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SPECIAL ARTICLE

The Toxicology Investigators Consortium Case Registry—the 2014 Experience

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Abstract The Toxicology Investigators Consortium (ToxIC) Case Registry was established in 2010 by the American College of Medical Toxicology. The Registry includes all medical toxicology consultations performed at participating sites. The Registry was queried for all cases entered between January 1 and December 31, 2014. Specific data reviewed for analysis included demographics (age, gender, ethnicity), source of consultation, reasons for consultation, agents involved in toxicological exposures, signs, symptoms, clinical findings, fatalities, and treatment. In 2014, 9172 cases were entered in the Registry across 47 active member sites. Females accounted for 51.1 % of cases. The majority (65.1 %) of cases were adults between the ages of 19 and 65. Caucasians made up the largest identified ethnic group (48.9 %). Most Registry cases originated from the inpatient setting (93.5 %), with a large majority of these consultations coming from the emergency department or inpatient admission services. Intentional and unintentional pharmaceutical exposures continued to be the most frequent reasons for consultation, accounting for 61.7 % of cases. Among cases of intentional pharmaceutical exposure, 62.4 % were associated with a self-harm attempt. Non-pharmaceutical exposures accounted for 14.1 % of Registry cases. Similar to the past years, non-opioid analgesics, sedative-hypnotics, and opioids were the most commonly encountered agents. Clinical signs or symptoms were noted in 81.9 % of cases. There were 89 recorded fatalities (0.97 %). Medical treatment (e.g., antidotes, antivenom, chelators, supportive care) was rendered in 62.3 % of cases. Patient demographics and exposure characteristics in 2014 Registry cases remain similar to prior years. The majority of consultations arose in the acute care setting (emergency department or inpatient) and involved exposures to pharmaceutical products. Among exposures, non-opioid analgesics, sedative/hypnotics, and opioids were the most frequently encountered. A majority of cases required some form of treatment, but fatalities were rare.

Keywords Poisonings · Overdose · Surveillance · Epidemiology

Data contained in this manuscript has not been previously presented in any form.

Electronic supplementary material The online version of this article (doi:10.1007/s13181-015-0507-7) contains supplementary material, which is available to authorized users.

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Introduction

The American College of Medical Toxicology (ACMT) created the Toxicology Investigators Consortium (ToxIC) in 2010 as a means to provide a tool for clinical toxicology research and toxico-surveillance [1]. Unlike other poisoning databases, ToxIC cases are prospective and based on patients seen in clinical consultation by medical toxicologists in both inpatient and ambulatory settings. Beginning with four sites in 2010, the ToxIC registry has since expanded, including eight

sites added in 2014. Investigators from 47 active sites, involving 77 separate facilities, submitted cases in 2014. Currently, 80.7 % of the active accredited medical toxicology fellowship programs in the USA participate in the ACMT ToxIC Registry. The objective of this report is to summarize the Registry's 2014 data. Cases entered from January 1, 2014 through December 31, 2014 are described in this fifth annual report for the Registry [2–5].

Since its inception, several supplemental or subregistries have been created within ToxIC. In 2014, subregistries focusing on novel drugs of abuse and metal-on-metal hip implants were added. These, in addition to existing supplemental registries studying caustic ingestion, lipid resuscitation therapy, prescription drug misuse, snake bites, and a clinical poisoning severity score, bring the total number of current subregistries active in 2014 to seven. Additional changes to the Registry data include more detailed patient demographic information and further specification of reasons for exposures to medications or other chemical substances. In 2014, 18 abstracts based on Registry data were presented at three national meetings and three manuscripts utilizing Registry data were published [5–7].

In addition to the support from ACMT, extramural funding for the Registry came from both governmental and industry sources in 2014. Government funding was provided via three National Institute of Health (NIH) grant subawards, while industry funding was in the form of an unrestricted grant from BTG International Inc. (North America) utilized for the support of the North American Snakebite Registry.

Methods

Participating investigators agree to enter data on all medical toxicology consultations into the Registry. Cases are entered on a password-protected, online data collection form. The site is maintained by ACMT with oversight by the ToxIC Registry Steering Committee. The Registry is compliant with the Health Insurance Portability and Accountability Act and does not collect any protected health information or otherwise identifying patient data fields. Registry participation is compliant with local Institutional Review Board policies and procedures, as well as the Western Institutional Review Board (WIRB). WIRB has determined that the collection protocol based on submission of de-identified data from a clinical visit under the maintenance and control of the medical toxicologist does not meet the threshold of human subjects research under federal regulation 45 CFR 46 and associated guidance.

Collected data include presenting signs, symptoms, clinical course, treatments, limited patient demographics, outcome, and the type of and reason for toxicological exposure. The term "consultation" is used in this report to describe any encounter with a medical toxicologist. Such encounters may include admission to a toxicology inpatient service or evaluation by a medical toxicologist in the emergency department, inpatient unit, or outpatient clinic. The online collection form is formatted to ensure data remains organized and easily searchable. Free-text entry fields allow caregivers to provide further detail or supplementary information. As part of the Registry's mission of providing a real-time toxico-surveillance tool, a component of the standard data form is a sentinel detection field that signals novel or unusual cases.

For this report, a search of the database was performed to identify cases recorded from January 1, 2014 through December 31, 2014. Additional data from the subregistries will be published separately.

This descriptive report summarizes case demographics, source and location of consultation, and reason for encounter and provides proportion of cases by individual agent, agent class, and treatment provided. Summary statistics for cases involving fatalities and adverse drug reactions are also described. In the following tables describing individual agent or agent classes, unless otherwise indicated, values with fewer than five occurrences were not listed as separate items, but are further grouped in "Miscellaneous." Percentages noted in tables for individual agents represent their relative proportion within their respective agent class. For clinical signs or symptoms, the tables provide the percentage of any individual signs or symptom relative to the total number of registry cases. In the detailed treatment tables, percentages for each treatment modality represent the relative frequency among the subset of cases receiving at least one type of treatment. In instances of limited data for an entire class or clinical effects (e.g., such as ten or fewer cases overall or one agent contributing the majority (>80 %) of a class), no detailed table is presented, but information may be described in the text section or available in the Supplementary Material.

Results

Tables 1 and 2, respectively, show the state and city (country and city for non-US sites) listings of the individual institutions participating in the ACMT ToxIC Registry. Institutions varied substantially in the number of cases entered in 2014, ranging from 1 to 833 cases submitted for this reporting year. The growth in annual case counts continued in 2014 (Fig. 1). The 47 ToxIC member sites active in 2014 entered a total of 9172 cases across 77 individual clinical facilities, representing a 6.7 % increase over 2013.

