraquat death was reported in a 60-year-old who presented with hypotension, tachycardia, QRS and QTc prolongation, and gastrointestinal bleeding. He was treated with activated charcoal, NAC, steroids, vitamin C, and magnesium sulfate. A multi-agent death involving intentional verapamil exposure, with a subsequent lipid emulsion medication dosing error given intranasally, was reported in a 65-year-old. In addition to treatment for the verapamil exposure, she was treated with enhanced elimination and ECMO specifically related to the medication error.

In 2020 there were 13 pediatric (age 0–18 years) deaths due to a known toxicologic exposure (16.1%), compared with 20.0% in 2019 [2]. The age range was 13 months to 18 years. Nine were single agent exposures and 4 involved multiple agents. No pediatric exposures involved acetaminophen in 2020, whereas 35.7% of pediatric exposures in 2019 involved acetaminophen. Three deaths involved opioids in pediatric patients. One single agent methamphetamine death was reported in a 13-month old.

There were 46 fatality cases in which life support was withdrawn, representing 0.7% of Core Registry cases. It was unknown whether life support was withdrawn in an additional 7 cases. Brain death was declared in 19 cases.

Table 38 2020 Fatalities reported in ToxIC Registry with known toxicological exposure[a]: single agent

Age/ gender[b]	Agents involved	Clinical findings[c]	Life support withdrawn	Brain death confirmed	Treatment[d]
25 M	Acetaminophen	HT, RD, CNS, OG, HPT, CPT, AKI	Yes	No	NAC, vasopressors (norepinephrine), intubation
32 F	Acetaminophen	HT, TC, MA, HPT, AKI	Yes	No	Fomepizole, NAC, vasopressors (norepinephrine, phenylephrine, vasopressin), intubation, IV fluid resuscitation
69 F	Acetaminophen	HT, CNS, MA, HGY, AG, HPT, GIB, CPT, AKI	Yes	No	NAC, $NaHCO_3$, glucose >5%, vasopressors (norepinephrine, vasopressin), intubation, IV fluid resuscitation
73 M	Acetaminophen	QTC, WBC, SN	No		None
80 M	Acetaminophen	HT, MI, CNS, MA, AG, HPT, CPT	No		NAC, vitamin K, vasopressors (phenylephrine), IV fluid resuscitation
26 F	Acetylsalicylic acid	TC, CNS, SZ, AG, AKI	No		$NaHCO_3$, benzodiazepines, MDAC, urinary alkalinization, CPR, IV fluid resuscitation
69 F	Amitriptyline	HT, BC, QRS, QTC, CNS	Yes	Yes	Glucagon, HIE, $NaHCO_3$, vasopressors (norepinephrine), intubation, IV fluid resuscitation
59 M	Amlodipine	HT, BC, QRS, RD, CNS, MA, AG, PNC, GII, AKI	No		Calcium, folate, fomepizole, HIE, lipid therapy, methylene blue, NAC, $NaHCO_3$, thiamine, vasopressors (epinephrine, norepinephrine, phenylephrine, vasopressin), CPR, intubation, IV fluid resuscitation, pacemaker, transfusion
50 M	Amphetamine	SYS, TC, HYT, AP, RD, RFX, MA, AG, GII, CPT, PLT, AKI, RBM	Yes	No	Calcium, $NaHCO_3$, benzodiazepines, steroids, vasopressors (norepinephrine), continuous renal replacement, IV fluid resuscitation
38 F	Bupropion	HT, BC, BP, VD, QTC, MI, RD, CNS, SZ, MA, CA	Yes	Yes	Antiarrhythmics, benzodiazepines, vasopressors (epinephrine, norepinephrine, phenylephrine, vasopressin), CPR, intubation, IV fluid resuscitation
16 F	Cocaine	HT, QRS, QTC, MI, AP, RD, CNS, HGY, HPT, AKI, RBM	Yes	Yes	Naloxone/nalmefene, $NaHCO_3$, glucose > 5%, vasopressors (epinephrine), CPR, intubation, IV fluid resuscitation, therapeutic hypothermia
16 F	Colchicine	HT, CNS, MA	Yes	Yes	Benzodiazepines, activated charcoal, ECMO, intubation, IV fluid resuscitation
53 M	Digitoxin	HT, VD, MI, RD, CNS	Yes	No	Digoxin Fab, antiarrhythmics, vasopressors (epinephrine, norepinephrine), CPR, cardioversion, intubation

Table 38 (continued)