Table 1 Participating institutions providing cases in 2014—USA

Arizona	*Massachusetts*	*Oregon*
Phoenix	Worcester	Portland
Banner Good Samaritan	UMass Memorial Medical Center	Doernbecher Children's Hospital
Phoenix Children's Hospital	*Michigan*	Oregon Health and Science University Hospital
California	Grand Rapids	Oregon Occupational Toxicology
Fresno	Spectrum Health Hospitals	*Pennsylvania*
UCSF Fresno Medical Center	*Minnesota*	Harrisburg
Loma Linda	St. Paul	Harrisburg Hospital
Children's Hospital Boston	Regions Hospital	JC Blair Memorial Hospital
Los Angeles	*Missouri*	Philadelphia
University of Southern California Verdugo Hills	Kansas City	Einstein Medical Center
San Diego	Children's Mercy Hospitals & Clinics	Hahnemann University Hospital
Kaiser San Diego	St. Louis	Mercy Fitzgerald Hospital
San Francisco	Washington University School of Medicine	Mercy Hospital of Philadelphia
San Francisco General Hospital	*Nebraska*	St. Christopher's Hospital for Children
Colorado	Omaha	Pittsburgh
Denver	University of Nebraska Medical Center	UPMC Children's Hospital of Pittsburgh
Children's Hospital Colorado	*New Jersey*	UPMC Magee Women's Hospital
Denver Health Medical Center	Morristown	UPMC Presbyterian/Shadyside
Porter and Littleton Adventist Hospital	Morristown Medical Center	*Texas*
Swedish Medical Center	New Brunswick	Dallas
University of Colorado Medical Center	Robert Wood Johnson University Hospital	Children's Medical Center Dallas
Connecticut	Newark	Parkland Memorial Hospital
Hartford	New Jersey Medical School (Rutgers)	St Paul University Hospital (UT)
Connecticut Children's Medical Center	*New Mexico*	University of Texas (UT) Southwestern Medical
Hartford Hospital	Albuquerque	Houston
John Dempsey Hospital	University of New Mexico Hospital	Ben Taub General Hospital
Georgia	*New York*	Texas Children's Hospital
Atlanta	Manhasset	San Antonio
Grady Memorial Hospital	Long Island Jewish Medical Center	San Antonio Military Medical Center
Illinois	North Shore University Hospital	*Utah*
Chicago	Staten Island University Hospital	Salt Lake City
UIC Medical Center	New York	Primary Children's Hospital
Evanston	Bellevue Medical Center	University of Utah Hospital
Evanston North Shore University Health System	Mount Sinai Hospital	*Virginia*
Indiana	NYU Langone Medical Center	Charlottesville
Indianapolis	Rochester	University of Virginia Health Systems
IU-Indiana University Hospital	Highland Hospital	Richmond
IU-Methodist Hospital-Indianapolis	Huther-Doyle	Virginia Commonwealth University (VCU) Medical
IU-Riley Hospital for Children	Strong Memorial Hospital	*Wisconsin*
IU-Wishard Memorial Hospital	Syracuse	Milwaukee
Massachusetts	SUNY Upstate Medical University	Children's Hospital of Wisconsin
Boston	*North Carolina*	Froedtert Memorial Lutheran Hospital
Beth Israel Boston	Charlotte	
	Carolinas Medical Center	

Demographics

Tables 3 and 4 summarize case demographic data for gender, age, race, and Hispanic ethnicity. In 2014, females comprised a slight majority of the Registry cases: 4691 (51.1 %) to 4481 (48.9 %), females to males, respectively. Sixty female cases were identified as being pregnant (1.3 %), accounting for 0.7 % of all cases. Adults between the ages of 19 and 65 comprised the majority (65.1 %) of reported cases. Adolescents (13 to 18 years) were the next

Table 2 Participating institutions providing cases—international

Australia
Melbourne
Austin Hospital
Sydney
Sydney-Blacktown-Mt. Druitt Health
Canada
Toronto
Hospital for Sick Children
Israel
Haifa
Rambam Health Care Campus
Saudi Arabia
Riyadh
King Abdulaziz Medical City

ToxIC maintains a related Registry of other international sites not reflected in this report

most frequent age category at 17.1 % of the cases. Data fields to establish race and Hispanic ethnicity information were newly introduced to the Registry in August 2014. Table 3 summarizes the available race/ethnicity data for this subset of cases (N=4759 field eligible). Caucasians made up the largest identified race group at 48.9 %.

Source of Referral and Primary Reason for Encounter

Hospital emergency departments were the most frequent source of referral, accounting for 5607 (61.1 %) of all Registry cases combined. The vast majority of all ToxIC cases (93.5 %) were seen in the emergency department (ED) or as an inpatient (IP) (N=8570), with an order of magnitude fewer seen as outpatients (N=602 or 6.6 %). As shown on Table 5, ED/IP consultation referrals came via the ED (N=5590 or 65.2 % of ED/IP cases), admitting services (N=2036 or 23.8 %), with a limited number from outside hospital transfer or other hospital non-ED service request (N=901 or 10.5 %). In comparison, outpatient (OP) referrals were primarily via patient self-referral (N=264 or 43.9 % of OP cases) or primary care/

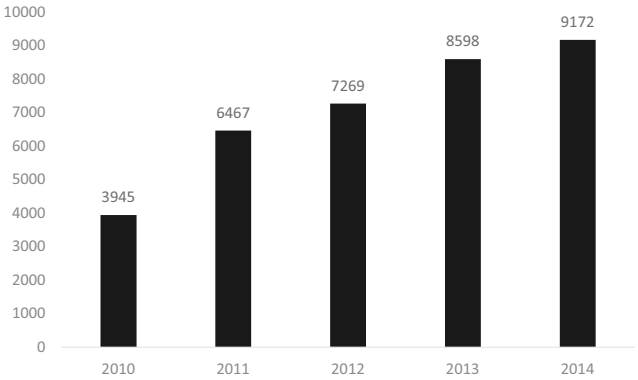

Fig. 1 ACMT ToxIC Registry total case count by year, 2010–2014

Table 3 ToxIC case demographics—age and gender

	N (%)
Gender	
Male	4481 (48.9)
Female	4691 (51.1)
Pregnant	60 (0.7)
Age (years)	
2–6	442 (4.8)
7–12	243 (2.6)
13–18	1567 (17.1)
19–65	5968 (65.1)
66–89	548 (6.0)
>89	29 (0.3)
Unknown	29 (0.3)
Total	9172 (100)

other provider referrals (N=221 or 36.7 %). Poison center referrals accounted for 4.8 % of the OP and 0.1 % of the ED/IP referrals in 2014.

Exposure to pharmaceutical products, both intentional and unintentional, was the most common reason for consultation, accounting for 61.7 % of all consultations (Table 6). By comparison, exposure to non-pharmaceuticals accounted for 14.1 %. All types of withdrawal combined were reported as the primary reason for encounter in 6.3 % or 575 cases, while all types of envenomation resulted 3.3 % or 304 cases. In 2014, additional data fields were added to the Registry for cases of intentional pharmaceutical exposure in order to further specify the presence of self-harm or suicidal intent. Within this subset of 4802 cases, self-harm attempt was reported in

Table 4 ToxIC case demographics—race and Hispanic ethnicity

	N (%)
Race	
Caucasian	2369 (48.9)
Unknown/uncertain	1563 (32.8)
Black/African	449 (9.4)
Other	230 (4.8)
Asian	86 (1.8)
Multiple	51 (1.1)
American Indian/Alaska Native	48 (1.0)
Australian Aboriginal	<5 (<0.1)
Native Hawaiian or Pacific Islander	<5 (<0.1)
Hispanic ethnicity[a]	
Hispanic	450 (9.5)
Non-Hispanic	2654 (55.8)
Unknown	1402 (29.5)
Total	9172 (100)

Race/ethnicity counts and frequency derived from 4759 cases with available data after July 2014 (51.9 % of the total number of cases in 2014)

[a] Hispanic ethnicity as indicated exclusive of race

Table 5 ToxIC registry case referral sources by inpatient/outpatient status

	N (%)
Emergency department (ED) or inpatient (IP)[a]	
ED	5590 (65.2)
Admitting service	2036 (23.8)
Outside hospital transfer	632 (7.4)
Request from another hospital service (not ED)	269 (3.1)
Primary care provider/other OP treating physician	26 (0.3)
Poison center	12 (0.1)
Employer/independent med evaluation/workman's comp	<5 (<0.1)
Self-referral	<5 (<0.1)
ED/IP total	8570 (100)
Outpatient (OP)/clinic/office consultation[b]	
Self-referral	264 (43.9)
Primary care provider or other OP treating physician	221 (36.7)
Employer/independent med eval/workman's comp	65 (10.8)
Poison center	29 (4.8)
ED	17 (2.8)
Request from another hospital service (not ED)	<5 (<0.9)
Admitting service	<5 (<0.9)
OP total	602 (100)

[a] Percentage based on the total number of cases (*N*=8570) seen by a medical toxicologist as consulting (ED or IP) or as attending (IP)

[b] Percentage based on the total number of cases (*N*=602) seen by a medical toxicologist as outpatient, clinic visit, or office consultation

Table 6 Reasons for medical toxicology encounter/consultation

	N (%)
Intentional exposure—pharmaceutical	4803 (52.4)
Intentional exposure—non-pharmaceutical	913 (10.0)
Unintentional exposure—pharmaceutical	853 (9.3)
Unintentional exposure—non-pharmaceutical	379 (4.1)
Organ system dysfunction	347 (3.8)
Not documented	297 (3.2)
Withdrawal—opioids	270 (2.9)
Envenomation—snake	234 (2.6)
Withdrawal—ethanol	227 (2.5)
Ethanol abuse	194 (2.1)
Interpretation of toxicology data	180 (2.0)
Environmental evaluation	162 (1.8)
Occupational evaluation	130 (1.4)
Withdrawal—sedative/hypnotic	51 (0.6)
Envenomation—spider	46 (0.5)
Malicious/criminal	27 (0.3)
Withdrawal—other	19 (0.2)
Envenomation—scorpion	15 (0.2)
Envenomation—other	9 (0.1)
Withdrawal—cocaine/amphetamine	8 (0.1)
Marine	7 (0.1)
Adverse drug reaction	<5 (<0.01)
Total	9172 (100)

2996 (62.4 %), with suicidal intent reported in 2327 (48.4 %) (Table 7).

Agent Classes

A total of 12,496 individual agents were listed among the 8040 Registry cases reporting a toxicological exposure. Reporting medical toxicologists indicated no suspected toxicological exposure in the remainder of cases (12.4 %). The distribution of these agents among the Registry's 40 predefined substance classes is shown in Table 8. Exposure to more than one agent was reported in 2755 (30.0 %) of cases. Similar to 2013 Registry data, non-opioid analgesics, sedative/hypnotic agents, opioids, and antidepressants constituted the most commonly encountered substance classes, collectively accounting for nearly one half (46.1 %) of all agents reported in 2014. Eight agent classes contributed to 37.7 % of the total cases: ethanol (6.8 %), anticholinergic/antihistamine (6.1 %), cardiovascular (5.7 %), antipsychotic (5.5 %), sympathomimetic (5.5 %), anticonvulsant (3.4 %), psychoactive (2.5 %), and envenomation (2.3 %). Table 8 provides comparative data from prior years of the Registry (2010–2013), again as the case number and relative frequency by agent class. Several classes have been added since 2010 as noted by "NR" in earlier years, including both pharmaceuticals (e.g., cough and cold, anticoagulant, other pharmaceutical, Parkinson's medication) and non-pharmaceuticals (e.g., household products, rodenticides).

Table 7 Detailed reasons for encounter—intentional pharmaceutical exposure

	N (%)
Reason for intentional pharmaceutical exposure subgroup[a]	
Attempt at self-harm	2996 (62.4)
Abuse/misuse	796 (16.6)
Therapeutic use	465 (9.7)
Unknown	384 (8.0)
None listed	161 (3.4)
	4802 (100)
Attempt at self-harm—suicidal intent subclassification[b]	
Suicidal intent	2327 (77.7)
Suicidal intent unknown	277 (9.2)
No data entered for suicidal intent	259 (8.6)
No data entered for suicidal intent	133 (4.4)
	2996 (100)

[a] Percentage of total number of cases (*N*=4802) indicating primary reason for encounter due to intentional pharmaceutical exposure

[b] Percentage of number of cases indicating attempt at self-harm (*N*=2996)

Table 8 Agent classes involved in medical toxicology consultation

	2014 *N* (%)	2013 *N* (%)	2012 *N* (%)	2011 *N* (%)	2010 *N* (%)
Analgesic (nonopioid)	1599 (12.8)	1490 (13.2)	1295 (12.3)	1368 (12.3)	854 (14.8)
Sedative-hypnotic/muscle relaxant	1546 (12.4)	1383 (12.3)	1422 (13.5)	1492 (13.4)	783 (13.6)
Opioid	1311 (10.5)	1250 (11.1)	1086 (10.3)	1100 (9.9)	619 (10.7)
Antidepressant	1301 (10.4)	1056 (9.4)	1039 (9.8)	1029 (9.3)	659 (11.4)
Ethanol	849 (6.8)	737 (6.5)	850 (8.1)	580 (5.2)	371 (6.4)
Anticholinergic/antihistamine	761 (6.1)	617 (5.5)	457 (4.3)	549 (4.9)	378 (6.5)
Cardiovascular	713 (5.7)	687 (6.1)	616 (5.8)	631 (5.7)	334 (5.8)
Antipsychotic	689 (5.5)	626 (5.6)	551 (5.2)	587 (5.3)	366 (6.3)
Sympathomimetic	684 (5.5)	702 (6.2)	692 (6.6)	774 (7.0)	247 (4.3)
Anticonvulsant	421 (3.4)	408 (3.6)	339 (3.2)	451 (4.1)	218 (3.8)
Psychoactive	312 (2.5)	302 (2.7)	460 (4.4)	360 (3.2)	135 (2.3)
Envenomation	282 (2.3)	188 (1.7)	196 (1.9)	183 (1.6)	105 (1.8)
Diabetic medications	210 (1.7)	181 (1.6)	138 (1.3)	113 (1.0)	65 (1.1)
Lithium	179 (1.4)	166 (1.5)	133 (1.3)	100 (0.9)	78 (1.4)
Cough and cold products	161 (1.3)	134 (1.2)	NR	NR	NR
Herbal products/dietary supplements	159 (1.3)	119 (1.1)	50 (0.5)	76 (0.7)	48 (0.8)
Metals	145 (1.2)	154 (1.4)	227 (2.2)	322 (2.9)	154 (2.7)
Gases/irritants/vapors/dusts	138 (1.1)	126 (1.1)	129 (1.2)	169 (1.5)	63 (1.1)
Household product	125 (1.0)	113 (1.0)	NR	NR	NR
Unknown agent	109 (0.9)	88 (0.8)	NR	NR	NR
Antimicrobial	104 (0.8)	113 (1.0)	62 (0.6)	107 (1.0)	38 (0.7)
Toxic alcohol	104 (0.8)	95 (0.8)	121 (1.1)	145 (1.3)	93 (1.6)
Hydrocarbon	84 (0.7)	84 (0.8)	45 (0.4)	67 (0.6)	50 (0.9)
Caustic	80 (0.6)	88 (0.8)	47 (0.4)	93 (0.8)	45 (0.8)
Plants and fungi	75 (0.6)	71 (0.6)	52 (0.5)	78 (0.7)	18 (0.3)
Anticoagulant	64 (0.5)	58 (0.5)	NR	NR	NR
Endocrine	43 (0.3)	34 (0.3)	49 (0.5)	37 (0.3)	9 (0.2)
Other non-pharmaceutical product	39 (0.3)	14 (0.1)	NR	NR	NR
Chemotherapeutic/immunological	37 (0.3)	23 (0.2)	12 (0.1)	20 (0.2)	5 (0.1)
Rodenticide	35 (0.3)	15 (0.1)	NR	NR	NR
Gastrointestinal agents	33 (0.3)	34 (0.3)	30 (0.3)	50 (0.4)	14 (0.2)
Insecticide	30 (0.2)	27 (0.2)	NR	NR	NR
Other pharmaceutical product	25 (0.2)	30 (0.3)	NR	NR	NR
Anesthetic	19 (0.2)	11 (0.1)	30 (0.3)	21 (0.2)	16 (0.3)
Anti-parkinsonism drugs	9 (0.1)	19 (0.2)	NR	NR	NR
Pulmonary	9 (0.1)	7 (0.1)	16 (0.2)	17 (1.5)	9 (0.2)
Ingested foreign object	6 (0.05)	<5 (<0.03)	NR	NR	NR
Herbicide	5 (0.04)	11 (0.1)	NR	NR	NR
Fungicide	<5 (<0.03)	<5 (<0.03)	NR	NR	NR
WMD/riot agent/radiological	<5 (<0.03)	<5 (<0.03)	<5 (<0.03)	7 (0.1)	0 (0.0)
Total annual agent entries	12,496	11,279	10,553	11,119	5774

Percentages are out of the total number of reported agent entries per year; 30 % of 2014 Registry cases reported exposure to multiple agents

NR no cases reported, class category not available

Individual Agents by Class

Tables 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, and 25 summarize specific pharmaceuticals and other substances reported as a toxic exposure by class, in order, based on relative contribution to the total number of agents reported to the Registry, with two exceptions. Single agent classes for ethanol and lithium are instead presented and discussed with toxic alcohols and anticonvulsants, respectively. Additional detailed information for agent classes with relatively smaller

Table 9 Analgesics

	N (%)
Acetaminophen	1051 (64.6)
Aspirin	270 (16.9)
Ibuprofen	194 (12.1)
Naproxen	52 (3.3)
Salicylamide	8 (0.5)
Meloxicam	7 (0.4)
Methylsalicylate	5 (0.3)
Miscellaneous[a]	12 (0.8)
Class total	1599 (100)

[a] Includes ketorolac, NSAID unspecified, phenazopyridine, analgesic unspecified, diclofenac, indomethacin, metamizole, piroxicam, and salsalate

case numbers and/or individual agents may be found in the online Supplementary Material.