Age/ gender[b]	Agents involved	Clinical findings[c]	Life support withdrawn	Brain death confirmed	Treatment[d]
14 F	Diphenhydramine	TC, VD, QRS, QTC, CNS, SZ	Yes	Yes	Calcium, lipid therapy, $NaHCO_3$, neuromuscular blockers, vasopressors (epinephrine), activated charcoal, CPR, cardioversion, intubation, IV fluid resuscitation, therapeutic hypothermia
25 M	Ethanol	SS, HT, TC, HYT, VD, QRS, QTC, MI, AP, CNS, SZ, HGY, HPT, PLT, AKI, RBM	No		$NaHCO_3$, anticonvulsants, vasopressors (norepinephrine), intubation, IV fluid resuscitation, therapeutic hypothermia
47 M	Ethanol	HT, QTC, CNS, RFX, MA, AG, GIB, HYS	Yes	No	Folate, fomepizole, NAC, benzodiazepines, neuromuscular blockers, intubation, IV fluid resuscitation
57 F	Ethanol	AP, AG, HPT, PNC, AKI	Unknown		Thiamine, benzodiazepines, glucose > 5%, opioids, vasopressors (norepinephrine)
16 M	Ethylene glycol	SHS, CNS	Yes	Unknown	Pyridoxine, thiamine, benzodiazepines, intubation, IV fluid resuscitation
26 F	Fentanyl	None listed	No		Naloxone/nalmefene, benzodiazepines, hemodialysis
39 M	Heroin	OT, RD, CNS	Yes	Yes	Buprenorphine/naloxone dual formulations (e.g. Suboxone)
56 M	Insulin	RD, CNS, SZ, HGY	Yes	Yes	Glucagon, octreotide, anticonvulsants, benzodiazepines, glucose >5%, opioids, intubation, IV fluid resuscitation
2 F	Lactulose	HT, TC, RD, CNS, SZ, HG, HN, MA, OG	No		Anticonvulsants, benzodiazepines, vasopressors (epinephrine), hemodialysis, CPR, intubation, IV fluid resuscitation
> 89 M	Laundry detergent pod	CRV	Unknown		None
64 M	Lithium	CNS, GIB	No		IV fluid resuscitation
60 F	Metformin	QTC, DLM, MA, AG, OG, PNC, WBC, AKI, RBM	Yes	Yes	Folate, fomepizole, methylene blue, pyridoxine, $NaHCO_3$, thiamine, glucose >5%, vasopressors (norepinephrine, phenylephrine, vasopressin), continuous renal replacement, IV fluid resuscitation
13mo F	Methamphetamine	HTN, TC, RD, CNS	Yes	Yes	Intubation
54 M	Methanol	HT, TC, CNS, SZ, MA, AG, OG, CPT, AKI	Yes	Yes	Folate, fomepizole, vasopressors (norepinephrine, phenylephrine, vasopressin), hemodialysis, intubation, transfusion
66 M	Methotrexate	ALI, DLM, CRV, GIB, CPT, PLT, PCT, AKI, RS	Yes	No	Opioids, intubation, IV fluid resuscitation, leucovorin

Table 38 (continued)

Age/ gender[b]	Agents involved	Clinical findings[c]	Life support withdrawn	Brain death confirmed	Treatment[d]
18 F	Nortriptyline	HT, BC, QRS, QTC, RD, CNS, SZ, MA	Yes	Yes	Lipid therapy, $NaHCO_3$, benzodiazepines, vasopressors (not specified), hemodialysis, CPR, ECMO intubation, IV fluid resuscitation
17 M	Opioid unspecified	OT, HT, AP, CNS	Unknown		None
7 F	Pancrelipase	HT, BC, MA, CA, CPT, PLT, WBC	No		Vasopressors (epinephrine), CPR, intubation, IV fluid resuscitation
60 M	Paraquat	HT, TC, QRS, QTC, AG, GIB	No		NAC, steroids, activated charcoal, vitamin C, magnesium sulfate
72 M	Rasburicase	MHG, AKI	No		Methylene blue
57 M	Unknown agent	AK, HT, TC, RD, CNS, MA	Yes	Yes	Hemodialysis, intubation

[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

[c] *AG:* anion gap, *AK:* alcoholic ketoacidosis, *AKI:* acute kidney injury, *ALI:* acute lung injury/ARDS, *AP:* aspiration pneumonitis, *BC:* bradycardia, *BP:* bradypnea, *CA:* cardiac arrest, *CNS:* coma/CNS depression, *CPT:* coagulopathy, *CRV:* corrosive injury, *DLM:* delirium, *GIB:* GI bleeding, *GII:* intestinal ischemia, *HG:* hyperglycemia, *HGY:* hypoglycemia, *HN:* hypernatremia, *HPT:* hepatoxicity, *HT:* hypotension, *HTN:* hypertension, *HYS:* hemolysis, *HY:* hypothermia, *HYT:* hyperthermia, *MA:* metabolic acidosis, *MHG:* methemoglobinemia, *MI:* myocardial injury/ischemia, *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, *SN:* dermal necrosis, *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, *MDAC* multiple dose activated charcoal, *NAC* n-Acetyl cysteine, *$NaHCO_3$* sodium bicarbonate

Table 39 2020 Fatalities reported in ToxIC Registry with known toxicological exposure[a]: multiple agents