Non-opioid analgesic entries for 2014 are shown in Table 9. Acetaminophen exposures accounted for 11.5 % of all Registry cases in 2014 and were the most common analgesic exposure (64.6 % within class frequency). Non-salicylate NSAIDS made up 24.6 % of this category, with ibuprofen the most common (12.1 %). Salicylates made up 27.0 % of the cases, primarily involving aspirin (16.9 %).

Sedative-hypnotic agents and muscle relaxants accounted for 12.4 % of all the agents reported (Table 8). As summarized in Table 10, benzodiazepines at 54.5 % accounted for the majority of the class as a whole, followed by muscle relaxants (20.7 %), other sedatives (17.4 %), nonbenzodiazepine agonists (8.9 %), and barbiturates (3.4 %). The two most common benzodiazepines, clonazepam (20.7 %) and alprazolam (15.1 %), accounted for over one third of the class. At least one benzodiazepine was reported in 9.1 % of all Registry cases. Zolpidem was the most common nonbenzodiazepine agent reported in this overall class (8.2 %), followed closely by the muscle relaxant cyclobenzaprine (7.5 %) and sedative gabapentin (7.4 %).

Table 11 summarizes the class of opioids, a category including natural opiates, semisynthetic and synthetic opioid agents. In 2014, 1311 individual opioid agents were reported, just over 10 % of all agents (Table 8). As in previous years, semisynthetic agents (heroin, oxycodone, hydrocodone, buprenorphine, hydromorphine, and oxymorphone) were the most common class subset at 63.3 % of all opioid entries. Heroin was the most common semisynthetic agent, at 26.7 %. Oxycodone was also relatively common, at 18.6 % of the class. The synthetic opioids (methadone, tramadol, fentanyl, naltrexone, loperamide, and naloxone) accounted for 25.7 % of the overall class, primarily due to methadone, tramadol, and fentanyl. The most common synthetic was methadone (12.1 %). The opiates morphine and codeine accounted for 5.7 % of the class.

Table 10 Sedative-hypnotics/muscle relaxants by subtype

	N (%)
Benzodiazepines	843 (54.5)
Clonazepam	320 (20.7)
Alprazolam	234 (15.1)
Lorazepam	127 (8.2)
Diazepam	80 (5.2)
Benzodiazepine unspecified	36 (2.3)
Temazepam	20 (1.3)
Chlordiazepoxide	13 (0.8)
Miscellaneous[a]	13 (0.8)
Muscle relaxants	320 (20.7)
Cyclobenzaprine	116 (7.5)
Carisoprodol	78 (5.0)
Baclofen	76 (4.9)
Tizanidine	24 (1.6)
Methocarbamol	10 (0.6)
Metaxalone	6 (0.4)
Miscellaneous[b]	10 (0.6)
Other sedatives	193 (12.5)
Gabapentin	115 (7.4)
Pregabalin	35 (2.3)
Buspirone	23 (1.5)
Sedative-hypnotic/muscle relaxant unspecified	9 (0.6)
Propofol	7 (0.5)
Miscellaneous[c]	<5 (<0.4)
Non-benzodiazepine agonists (“Z” drugs)	138 (8.9)
Zolpidem	126 (8.2)
Eszopiclone	7 (0.5)
Miscellaneous[d]	5 (0.3)
Barbiturates	52 (3.4)
Butalbital	37 (2.4)
Phenobarbital	12 (0.8)
Miscellaneous[e]	<5 (<0.3)
Class total	1546 (100)

[a] Includes midazolam, nitrazepam, bromazepam, oxazepam, etizolam, and flunitrazepam

[b] Includes meprobamate, chlorzoxazone, and orphenadrine

[c] Includes phenibut, chlorbutol, and ramelteon

[d] Includes zopiclone and zaleplon

[e] Includes pentobarbital and butabarbital

Antidepressants accounted for 10.4 % of the total agents reported in the Registry (Table 8). As shown in Table 12, the two most common individual antidepressants reported were bupropion (17.7 %) and trazodone (13.8 % class). By comparison, the tricyclic antidepressants combined (13.5 %) appeared at a considerable lower frequency. Over one third of the antidepressants reported were selective serotonin reuptake inhibitors (SSRIs). The most common SSRI, citalopram, accounted for 10.4 % of the antidepressant agents reported.

Table 11 Opioids

	N (%)
Heroin	350 (26.7)
Oxycodone	244 (18.6)
Methadone	158 (12.1)
Hydrocodone	128 (9.8)
Tramadol	124 (9.5)
Buprenorphine	80 (6.1)
Opioid unspecified	54 (4.1)
Morphine	52 (4.0)
Fentanyl	38 (2.9)
Codeine	30 (2.3)
Hydromorphone	15 (1.1)
Oxymorphone	12 (0.9)
Naltrexone	7 (0.5)
Loperamide	5 (0.4)
Naloxone	5 (0.4)
Miscellaneous[a]	9 (0.7)
Class total	1311 (100)

[a] Includes tapentadol, diphenoxylate, desomorphine, and papaverine

Table 12 Antidepressants

	N (%)
Other antidepressants	485 (37.3)
Bupropion	230 (17.7)
Trazodone	180 (13.8)
Mirtazapine	62 (4.8)
Vilazodone	6 (0.5)
Miscellaneous[a]	7 (0.5)
Selective serotonin reuptake inhibitors (SSRIs)	480 (36.9)
Citalopram	135 (10.4)
Sertraline	114 (8.8)
Fluoxetine	109 (8.4)
Escitalopram	78 (6.0)
Paroxetine	44 (3.4)
Tricyclic antidepressants (TCAs)	176 (13.5)
Amitriptyline	129 (9.9)
Nortriptyline	20 (1.5)
Doxepin	18 (1.4)
Imipramine	5 (0.4)
Miscellaneous[b]	<5 (0.1)
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	150 (11.5)
Venlafaxine	89 (6.8)
Duloxetine	47 (3.6)
Desvenlafaxine	7 (0.5)
Fluvoxamine	7 (0.5)
Class total	1301 (100)

[a] Includes antidepressant unspecified, nefazodone, tianeptine, and tranylcypromine

[b] Includes clomipramine and desipramine

Table 13 Anticholinergics and antihistamines

	N (%)
Diphenhydramine	406 (53.4)
Hydroxyzine	110 (14.5)
Doxylamine	45 (5.9)
Chlorpheniramine	42 (5.5)
Benztropine	37 (4.9)
Promethazine	26 (3.4)
Cetirizine	16 (2.1)
Loratadine	13 (1.7)
Antihistamine unspecified	7 (0.9)
Trihexyphenidyl	7 (0.9)
Dimenhydrinate	6 (0.8)
Oxybutynin	6 (0.8)
Anticholinergic unspecified	5 (0.6)
Dicyclomine	5 (0.6)
Meclizine	5 (0.6)
Miscellaneous[a]	25 (3.3)
Class total	761 (100)

[a] Includes fexofenadine, hyoscyamine, atropine, brompheniramine, scopolamine, belladonna, fesoterodine, pheniramine, pyrilamine, tiotropium, and tolterodine

Table 8 shows that 6.1 % of all agents reported in 2014 were anticholinergic/antihistamine agents. As seen in Table 13, diphenhydramine was the most common individual agent, equaling 53.4 % of all reported agents in this class, followed by hydroxyzine (14.5 %), then three agents accounting for 5–6 % of the class (doxylamine, chlorpheniramine, and benzotropine). Of note, hydroxyzine was represented in 4.4 % of all Registry cases.

As listed in Table 14, the most common groups of cardiovascular agents were beta blockers (27.5 %), sympatholytics (22.4 %), and calcium channel antagonists (15.0 %). Metoprolol and propranolol were the two most common beta blockers, accounting for 10.7 and 6.9 %, respectively. Clonidine was the most commonly reported sympatholytic, responsible for 18.2 % of all cardiovascular agents, while amlodipine was the most common calcium channel antagonist (7.4 %). Clonidine was reported in 1.4 % of all Registry cases. Digoxin was the predominate cardiac glycoside (69 of 70 cases). Ace inhibitors, diuretics, antidysrhythmics, and other antihypertensives and vasodilators appeared to a much lesser extent. However, lisinopril, the most common ACE inhibitor, accounted for 7.4 % of the cardiovascular class.

Antipsychotics contributed 5.5 % of all agent entries to the Registry (Table 8). Atypical antipsychotics represented over 83 % of the class, primarily due to quetiapine (48.0 %), risperidone (11.6 %), aripiprazole (11.0 %), and olanzapine (10.6 %) (Table 15). Quetiapine exposure was represented in 6.3 % of the Registry cases. Within the overall class, an array

Table 14 Cardiovascular agents by subtype

	N (%)
Beta blockers	196 (27.5)
Metoprolol	76 (10.7)
Propranolol	49 (6.9)
Carvedilol	27 (3.8)
Atenolol	23 (3.2)
Labetalol	8 (1.1)
Nadolol	6 (0.8)
Miscellaneous[a]	7 (1.0)
Sympatholytics	160 (22.4)
Clonidine	130 (18.2)
Guanfacine	30 (4.2)
Calcium channel antagonists	107 (15.0)
Amlodipine	53 (7.4)
Diltiazem	28 (3.9)
Verapamil	21 (2.9)
Miscellaneous[b]	5 (0.7)
Cardiac glycosides	70 (9.8)
Digoxin	69 (9.7)
Digitoxin	<5 (<0.2)
ACE inhibitors	57 (8.0)
Lisinopril	53 (7.4)
Miscellaneous[c]	5 (0.6)
Diuretics	44 (6.2)
Hydrochlorothiazide	21 (2.9)
Furosemide	13 (1.8)
Miscellaneous[d]	10 (1.4)
Other antihypertensives and vasodilators	28 (3.9)
Prazosin	10 (1.4)
Miscellaneous[e]	18 (2.5)
Antidysrhythmics	20 (2.8)
Amiodarone	6 (0.8)
Flecainide	5 (0.7)
Miscellaneous[f]	9 (1.3)
Other cardiovascular agents	17 (2.4)
Simvastatin	10 (1.4)
Miscellaneous[g]	7 (1.0)
Angiotensin receptor blockers	15 (2.1)
Losartan	8 (1.1)
Valsartan	5 (0.7)
Miscellaneous[h]	<5 (<0.4)
Class total	713 (100)

[a] Includes nebivolol and timolol

[b] Includes nifedipine and felodipine

[c] Includes benazepril, perindopril, and quinapril

[d] Includes chlorthalidone, acetazolamide, bumetanide, spironolactone, and torsemide

[e] Includes tamsulosin, isosorbide, antihypertensive unspecified, hydralazine, terazosin, alfuzosin, cilostazol, doxazosin, minoxidil, and nitroglycerin

[f] Includes propafenone, mexiletine, dofetilide, and dronederone

[g] Includes atorvastatin, colesevalm, fenofibrate, lovastatin, and ranolazine

[h] Includes olmesartan and telmisartan

Table 15 Antipsychotics

	N (%)
Quetiapine	331 (48.0)
Risperidone	80 (11.6)
Aripiprazole	76 (11.0)
Olanzapine	73 (10.6)
Haloperidol	35 (5.1)
Clozapine	23 (3.3)
Ziprasidone	19 (2.8)
Chlorpromazine	18 (2.6)
Paliperidone	9 (1.3)
Lurasidone	8 (1.2)
Miscellaneous[a]	17 (2.2)
Class total	689 (100)

[a] Includes prochlorperazine, fluphenazine, loxapine, antipsychotic unspecified, trifluoperazine, asenapine, iloperidone, and thioridazine

of "first-generation" phenothiazines resulted in 3.5 % of agent entries.

Table 16 shows agents reported as sympathomimetics, including a range of pharmaceuticals, illicit drugs, and other designer stimulants associated with toxic exposures/consultations. Overall, this class contributed 5.5 % of all agent entries in 2014 (Table 8). At 37.1 %, cocaine was the majority contributor to this class, followed by methamphetamine and amphetamine, which combined accounted for another 32.6 %. Pharmaceutical stimulants of interest, such as those for

Table 16 Sympathomimetics

	N (%)
Cocaine	252 (37.1)
Methamphetamine	145 (21.3)
Amphetamine	77 (11.3)
Methylphenidate	50 (7.4)
Dextroamphetamine	33 (4.9)
Methylenedioxy-*N*-methamphetamine	26 (3.8)
Lisdexamfetamine	18 (2.6)
Phenylephrine	15 (2.2)
Phentermine	14 (2.1)
Sympathomimetic unspecified	10 (1.5)
25I-NBOMe	6 (0.9)
Atomoxetine	6 (0.9)
Cathinone	6 (0.9)
Dexmethylphenidate	6 (0.9)
Miscellaneous[a]	20 (2.9)
Class total	684 (100)

[a] Includes clenbuterol, 2C series drugs, pseudoephedrine, epinephrine, alpha-pyrrolidinopentiophenone, ephedrine, ethylphenidate, methylenedioxypyrovalerone (MDPV), methylenedioxyethylamphetamine (MDEA), phendimetrazine, phenylethylamine designer drugs, and tetrahydrozoline

Table 17 Anticonvulsants and mood stabilizers

	N (%)
Lithium[a]	179 (100)
Valproic acid	116 (27.6)
Lamotrigine	94 (22.3)
Phenytoin	59 (14.0)
Carbamazepine	54 (12.8)
Topiramate	42 (10.0)
Oxcarbazepine	26 (6.2)
Levetiracetam	16 (3.8)
Zonisamide	7 (1.7)
Miscellaneous[b]	7 (1.7)
Class total	421 (100)

[a] Lithium is considered a separate agent class

[b] Includes clobazam, felbamate, and lacosamide

Table19 Envenomations and marine poisonings

	N (%)
Crotalus spp.	102 (36.2)
Agkistrodon spp.	80 (28.4)
Snake unspecified	30 (10.6)
Loxosceles spp.	19 (6.7)
Latrodectus spp.	18 (6.4)
Centruroides spp.	13 (4.6)
Miscellaneous[a]	20 (7.1)
Class total	282 (100)

[a] Includes envenomation unspecified, *Vipera palaesinae*, scombroid poisoning, scorpion unspecified, ciguatera poisoning, hymenoptera, insect unspecified, jellyfish, *Pterios* spp. (lionfish), palytoxin, *Scolopendra* spp. (centipedes), spider unspecified, stingray, and *Trimeresurus abolabris*

treating attention deficit/hyperactivity disorder, contributed for 2 % or more to this class. These drugs included methylphenidate (7.4 %), dextroamphetamine (4.9 %), and lisdexamfetamine (2.6 %). The most common designer amphetamine reported was methylenedioxy-*N*-methamphetamine at 3.8 % of the class. A range of other designer stimulants were reported in smaller numbers, including 4-iodo-2,5-dimethoxy-*N*-(2-methoxybenzyl) phenethylamine (25I-NBOMe), cathinone, methylenedioxypyrovalerone (MDPV), methylenedioxyethylamphetamine (MDEA), and alpha-pyrrolidinopentiophenone.

Anticonvulsants comprised 3.4 % of the agent entries, primarily due to valproic acid (27.6 %) and lamotrigine (22.3 %) (Table 17). The mood stabilizer lithium constitutes a single agent class in the Registry. In 2014, 179 occurrences, representing 2.0 % of the Registry cases, were entered.