Age/ gender[b]	Agents involved	Clinical findings[c]	Life support withdrawn	Brain death confirmed	Treatment[d]
29 M	Acetaminophen, aripiprazole, bupropion, clonazepam, hydroxychloroquine, metformin	None	No		NAC, IV fluid resuscitation
42 F	Acetaminophen, alprazolam, insulin, venlafaxine	CNS, DLM, HGY, MA, HPT	Yes	Unknown	NAC
49 F	Acetaminophen, butabarbital, caffeine	HT, CNS, MA, AG, HPT, CPT, WBC, AKI, RBM	Yes	No	NAC, benzodiazepines, neuromuscular blockers, opioids, vasopressors (norepinephrine), continuous renal replacement, intubation, IV fluid resuscitation
51 F	Acetaminophen, benzonatate	HT, TC, RD, CNS, HGY, MA, AG, HPT	Yes	No	Calcium, fomepizole, NAC, $NaHCO_3$, thiamine, vitamin K, opioids, steroids, vasopressors (epinephrine), hemodialysis, intubation
59 F	Acetaminophen, hydrocodone	SHS, CNS	No		NAC, naloxone/nalmefene
73 M	Acetaminophen, iron	HT, QRS, QTC, CNS, HGY, MA, AG, CPT, AKI, RBM	No		Fomepizole, NAC, octreotide, vitamin K, deferoxamine, glucose >5%, opioids, vasopressors (norepinephrine, vasopressin), hemodialysis, intubation, transfusion
32 F	Alprazolam, cyclobenzaprine, tramadol	SHS, BP, RD, CNS	Yes	Unknown	benzodiazepines, steroids, intubation, IV fluid resuscitation, therapeutic hypothermia
60 F	Alprazolam, zolpidem	SHS, QTC, AP, RD, CNS, MA, AG, HPT	Yes	No	None
15 F	Amlodipine, hydrocodone, ibuprofen, pravastatin	HT, TC, MA, CPT, WBC	Yes	Yes	Calcium, HIE, lipid resuscitation therapy, glucose >5%, neuromuscular blockers, vasopressors (epinephrine, norepinephrine, vasopressin), ECMO, transfusion
36 M	Amlodipine, hydrochlorothiazide, ibuprofen, lisinopril	HT, BC, RD, CNS, MHG	Yes	Unknown	Calcium, glucagon, HIE, lipid resuscitation therapy, methylene blue, $NaHCO_3$, benzodiazepines, glucose >5%, opioids, vasopressors (epinephrine, phenylephrine), hemodialysis, ECMO
50 M	Amlodipine, hydroxyzine	HT, CNS	Yes	No	HIE, methylene blue, vasopressors (epinephrine, norepinephrine)
52 F	Amlodipine, gabapentin, meloxicam, metoprolol, potassium	HT, TC, BC, AVB, CNS, MA	No		Atropine, calcium, glucagon, lipid resuscitation therapy, antiarrhythmics, glucose >5%, activated charcoal, continuous renal replacement, CPR, intubation, IV fluid resuscitation, pacemaker
41 M	Amphetamine, cocaine, opioid unspecified	HT, TC, BP, HYT, QTC, MI, AP, RD, CNS, AG, HPT, HYS, CPT, PLT, WBC, AKI, RBM, RS	Yes	Unknown	Calcium, naloxone/nalmefene, antiarrhythmics, anticonvulsants,

Table 39 (continued)

Age/ gender[b]	Agents involved	Clinical findings[c]	Life support withdrawn	Brain death confirmed	Treatment[d]
					antihypertensives, benzodiazepines, beta-blockers, neuromuscular blockers, opioids, steroids, vasopressors (norepinephrine), continuous renal replacement, exchange transfusion, intubation, IV fluid resuscitation
50 F	Baclofen, pregabalin	SHS, RD, CNS	No		Intubation, IV fluid resuscitation
64 M	Baclofen, clonazepam	RD, RFX	Unknown		Benzodiazepines, CPR, intubation, IV fluid resuscitation
62 M	Benzodiazepine unspecified, ethanol	SHS, CNS	Yes	Yes	Flumazenil, benzodiazepines, IV fluid resuscitation
84 F	Carbon monoxide, cyanide	HT, VD, MI, AP, RD, CNS, MA, CPT, WBC, BL	Yes	Yes	Hydroxocobalamin, opioids, vasopressors (epinephrine, norepinephrine), CPR, IV fluid resuscitation
22 F	Citalopram, morphine	OT, CNS, RFX	Yes	Unknown	None
17 M	Cocaine, ethanol	HT, TC, QRS, QTC, RD, CNS, MA, AKI, RBM	No		$NaHCO_3$, vasopressors (epinephrine, norepinephrine), intubation
18 M	Cocaine, heroin	OT, SYS, HT, TC, AP, RD, CNS, MA, HPT, AKI	Yes	Yes	Naloxone/nalmefene, benzodiazepines, neuromuscular blockers, opioids, vasopressors (norepinephrine), intubation, IV fluid resuscitation
15 M	Empagliflozin, ibuprofen, lisinopril, lisdexamfetamine, metformin, quetiapine	HT, RD, CNS, MA, AG	Yes	No	Anticonvulsants, benzodiazepines, whole bowel irrigation, continuous renal replacement, CPR, ECMO, intubation, IV fluid resuscitation
58 F	Ethanol, heroin	AGT, DLM	Unknown		benzodiazepines
61 F	Ethanol, hydromorphone, lorazepam, oxycodone	CHO, AGT, DLM	Unknown		Flumazenil, folate, thiamine, antipsychotics, benzodiazepines, opioids, IV fluid resuscitation
39 F	Fentanyl, heroin	None	No		Buprenorphine/naloxone dual formulations (e.g. Suboxone)
29 F	Heroin, methadone	QTC, RFX, SZ, MA, WBC	Yes	Yes	Calcium, naloxone/nalmefene, $NaHCO_3$, anticonvulsants, benzodiazepines, neuromuscular blockers, opioids, CPR
65 F	Lipid emulsion, verapamil	HT, TC, BC, MA, AG, HPT, HYS, CPT, PLT, AKI	Yes	Unknown	Calcium, glucagon, HIE, lipid resuscitation therapy, antiarrhythmics, benzodiazepines, glucose >5%, opioids, vasopressors (epinephrine, norepinephrine, vasopressin), continuous renal replacement, ECMO,

Table 39 (continued)

Age/ gender[b]	Agents involved	Clinical findings[c]	Life support withdrawn	Brain death confirmed	Treatment[d]
					intubation, IV fluid resuscitation, pacemaker, transfusion

[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.