Table 18 Psychoactives

	N (%)
Marijuana	101 (32.4)
Cannabinoid—synthetic	81 (26.0)
Phencyclidine	27 (8.7)
Lysergic acid diethylamide (LSD)	25 (8.0)
Nicotine	21 (6.7)
Cannabinoid—nonsynthetic	14 (4.5)
Gamma hydroxybutyrate (GHB)	13 (4.2)
Miscellaneous[a]	30 (9.6)
Class total	312 (100)

[a] Includes ketamine, donepezil, ibogaine, 1,4-butanediol, dimethyltryptamine, γ-butryolactone, mephedrone, methoxetamine, psychoactive unspecified, 2,6-dimethoxy-4-methylamphetamine, *Argyeria nervosa*, disulfiram, hallucinogen unspecified, hallucinogenic amphetamine, methylone, tetrahydropalmatine, and vareniciline

Cases classified as involving other psychoactive drugs of abuse are shown in Table 18. Marijuana was the most frequent entry in this category in 2014, representing 32.4 % of all entries in this group. Synthetic cannabinoids, such as those referred to as "spice" or "K2," were reported in 26.0 % of all class entries. Other psychoactive compounds included phencyclidine, lysergic acid diethylamide (LSD), and gamma hydroxybutyrate (GHB).

Among envenomations and marine poisonings, over 70 % were related to *Crotalus* spp. (rattlesnake), *Agkistrodon* spp. (water moccasin), or snake species unspecified (Table 19); 17.7 % of envenomations were attributed to *Loxsocoles* spp. (recluse spider), *Latrodectus* spp. (widow spider), and *Centruroides* spp. (bark scorpions).

Antidiabetic medications metformin (29.5 %), insulin (24.3 %), glipizide (18.6 %), and glyburide (15.7 %) were responsible for the majority of entries among the diabetes-related medications reported (Table 20). Dextromethorphan accounted for 87.0 % of cough and cold product entries (see Supplementary Material).

Table 20 Diabetic medications

	N (%)
Metformin	62 (29.5)
Insulin	51 (24.3)
Glipizide	39 (18.6)
Glyburide	33 (15.7)
Glimepiride	11 (5.2)
Sulfonylurea unspecified	5 (2.4)
Miscellaneous[a]	9 (4.3)
Class total	210 (100)

[a] Includes sitagliptin, pioglitazone, gliclazide, liraglutide, and repaglinide

Table 21 Ethanol and toxic alcohols

	N (%)
Ethanol[a]	849 (100.0)
Nonethanol alcohols and glycols	
Ethylene glycol	40 (38.5)
Isopropanol	29 (27.9)
Methanol	14 (13.5)
Acetone	9 (8.7)
Miscellaneous[b]	12 (11.5)
Class total	104 (100)

[a] Ethanol is considered a separate agent class

[b] Includes methyl ethyl ketone, propylene glycol, glycol ether unspecified, butyl ethylene glycol, and toxic alcohol unspecified

Table 23 Metals

	N (%)
Lead	37 (25.5)
Iron	22 (15.2)
Cobalt	17 (11.7)
Chromium	14 (9.7)
Mercury	13 (9.0)
Arsenic	6 (4.1)
Copper	6 (4.1)
Miscellaneous[a]	30 (20.7)
Class total	145 (100)

[a] Includes gadolinium, manganese, magnesium, selenium, titanium, aluminum, metal unspecified, silver, antimony, beryllium, cadmium, cesium, thallium, uranium, and zinc sulfate

Nine additional classes comprised the remaining pharmaceutical group classifications, accounting for 0.1–0.9 % of all agent entries (Table 8). A large number of individual agents contributed to the 69 antibiotics, 21 antivirals, antifungals, and other types of antimicrobials (both pharmaceutical and nonpharmaceutical uses). Warfarin accounted for 71.2 % of the anticoagulants, followed by rivaroxaban (10.6 %), with a variety of other agents in the class accounting for a limited number of entries (see Supplementary Material). For the remaining drug classes, the most common agents were the following: levothyroxine (endocrine agents), hydrogen peroxide and pyridostigmine (other pharmaceuticals), benzonatate (anesthetics), omeprazole (gastrointestinal), levodopa/carbodopa (anti-parkinsonism), theophylline (pulmonary), and hydroxychloroquine (chemotherapeutic and immunological).

Alcohols were classified into two categories, ethanol and other toxic alcohols (Table 21). As a single agent class, ethanol was responsible for 6.8 % of all agents. Table 21 summarizes case numbers for the other, less common toxic alcohols including ethylene glycol, isopropanol, methanol, and acetone, which as a group accounted for 0.8 % of the agent entries.

The agent class herbals and dietary supplements captured a broad range of products from a variety of sources (herbal, mineral, or chemical). Three single agents were responsible for 64.1 % of the 159 entries: caffeine, melatonin, and multivitamins. Over 30 other agents were responsible for the remaining 35.9 %. Table 22 shows a similar situation for the plant and fungi class, and mold (unspecified) was the most common agent class entry (34.7 %), followed by mushroom unspecified (16.0 %) and mushroom, *Psilocybe* spp. (8.0 %), with 22 other specific agents accounting for the remaining 41.3 % (31 cases) (data in Supplementary Materials).

Eight classes of agents were most often reported in occupational and environmental exposures: metals, hydrocarbons, pesticides, gases, caustics, irritants, vapors, and dusts. In the metal class, lead, iron, and cobalt accounted for over one half

Table 22 Plants and fungi

	N (%)
Mold	26 (34.7)
Mushroom unspecified	12 (16.0)
Mushroom (*Psilocybe* spp.)	6 (8.0)
Miscellaneous[a]	31 (41.3)
Class total	75 (100)

[a] Includes *Nerium oleander*, *Datura stramonium*, *Dieffenbachia*, Kombucha tea, *Mitragyna speciosa* (kratom), mycotoxins, *Amanita muscaria*, *Chrysanthemum parthenium*, *Cucurita pepo*, *Gyromitra*, lavender, *Glycyrrhiza glabra* (licorice), marigold, *Morinda officinalis* (Ba Ji Tian), *Phytolacca* (pokeweed), plants or fungi unspecified, solanines, toxalbumins, valerian root, dandelion, primrose, and *Scutellaria* (skullcap)

Table 24 Gases, irritants, vapors, and dusts

	N (%)
Carbon monoxide	81 (58.7)
Cyanide	10 (7.2)
Hydrogen sulfide	7 (5.1)
Smoke	7 (5.1)
Unspecified gas	6 (4.3)
Sulfur dioxide	5 (3.6)
Miscellaneous[a]	22 (15.9)
Class total	138 (100)

[a] Includes dust, asbestos, carbon disulfide, chlorine, nitrogen oxides, petroleum vapors, arsine, carbon dioxide, chloramine, phosgene, phosphine, polyurethane vapors, radon, and silica

Table 25 Household products

	N (%)
Sodium hypochlorite ≤6 %	35 (28.0)
Detergent pods	26 (20.8)
Cleaning solutions and disinfectants	24 (19.2)
Soaps and detergents unspecified	13 (10.4)
Household product unspecified	11 (8.8)
Miscellaneous[a]	16 (12.8)
Class total	125 (100)

[a] Includes hair products, paints, ammonia <10 %, hand sanitizer unspecified, deodorants/antiperspirants, dishwasher detergent, and sunscreens

of the class entries (51.7 %), followed by chromium, mercury, arsenic, and copper (Table 23). Carbon monoxide was the most common entry in the gases, irritants, vapors, and dust class (Table 24). A large fraction of the entries for the hydrocarbon class were unspecified (38.1 %); toluene and gasoline were the only specific agents with five or more reported cases. Brodifacoum, a 4-hydroxycoumarin vitamin K antagonist (anticoagulant) poison, was the most common rodenticide entry (23 cases). Only a limited number of herbicides and fungicides were reported (total n=6), with no agent with more than 2 entries. Organophosphates accounted for the majority of insecticide cases as indicated by entries for malathion, acephate, chlorpyrifos, and organophosphates unspecified, with several entries related to pyrethroids (permethrin, cypermethrin, pyrethrin unspecified). The caustic agent class also captured a broad range of agents, with only three individual agents with more than 5 occurrences (sodium hydroxide, hydrofluoric and hydrochloric acid), that combine to represent 36.3 % of the class entries (see Supplementary Material).

Additional non-pharmaceutical agents are included across four classes: household products, caustics, other nonpharmaceuticals, and ingested foreign objects (Table 25 and Supplementary Material). Other than sodium hypochlorite<6 % in concentration (28 % of class), the majority of agent entries are chemically nonspecific as compared to the pharmaceuticals; however, these agents were still associated with 1.0 % of all agent entries (Table 8). In the class other nonpharmaceuticals, only "unspecified" agents had more than 3 entries, while batteries were the most commonly reported ingested foreign object.

Clinical Signs and Symptoms

At least one clinical sign or symptom was reported in 7512 (81.9 %) cases. These findings are summarized in Tables 26, 27, 28, 29, and 30, organized by either syndrome or organ system. Sedative-hypnotic and anticholinergic were the two most common toxidromes reported (both reported in over 5 % of all cases), followed by opioid, sympathomimetic, and serotonin syndrome (Table 26). Tachycardia was the most common major vital sign abnormality (9.9 % cases) followed by hypotension (5.7 % cases) and bradycardia (3.5 % cases) (Table 27). Neurological effects were encountered most frequently among all signs and symptoms. Coma or CNS depression was observed in 2641 (28.8 %) cases (Table 28). Delirium, agitation, and rigidity/dystonia were relatively common as well, appearing in 10.7, 10.2, and 7.3 % of cases, respectively. Among pulmonary signs or symptoms, respiratory depression occurred most frequently (6.5 %), while prolonged QTc (>500 ms) or QRS (>120 ms) was the frequently reported cardiovascular effect (Table 29). All other individual signs or symptoms were reported in less than 6 % of Registry cases (Table 30).

Table 26 Toxidromes

	N (%)[a]
Sedative-hypnotic	631 (6.9)
Anticholinergic	467 (5.1)
Opioid	330 (3.6)
Sympathomimetic	232 (2.5)
Serotonin syndrome	210 (2.3)
Sympatholytic	36 (0.4)
Alcoholic ketoacidosis	26 (0.3)
NMS	15 (0.2)
Washout syndrome	11 (0.1)
Anticonvulsant hypersensitivity	8 (0.1)
Overlap syndromes	7 (0.1)
Cholinergic	5 (0.05)
Fume fever	<5 (<0.05)
Total	1980 (21.6)

NMS neuroleptic malignant syndrome

[a] Percentage equals the number of cases reporting specific treatment relative to the total number of Registry cases in 2014 (N=9172)

Table 27 Major vital sign abnormalities

	N (%)[a]
Tachycardia (HR>140)	910 (9.9)
Hypotension (systolic BP<80 mmHg)	525 (5.7)
Bradycardia (HR<50)	319 (3.5)
Hypertension (systolic BP>200 mmHg or diastolic BP>120 mmHg)	182 (2.0)
Bradypnea (RR<10)	149 (1.6)
Hyperthermia (temp>105 °F)	37 (0.4)
Total	1733 (18.9)[a,b]

HR heart rate, *BP* blood pressure

[a] Percentage equals the number of cases relative to the total number of Registry cases in 2014 (N=9172)

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

Table 28 Clinical signs and symptoms—neurological

	N (%)[a]
Coma/CNS depression	2641 (28.8)
Delirium	979 (10.7)
Agitation	937 (10.2)
Hyperreflexia/myoclonus/tremor	667 (7.3)
Seizures	405 (4.4)
Hallucinations	276 (3.0)
Dystonia/rigidity/extrapyramidal symptoms	164 (1.8)
Weakness/paralysis	97 (1.1)
Numbness/paresthesia	74 (0.8)
Peripheral neuropathy	31 (0.3)
Total	4500 (49.1)[a,b]

CNS central nervous system

[a] Percentage equals the number of cases relative to the total number of Registry cases in 2014 (*N*=9172)

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

Fatalities

There were 89 fatalities reported in the Registry in 2014, comprising 0.97 % of all cases (Tables 31 and 32, Supplementary Material). Forty-eight (53.4 %) of these cases were female. The average age of fatalities was 45.1 years, ranging from 8 weeks to 80 years of age. As in 2013, nonopioid analgesics and opioids were the most frequently reported agents among these cases. For cases reporting a single agent poisoning (38 cases or 42.7 % of all fatalities), acetaminophen was the agent reported for all 12 analgesic-related events. One half of the six opioid-related deaths were related to heroin, with the remainder of single agent opioid-related events due to methadone, oxycodone, and tramadol.

Among the 31 multiple agent fatalities (34.8 % of the total), 10 cases involved one or more opioids: oxycodone (4 cases), methadone (3 cases), and heroin (3 cases). Non-opioid analgesics were reported in seven multiple agent poisonings (primarily acetaminophen, nine cases).

In a substantial portion of cases, 22 of 89 (24.7 %), no agent was entered into the ToxIC Registry (see Supplementary Material). For the majority of this subset, 19 of 22 cases

Table 29 Clinical signs—cardiovascular and pulmonary

	N (%)[a]
Cardiovascular	
Prolonged QTc (≥500 ms)	265 (2.9)
Prolonged QRS (≥120 ms)	127 (1.4)
Ventricular dysrhythmia	69 (0.8)
AV block (>1st degree)	39 (0.4)
Total	417 (4.5)[b]
Pulmonary	
Respiratory depression	598 (6.5)
Aspiration pneumonitis	136 (1.5)
Acute lung injury/ARDS	75 (0.8)
Asthma/reactive airway disease	56 (0.6)
Total	772 (8.4)[b]

ARDS acute respiratory distress syndrome

[a] Percentage equals the number of cases reporting specific treatment relative to the total number of Registry cases in 2014 (*N*=9172)

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

Table 30 Clinical signs—other organ systems

	N (%)[a]
Metabolic	
Metabolic acidosis (pH<7.2)	323 (3.5)
Elevated anion gap (>20)	276 (3.0)
Hypoglycemia (glucose<50 mg/dL)	182 (2.0)
Elevated osmole gap (>20)	40 (0.4)
Total	624 (6.8)[b]
Gastrointestinal/hepatic	
Hepatotoxicity (AST≥1000 IU/L)	316 (3.4)
Gastrointestinal bleeding	48 (0.5)
Corrosive injury	35 (0.4)
Pancreatitis	31 (0.3)
Intestinal ischemia	8 (0.1)
Total	409 (4.5)[b]
Hematological	
Coagulopathy (PT>15 s)	179 (2.0)
Thrombocytopenia (platelets<100 K/μL)	75 (0.8)
Leukocytosis (WBC>20 K/μL)	65 (0.7)
Hemolysis (Hgb<10 g/dL)	23 (0.3)
Methemoglobinemia (MetHgb≥2 %)	13 (0.1)
Pancytopenia	13 (0.1)
Coagulopathy (PT>15 s)	179 (2.0)
Thrombocytopenia (platelets<100 K/μL)	75 (0.8)
Total	306 (3.3)[b]
Renal/musculoskeletal	
Acute kidney injury (creatinine>2.0 mg/dL)	346 (3.8)
Rhabdomyolysis (CPK>1000 IU/L)	317 (3.5)
Total	573 (6.2)[b]
Dermatological	
Rash	122 (1.3)
Blister/bullae	76 (0.8)
Necrosis	22 (0.2)
Angioedema	14 (0.2)
Total	199 (2.2)[b]

PT prothrombin time, *WBC* white blood cells, *Hgb* hemoglobin, *CPK* creatinine phosphokinase

[a] Percentage equals the number of cases reporting specific treatment relative to the total number of Registry cases in 2014 (*N*=9172)

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

Table 31 2014 fatalities reported in toxic registry with known toxicological exposure: single agent