[c] AG: anion gap, AGT: agitation, AKI: acute kidney injury, AP: aspiration pneumonitis, AVB: AV block, BC: bradycardia, BL: blisters/bullae, BP: bradypnea, CHO: cholinergic, CNS: coma/CNS depression, CPT: coagulopathy, DLM: delirium, HGY: hypoglycemia, HPT: hepatoxicity, HT: hypotension, HYS: hemolysis, HYT: hyperthermia, MA: metabolic acidosis, MHG: Methemoglobinemia, MI: myocardial injury/ischemia, OT: opioid toxidrome, PLT: thrombocytopenia, QRS: QRS prolongation, QTC: QTc prolongation, RBM: rhabdomyolysis, RD: respiratory depression, RFX: hyperreflexia/clonus/tremor, RS: rash, SHS: sedative-hypnotic 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

Adverse drug reactions

Table 41 presents the common drugs associated with adverse drug reactions reported to the Core Registry in 2020. One hundred seventy-seven ADRs (2.7% of cases) were reported in 2020. Lithium was again the most common drug reported (10.2%), similar to recent years.

Treatment

Antidotal therapy

Table 42 describes the 2777 antidotes reported to the Core Registry in 2020. Similar to last year, N-acetylcysteine (28.3%), followed by naloxone/nalmefene (15.5%), and thiamine (15.0%) were the three most common antidotes reported [2]. In 2020, 31.0% of Core Registry cases received at least one antidote compared with 26.3% in 2019 [2].

Antivenom therapy

Table 43 presents data on antivenom therapies reported to the Core Registry. Crotalidae polyvalent immune Fab (ovine) again made up the majority (65.7%) of antivenom administered, however its relative contribution continued to decline (73.9% in 2019 from 94.2% in 2018) in this year.[2, 3] Crotalidae immune Fab2 (equine) antivenom, introduced in 2019 (19.9%) increased to 31.0% of cases of administered antivenom in 2020.

Pharmacologic supportive care

Table 44 describes the 3260 pharmacologic supportive care treatments reported in 2020. Benzodiazepines were again the most commonly reported agents (47.1%), followed by opioids (12.8%) and vasopressors (8.1%).

Non-pharmacologic supportive care

Table 45 presents non-pharmacologic supportive care treatments reported to the Core Registry in 2020. IV fluid resuscitation (76.1%) and intubation/ventilatory management (19.3%), remain the most common treatments in this category.

Chelation therapy administered

Table 46 presents data on chelation therapy administered. There were 22 chelation agents reported in 2020. Deferoxamine was the most common chelator administered (36.4%).

Table 40 2020 Fatalities reported in ToxIC Registry with unknown toxicological exposure[a]

Age/gender[b]	Clinical findings[c]	Life support Withdrawn	Brain death Confirmed	Treatment reported[d]
9mo M	None	Yes	Yes	None
9mo F	HTN, TC, RD, CNS, MA, HYS, CPT, PLT	No		None
5 F	TC, CNS, SZ	Yes	Unknown	None
17 M	HT, TC, VD, QRS, QTC, AP, CNS, MA, AG, WBC	Yes	Yes	$NaHCO_3$, vasopressors (epinephrine, norepinephrine), CPR, cardioversion, intubation, IV fluid resuscitation
19 F	HT, TC, VD, MI, ALI, CNS, HPT, WBC, AKI	Yes	No	None
20 F	ALI, MA, HPT, HYS, PLT, AKI	Yes	No	NAC, opioids, steroids, intubation, IV fluid resuscitation, therapeutic hypothermia, cyclophosphamine
28 F	HT, MI, CNS, MA, AG, OG, HPT, HYS, CPT, PLT, AKI	Yes	No	Calcium, fomepizole, HIE, methylene blue, NAC, $NaHCO_3$, thiamine, vitamin K, benzodiazepines, neuromuscular blockers, opioids, vasopressors (epinephrine, norepinephrine, phenylephrine, vasopressin), hemodialysis, intubation, IV fluid resuscitation
39 F	SHS, HT, ALI, CNS, MA, AG, OG, CA	Yes	No	Fomepizole, methylene blue, NAC, $NaHCO_3$, glucose >5%, neuromuscular blockers, vasopressors (epinephrine, norepinephrine, phenylephrine, vasopressin), hemodialysis, CPR, ECMO, intubation, IV fluid resuscitation, exlap for increased abdominal pressure
39 F	HTN, MI, CNS, PAR	Yes	No	None
39 M	HT, HYT, MI, RD, CNS, AKI	No		Naloxone/nalmefene, benzodiazepines, vasopressors (epinephrine, norepinephrine, vasopressin), intubation, IV fluid resuscitation
47 F	HT, TC, MI, ALI, MA, AG, HYS, CPT, PLT	No		None
50 F	QTC, CNS, MA, AG, HPT, AKI	No		NAC, steroids, vasopressors (norepinephrine, vasopressin), hemodialysis, intubation, IV fluid resuscitation
54 M	AK, HT, ALI, CNS, SZ, MA, AG, OG, AKI	Yes	Unknown	None
55 M	HT, QTC, RD, CNS, MA, AG, HPT, PNC, GIB, CPT, WBC, AKI	Yes	No	None
55 M	HT, TC, HYT, VD, MI, RD, AGT, MA, AG, CPT, PLT, AKI	No		NAC, antiarrhythmics, neuromuscular blockers, opioids, vasopressors (norepinephrine), intubation, IV fluid resuscitation
56 F	HT, TC, CNS, HGY, AG, HPT	No		None
57 M	HT, QRS, QTC, CNS	No		$NaHCO_3$, vasopressors (phenylephrine), CPR, IV fluid resuscitation
57 M	RD, CNS, MA, AG, OG, HPT, CPT	No		NAC, vasopressors (epinephrine, norepinephrine, vasopressin), hemodialysis,
66 F	HT, TC, ALI, CNS, MA, AG, OG, AKI	No		None
77 M	TC, HGY, CPT, AKI, ECH	No		Vitamin K,
84 F	HT, BC, HGY, AKI	Unknown		None

[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. mo: months

[c] AG: anion gap, AGT: agitation, AK: alcoholic ketoacidosis, AKI: acute kidney injury, ALI: acute lung injury/ARDS, AP: aspiration pneumonitis, BC: bradycardia, CA: cardiac arrest, CNS: coma/CNS depression, CPT: coagulopathy, ECH: ecchymosis, GIB: GI bleeding, HGY: hypoglycemia, HPT: hepatoxicity, HT: hypotension, HTN: hypertension, HYS: hemolysis, HYT: hyperthermia, MA: metabolic acidosis, MI: myocardial injury/ischemia, OG: osmolar gap, OT: opioid toxidrome, PAR: paralysis/weakness, PLT: thrombocytopenia, PNC: pancreatitis, QRS: QRS prolongation, QTC: QTc prolongation, RD: respiratory depression, SHS: sedative-hypnotic 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-acetylcysteine, $NaHCO_3$: Sodium bicarbonate

Table 41 Most common drugs associated with adverse drug reactions

	N (%)
Lithium	18 (10.2)
Valproic acid	6 (3.4)
Baclofen	6 (3.4)
Digoxin	5 (2.8)
Quetiapine	5 (2.8)
Metformin	5 (2.8)
Miscellaneous[a]	132 (74.6)
Class total	**177 (100)**

[a] Includes gabapentin, morphine, citalopram, propofol, ondansetron, risperidone, benztropine, fluoxetine, haloperidol, guanfacine, metoprolol, phenytoin, linezolid, methadone, naloxone, olanzapine, diphenhydramine, duloxetine, lamotrigine, paliperidone, scopolamine, verapamil, aripiprazole, sertraline, carbamazepine, bupropion, amlodipine, amitriptyline, etanercept, diltiazem, amiodarone, dextromethorphan, ethinyl estradiol, ferric carboxymaltose (iron dextran), flumazenil, alprazolam, acyclovir, ethanol, arsenic, corticosteroid, bupivacaine, clozapine, dexmedetomidine, dapsone, cyproheptadine, crotalus (rattlesnake), Crotalidae Immune Fab2 (Equine, Anavip), carvedilol, chlordiazepoxide, clomipramine, clonidine, cocaine, atenolol, succinylcholine, lidocaine, pregabalin, prilocaine, rasburicase, rifampin, ropivacaine, sed-hypnotic/muscle relaxant unspecified, piperacillin, sotalol, physostigmine, sumatriptan, tazobactam, temazepam, tramadol, triamcinolone, unknown agent, valacyclovir, vecuronium, sitagliptin, LSD, glyburide, hydromorphone, insulin, isoflurane,itraconazole, acetaminophen, lisdexamfetamine, pramipexole, lisinopril, glipizide, methotrexate, methylphenidate, metoclopramide, nadolol, nicardipine, nifedipine, nortriptyline, phenazopyridine, and ziconotide

Decontamination interventions administered

Table 47 describes the 246 decontamination interventions administered. Activated charcoal again represented the significant majority (91.5%) in this class.

Enhanced elimination interventions administered

Table 48 presents the enhanced elimination interventions reported. Hemodialysis for toxin removal (28.4%), continuous renal replacement therapy (25.3%), followed by urinary alkalinization (22.1%) and hemodialysis for other reasons (17.9%) topped the reported interventions in this class.

Discussion

This report describes the 11th year of data collected for the Toxicology Investigators' Consortium Registry. Core Registry case numbers decreased slightly this year; however in light of the COVID-19 pandemic, that drop was not unexpected. Despite this, the Core Registry continued to grow, adding six new sites this year and increasing quality control measures.

Table 42 Antidotal therapy

	N (%)[a]
N-acetylcysteine	788 (28.4)
Naloxone/nalmefene	431 (15.5)
Thiamine	147 (14.1)
Folate	371 (13.4)
Sodium bicarbonate	199 (7.2)
Fomepizole	95 (3.4)
Physostigmine	83 (3.0)
Calcium	59 (2.1)
Flumazenil	43 (1.5)
Cyproheptadine	38 (1.4)
Glucagon	36 (1.3)
Atropine	34 (1.2)
Octreotide	30 (1.1)
Insulin-Euglycemic therapy	27 (1.0)
Carnitine	22 (0.8)
Vitamin K	18 (0.6)
Lipid resuscitation therapy	17 (0.6)
Pyridoxine	17 (0.6)
Methylene blue	16 (0.6)
Fab for digoxin	10 (0.4)
Hydroxocobalamin	8 (0.3)
Dantrolene	5 (0.2)
Botulinum antitoxin	4 (0.1)
Anticoagulation reversal	2 (0.1)
Bromocriptine	2 (0.1)
Thiosulfate	2 (0.1)
2-PAM	1 (< 0.1)
Ethanol	1 (< 0.1)
Silimarin	1 (< 0.1)
Class total	**2777 (100)**

[a] Percentages are based on the total number of antidotes administered (*N* = 2777); 2066 (31.0%) cases received at least one antidote. Cases may have involved the use of multiple antidotes

Although the Core Registry is not strictly population based, it represents a wide geographic distribution of cases evaluated by medical toxicologists. These data can be used in conjunction with data from other registries including the National Poison Data System to provide a more detailed picture of poisoning trends, novel exposures, and their public health implications.

This 11th annual report finds overall trends in agent classes, agents, demographics, types of encounters, clinical signs and symptoms, and treatments to be largely unchanged from recent years. Notable findings or trends in the Core Registry are discussed below.

In 2019, the opioid class jumped to the second most common agent class reported to the Core Registry; this trend

Table 43 Antivenom therapy

	N (%)[a]
Crotalidae polyvalent immune fab (ovine)	142 (65.7)
Crotalidae immune fab_2 (equine)	67 (31.0)
Other snake antivenom	4 (1.9)
Scorpion antivenom	2 (0.9)
Spider antivenom	1 (0.5)
Class total	**216 (100)**

[a] Percentages are out of the total number of antivenom treatments administered (*N* = 216)

continued again this year. Despite that increase, relative percentage of reported opioid-related deaths has fallen over the last several years (14.8% vs 19.8% vs 34.0% for 2020, 2019, and 2018, respectively).[2, 3]

Relative contribution of fentanyl to the opioid class exposures continues to increase (25.4% vs 14.6% vs 10.1% for 2020, 2019, and 2018, respectively) [2, 3] and remains the second most common opioid reported in 2020. Oral opioids such as oxycodone, methadone, buprenorphine, tramadol, and hydrocodone remained relatively stable this year.

In 2020 ethanol became the 4th most common agent class reported, overtaking the sedative hypnotic/muscle relaxant class.

Marijuana and THC/CBD-related products continues to represent the majority of the psychoactive class (65.7%) and relative contribution of synthetic cannabinoid cases continued to fall.

Table 44 Supportive care-pharmacologic

	N (%)[a]
Benzodiazepines	1535 (47.1)
Opioids	418 (12.8)
Vasopressors	263 (8.1)
Phenobarbital	249 (7.6)
Antipsychotics	217 (6.7)
Glucose > 5%	113 (3.5)
Neuromuscular blockers	111 (3.4)
Anticonvulsants	110 (3.4)
Antihypertensives	73 (2.2)
Steroids	65 (2.0)
Albuterol and other bronchodilators	39 (1.2)
Beta-blockers	34 (1.0)
Antiarrhythmics	31 (1.0)
Miscellaneous[a]	2 (0.1)
Class total	**3260 (100)**

[a] Percentages based on the total number of pharmacologic interventions (*N* = 3260); 2243 Registry cases (33.6%) received at least one pharmacologic intervention. Cases may have involved the use of multiple interventions

Table 45 Supportive care—non-pharmacologic

	N (%)[a]
IV fluid resuscitation	2446 (76.1)
Intubation/ventilatory management	621 (19.3)
CPR	56 (1.7)
Transfusion	20 (0.6)
Therapeutic hypothermia	20 (0.6)
ECMO	19 (0.6)
Cardioversion	14 (0.4)
Pacemaker	8 (0.2)
Hyperbaric oxygen	6 (0.2)
Transplant	2 (0.1)
Cardiopulmonary bypass	1 (< 0.1)
Class total	**3213 (100)**

[a] Percentages are based on the total number of treatments administered (*N* = 3213); 2619 Registry cases (39.3%) received at least one form of nonpharmacologic treatment. Cases may have involved the use of multiple forms of treatment. *CPR* Cardiopulmonary resuscitation, *ECMO* extracorporeal membrane oxygenation

With regards to envenomations, 2020 saw new trends including an increase in relative Agkistrodon cases (34.4% in 2020 vs 16.9% in 2019). Two of the six new sites added to the Core Registry in 2020 commonly report Agkistrodon cases, possibly driving this year's trend. In addition, the use of Crotalidae immune Fab2 (equine) antivenom continued to increase this year (31.0% in 2020 vs 19.9% 2019) [2].

Telemedicine encounters

Table 49 presents data on the 144 telemedicine encounters reported in 2020. This was the first year such data was collected in the Core Registry, prompted by the COVID-19 pandemic and national rise of telemedicine as a mode of patient care. Most evaluations were for patients physically located in the emergency department at the time of the encounter (*n* = 74;

Table 46 Chelation therapy

	N (%)[a]
Deferoxamine	8 (36.4)
DMSA	7 (31.8)
EDTA	5 (22.7)
Dimercaprol	2 (9.1)
Class Total	**22 (100)**

[a] Percentages are out of the total number of chelation treatments administered (N=22); 20 Registry cases (0.3%) received at least one form of chelation treatment. *DMSA* dimercaptosuccinic acid, *EDTA* ethylenediamine-tetraacetic acid

Table 47 Supportive care—decontamination

	N (%)[a]
Activated charcoal	225 (91.5)
Whole bowel irrigation	14 (5.7)
Irrigation	5 (2.0)
Gastric lavage	2 (0.8)
Class total	**246 (100)**

[a] Percentages based on the total number of decontamination interventions (*N* = 246); 240 Registry cases (3.6%) received at least one decontamination intervention. Cases may have involved the use of multiple interventions

51.4%). Sixty-five (45.1%) occurred via telemedicine instead of in person because of concerns for infection, while 14 (9.7%) were due to a hospital policy. COVID-19 status was only known in 19 (13.2%) patients; 3 were positive and 16 were negative. Half of the telemedicine consults consisted of chart reviews (50.7%).

Only seven evaluations (4.9%) were primarily addiction medicine evaluations, five of which were for initiation of opioid agonist therapy. No telemedicine evaluations were for adverse drug reactions or medication errors. Toxicology therapeutic intervention was administered to 94 (65.3%) patients, but only 75 (52.1%) of telemedicine evaluations were billed.

COVID

A new set of COVID-19 specific questions were incorporated into the ToxIC Core Registry on August 1, 2020. After this implementation, a total of 3119 toxicological exposure cases were reported in 2020. Fifty-one cases (1.6%) were COVID-19 positive, 1397 (44.8%) were COVID-19 negative, and 1671 (53.6%) were unknown. Regarding the COVID-19 cases, males represented 54.9%; there were no transgender COVID-19-positive patients. Age and gender breakdown of COVID-19 cases are described in Table 50. The toxic exposures in COVID-19 patients were largely unrelated to COVID-19; only 5 (9.8%) exposures were related to COVID-19 treatment or prophylaxis. Of the patients presenting with a toxic exposure, the four most common reasons for encounter include intentional pharmaceutical (50.9%), intentional non-pharmaceutical (15.7%) and unintentional pharmaceutical (9.8%) and withdrawal of ethanol or opioids (9.8%).

Table 48 Enhanced elimination

	N (%)[a]
Hemodialysis (toxin removal)	54 (28.4)
Continuous renal replacement therapy	48 (25.3)
Urinary alkalinization	42 (22.1)
Hemodialysis (other indication)	34 (17.9)
Multiple-dose activation charcoal	11 (5.8)
Exchange transfusion	1 (0.5)
Class total	**190 (100)**

[a] Percentages are based on the total number of treatments administered (*N* = 190); 168 Registry cases (2.5%) received at least one form of enhanced elimination

Table 49 Telemedicine encounters

	N (%)
Source of referral	
ED[a]	74 (51.4)
Admitting service	50 (34.7)
Poison center	1 (0.7)
Outside hospital transfer	3 (2.1)
Nature of consultation	
Consult from ED or inpatient service	126 (87.5)
Admitting toxicology service	5 (3.5)
Outpatient clinic	13 (9.0)
Nature of telemedicine consult	
Chart review	73 (50.7)
Over the phone	16 (11.1)
Over video/Internet	54 (37.5)
Unknown	1 (0.7)
Reason for encounter	
Attempt at self-harm	38 (26.4)
ETOH[b] withdrawal	3 (2.1)
Opioid withdrawal	1 (0.7)
Occupational evaluation	5 (3.5)
Interpretation of laboratory data	3 (2.1)
Organ system dysfunction	5 (3.5)
Envenomation	9 (6.3)
Total telemedicine encounters	**144 (100)**

[a] *ED* emergency department

[b] *ETOH* ethanol

Table 50 Encounters for toxic exposures in COVID-19 positive patients by age and gender

	Female *N* (%)[a]	Male *N* (%)[a]	Total N (%)[a]
Age 2–6	2 (3.9)	1 (2.0)	3 (5.9)
Age 7–12	1 (2.0)	1 (2.0)	2 (3.9)
Age 13–18	7 (13.7)	7 (13.7)	14 (27.4)
Age 19–65	10 (19.6)	18 (35.3)	28 (54.9)
Age 66–89	3 (5.9)	1 (2.0)	4 (7.8)
Class total	23 (45.1)	28 (54.9)	51 (100)

[a] Percent based on total number of cases (*N* = 51)

Table 51 Reasons for encounter and primary agent in toxic exposures related to COVID-19 treatment and prophylaxis

Age	Gender	Reason for encounter	Self-harm	Agent(s)	Treatment
27	M	Intentionally taking higher dose than indicated	Yes	Benzonatate, ibuprofen, EtOH	None
49	M	Intentionally taking higher dose than indicated	No	Acetaminophen	NAC
50	M	Intentionally taking higher dose than indicated	No	Acetaminophen	NAC
29	M	Accidental supratherapeutic dosing by parent	No	Acetaminophen	NAC
60	M	Intentionally taking higher dose than indicated	No	Acetaminophen	NAC

NAC = N-acetylcystine

Agent exposures related to COVID-19 treatment or prophylaxis are described in Table 51. There were no children in this group. Only one case was related to a self-harm attempt. The remaining cases were intentional (3/4) or unintentional (1/4) supratherapeutic dosing. Acetaminophen was the most common agent (4 of 5 cases; 80.0%); all acetaminophen cases required NAC treatment and 3/4 developed a transaminitis.

Limitations

The ToxIC Core Registry is a unique prospective database of cases in which bedside or telemedicine consultation is performed by medical toxicologists, enabling an informed relationship between exposures and clinical outcomes. Limitations, however, do exist for the Core Registry. One of these is a bias towards inclusion of more severe case presentations, as cases are only included if they undergo subspecialty consultation. Cases for which a medical toxicology consultation was not requested are not reported and may represent a group with less severe illness. Therefore, the Core Registry likely represents a different population from other data sources such as Poison Control Centers. Regional differences may lead to a disproportionate number of specific cases reported based on variations in drug use, abuse, and other toxic exposures. The ToxIC Core Registry includes sites from multiple, diverse locations, but the entire country is not uniformly represented. Larger academic medical centers with greater amounts of medical toxicology faculty may be over-represented in the database.

At the level of the individual sites, there may be a reporting bias towards more complicated or interesting cases. Although the express intent of the Core Registry, as defined in written agreements with all sites, is to obtain a consecutive sample of all cases at a given site, individual cases may be missed. Data regarding substances of exposure or species of envenomation relies heavily on patient self-report and may be misclassified; this limitation is likely of most significance with regard to illicit drug exposure and patient hesitancy to disclose detailed information. Lastly, efforts are made to continually improve the quality of data collected. While member sites are instructed to complete all applicable data fields, there are still a number of cases and data fields with incomplete information. This remains an issue for collection of race and ethnicity, for example. Efforts continue to support quality data collection and follow up on missing data where applicable.

Conclusions

The ToxIC project continues to grow and evolve, including the Core Registry and additional surveillance projects. The Core Registry remains unique amongst databases in that it represents prospective data collected from cases evaluated by medical toxicologist specialists. Although this feature limits extrapolation to the population as a whole, it increases the potential for high-quality data and for increased correlation between exposure cases and clinical findings. Continued quality improvement and surveillance efforts remain areas of focus for the Core Registry and of ToxIC as a whole.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13181-021-00854-3.

Funding sources The Toxicology Investigators Consortium received funding from the US National Institute of Drug Abuse (1RO1DA037317- 02) and the American Academy of Addiction Psychiatry (1H79TI083343) and has data-sharing contracts with the U. S. Food and Drug Administration, Centers for Disease Control and Prevention (CDC), and BTG International, Inc. (North America).

Toxicology Investigators Consortium (ToxIC) 2020 Study Group Collaborators: Acciani J, Akpunonu PD, Aks S, Algren DA, Atti S, Avera R, Baum RA, Beauchamp GA, Bentur D, Beuhler M, Boyle KL, Brenner M, Bruccoleri R, Burns M, Button B, Calello DP, Canning J, Cannon RD, Cao D, Carey JL, Carpenter J, Castaneda J, Castelli R, Cates A, Ceretto V, Chen R, Christian MR, Conner K, Cook MD, Correia M, Dargan P, De Olano J, DeGelorm T, Devgun J, Dribben W, Eisenga BE, Epperson C, Falkowitz D, Farrar HC, Feng S, Fernandez D, Fikse DJ, Filip AB, Finkelstein Y, Fisher E, Ford J, Furmaga J, Gittinger M, Goldberger DJ, Gorodetsky RM, Greene SC, Griswold M, Hail S, Hartmann RJ, Hendrickson RG, Hieger MA, Hodgman MJ, Holstege C, Hoyte C, Hughes AR, James LP, Jefri MY, Judge BS, Kao L, Katz KD, Kazzi ZN, Kiernan E, Kim H, Kirschner R, Koons AL, Kowalski JM, Kusin SG, Latch RL, Levine M, Liebelt EL, Liss DB, Liu YS, Lo

CY, Loughran DE, Lucyk SN, Lydecker A, Makar G, Manini A, Marlin M, McFalls J, McGillis ES, McKeown N, Meaden CW, Meadors K, Mink M, Minns A, Morgan BW, Mullins ME, Nacca NE, Nanagas K, Niruntarai S, Ng P, Noble MJ, Nogar J, Obilom C, Onisko N, Ontiveros S, Othong R, Pizon AF, Podmoroff H, Priya S, Quang LS, Rianprakaisang TN, Rickner-Schmidt S, Riley BD, Ross B, Roth B, Rowden A, Schaack-Rothstein L, Schauben J, Schult R, Seifert SA, Shaker K, Sharma K, Sheikh S, Simpson SE, Sollee D, Steck A, Stephani JA, Surmaitis RM, Temple C, Thompson JA, Thompson M, Thornton SL, Tormoehlen L, Ubani C, Walsh SJ, Warpinski G, Warrick BJ, Wermuth M, Wiegand TJ, Winkler G, Wolk BJ, Yarema MC, Young A, Zosel AE

We also wish to thank study coordinators: Aubin C, Beauchamp GA, Crawley LJ, Delatte S, Falter T, Fankhauser K, Garcia DA, Hieger MA, Irvin E, Krueger JA, Kurt A, Lymon KJ, Othong R, Padilla-Jones A, Phan T

Sources of funding US National Institutes of Health
US Food and Drug Administration
BTG International
Center for Disease Control and Prevention (CDC)

Declarations

Conflict of interest The authors have no conflicts of interest to declare.

Previous presentation of data This data has not been previously presented.

References

1. Brent J, Wax PM, Schwartz T, et al. The toxicology investigators consortium case registry-the 2010 experience. *J Med Toxicol*. 2011;7(4):266–76.
2. Spyres MB, Farrugia LA, Kang AM, Aldy K, Calello DP, Campleman SL, On behalf of the toxicology investigators consortium study group, et al. The Toxicology Investigators Consortium Case Registry—the 2019 Annual Report. *Journal of Medical Toxicology*. 2020;*16*(4):361–87. https://doi.org/10.1007/s13181-020-00810-7.
3. Spyres MB, Farrugia LA, Kang AM, Calello DP, Campleman SL, On behalf of the Toxicology Investigators Consortium (ToxIC) Study Group, et al. The Toxicology Investigators Consortium Case Registry-the 2018 Annual Report. *Journal of Medical Toxicology*. 2019;*15*(4):228–54. https://doi.org/10.1007/s13181-019-00736-9.
4. Farrugia LA, Rhyee SH, Campleman SL, Judge B, Kao L, Pizon A, Porter L, Riederer AM, Wiegand T, Calello D, Wax PM, Brent J, On behalf of the Toxicology Investigators Consortium (ToxIC) Study Group. The Toxicology Investigators Consortium Case Registry—the 2017 Annual Report. *Journal of Medical Toxicology*. 2018;*14*(3):182–211. https://doi.org/10.1007/s13181-018-0679-z.
5. Farrugia LA, Rhyee SH, Calello DP, Campleman SL, Riederer AM, On behalf of the Toxicology Investigators Consortium Study Group, et al. The Toxicology Investigators Consortium Case Registry—the 2016 Experience. *Journal of Medical Toxicology*. 2017;*13*(3):203–26. https://doi.org/10.1007/s13181-017-0627-3.