Age/gender[a]	Agents involved	Clinical findings	Life support withdrawn	Brain death confirmed	Treatment[b]
2 F	Propofol	HT, TC, BP, AGT, AG, AKI, RBM	Yes	Unknown	Carnitine
14 M	Oxycodone	HT, VD, RD, CNS	Yes	Unknown	Naloxone
19 F	Methanol	HT, VD, ALI, CNS, SZ, MA, AG	No	Unknown	Folate, fomepizole, pyridoxine, $NaHCO_3$, thiamine, vasopressors, anticonvulsants, steroids, hemodialysis, continuous renal replacement, intubation, IV fluids
21 F	Acetaminophen	HT, CNS, MA, HPT, GIB, HYS, CPT, PLT, AKI	Yes	Unknown	Factor replacement, NAC, vitamin K, vasopressors, continuous renal replacement, intubation, IV fluids, therapeutic hypothermia, transfusion
23 F	Acetaminophen	HT, TC, CNS, DLM, HGY, MA, CPT, WBC, AKI	No	Unknown	Fomepizole, NAC, $NaHCO_3$, vasopressors, benzodiazepines, glucose, neuromuscular blockers, steroids, hemodialysis, CPR, intubation, IV fluids, therapeutic hypothermia
24 F	Acetaminophen	CNS, HGY, MA, AG, HPT, CPT, AKI, RBM	Yes	Yes	NAC, vasopressors, glucose, intubation, IV fluids
25 M	Sodium hydroxide	HT, TC, AP, CRV, PLT, WBC	Yes	No	None listed
27 M	Heroin	BP, RD, CNS	Yes	No	Vasopressors, CPR, intubation
29 F	Acetaminophen	HT, TC, CNS, MA, AG, HPT, CPT, AKI,	Yes	No	NAC, vasopressors,
31 F	Acetaminophen	HT, TC, VD, RD, CNS, MA, AG, HPT, HYS, CPT, WBC, AKI	Yes	No	NAC, $NaHCO_3$, vitamin K, vasopressors, antiarrhythmics, benzodiazepines, continuous renal replacement, CPR, intubation, IV fluids, transfusion
34 F	Acetaminophen	HT, TC, RD, CNS, DLM, RFX, HGY, MA, AG, HPT, CPT, PLT, WBC, AKI	Yes	No	NAC, vasopressors, bronchodilators, benzodiazepines, glucose, neuromuscular blockers, opioids, intubation
36 M	Ethanol	HT, CNS, HGY, MA, AG, HPT, GIB, CPT, AKI	No	Unknown	Fomepizole, NAC, $NaHCO_3$, thiamine, vasopressors, benzodiazepines, glucose, continuous renal replacement, intubation, IV fluids
40 M	Ibogaine	None listed	Yes	Yes	None listed
41 F	Acetaminophen	HPT, PLT	No	Unknown	NAC
44 M	Methamphetamine	HT, TC, RD, CNS, MA, AG, PNC, WBC, PLT, AKI, RBM	No	Unknown	Fomepizole, benzodiazepines, glucose, intubation, IV fluids
46 F	Acetaminophen	CNS, HGY, HPT, CPT, AKI	No	Unknown	NAC, IV fluids, pacemaker, transplantation
47 M	Heroin	HT, CNS, RBM	Missing	Missing	Naloxone
47 M	Insulin	CNS, HGY	Yes	Yes	Octreotide, glucose, intubation
48 F	Acetaminophen	CNS, DLM, MA, HPT, PNC, CPT, WBC, AKI	Yes	Unknown	NAC, thiamine, hemodialysis
48 F	Heroin	QTc, RD, AGT, MA, PNC, HYS, CPT	No	Unknown	Naloxone, opioids, intubation
49 M	Phenytoin	CNS, HPT	Yes	Unknown	None listed
52 F	Acetaminophen	RD, CNS, MA, AG, HPT, CPT	Yes	No	Flumazenil, NAC, naloxone, vasopressors
56 F	Tramadol	HT, VD, SZ, MA, WBC, AKI	Unknown	Unknown	Atropine, vasopressors, intubation
57 F	Methadone	HT, BP, AP, RD, CNS, DLM, WKN, PLT	Yes	No	Flumazenil, naloxone, bronchodilators, benzodiazepines, opioids, intubation
59 M	Verapamil	HT, BC, AKI	Yes	No	Lipid resuscitation, IV fluids
60 M	Amlodipine	HT, ALI, RD, CNS, MA, AKI	No	Unknown	Calcium, glucagon, insulin-euglycemic therapy, vasopressors, glucose, intubation, IV fluids

Table 31 (continued)

Age/gender[a]	Agents involved	Clinical findings	Life support withdrawn	Brain death confirmed	Treatment[b]
62 M	Ethylene glycol	None listed	Yes	No	Fomepizole
63 M	Metformin	TC, CNS, MA, HPT, AKI	Yes	Yes	Vasopressors, antiarrhythmics, hemodialysis, intubation, IV fluids
66 M	Ethanol	HT, TC, AP, ALI, CNS, HGY, MA, AG, GIB, INT, PLT, PCT, AKI	Yes	No	Folate, fomepizole, $NaHCO_3$, thiamine, hemodialysis, IV fluids
67 F	Ethylene glycol	HT, BC, AP, ALI, CNS, MA, AG	No	Unknown	Fomepizole, $NaHCO_3$, vasopressors, glucose
68 M	Temazepam	HT, ALI, CNS	Yes	Yes	Naloxone, vasopressors, intubation
71 M	Insulin	HGY	No	Unknown	Glucose
75 F	Acetaminophen	ALI, RD, CNS, WBC, AKI	No	No	None listed
77 F	Acetaminophen	HT, CNS, MA, HPT	Yes	Yes	NAC, vasopressors
78 F	Digoxin	HT, VD, RD, CNS	Yes	Yes	Digoxin Fab, vasopressors, continuous renal replacement, CPR, cardioversion
78 M	Smoke	HT, ALI	Unknown	Unknown	Thiosulfate
83 F	Digoxin	BC, CNS, HGY, MA, AG, AKI	No	Unknown	Atropine, digoxin Fab
86 F	Warfarin	CPT	Yes	Yes	Anticoagulant reversal

Based on the response from a medical toxicologist "Did the patient have a toxicological exposure?" equals Yes with known agent(s)

AG anion gap, *AGT* agitation, *AKI* acute kidney injury, *ALI* acute lung injury/ARDS, *AP* aspiration pneumonia, *AVB* AV block, *BC* bradycardia, *BP* bradypnea, *CNS*: Coma/CNS depression, *CPT* coagulopathy, *CRV* corrosive injury, *DLM* delirium, *EPS* dystonia, *GIB* GI bleeding, *HCN* hallucinations, *HGY* hypoglycemia, *HPT*: Hepatoxicity, *HT* hypotension, *HTN* hypertension, *HYS* hemolysis, *HYT* hyperthermia, *INT* intestinal ischemia, *MA* metabolic acidosis, *MET* methemoglobinemia, *NP* neuropathy, *OG* osmole gap, *PCT* pancytopenia, *PLT* thrombocytopenia, *PNC* pancreatitis, *PST* paresthesia, *QRS* QRS prolongation, *QTc* QTc prolongation, *RAD* asthma/reactive airway disease, *RBM* rhabdomyolysis, *RD* respiratory depression, *RFX* hyperreflexia/tremor, *SZ* seizures, *TC* tachycardia, *VD* ventricular dysrhythmia, *WBC* leukocytosis, *WKN* weakness/paralysis, *CPR* cardiopulmonary resuscitation, *NAC N*-acetylcysteine, *$NaHCO_3$* sodium bicarbonate

[a] Age in years unless otherwise stated

[b] Pharmacological and nonpharmacological support as reported by a medical toxicologist

Table 32 2014 fatalities reported in toxic registry with known toxicological exposure: multiple agents

Age/gender[a]	Agents involved	Clinical findings	Life Support Withdrawn	Brain Death Confirmed	Treatment[b]
8 weeks F	Atorvastatin, omega-3-acid ethyl esters	HT, TC, RD, CNS, MA, HPT, HYS, CPT, PLT	Yes	No	Intubation
14 months M	Amphetamine, dextroamphetamine	TC, AGT, RFX	Yes		Benzodiazepines
14 M	Metformin, clonidine, quetiapine, valproic acid	HT, TC, CNS, MA	No	Unknown	Lipid resuscitation, gastric lavage, charcoal, CPR, cardioversion, IV fluids
14 M	Heroin, cocaine	CNS	Unknown	Unknown	Naloxone
16 M	Methadone, alprazolam	HT, BC, VD, QTc,	Yes	Unknown	Vasopressors, antiarrhythmics
21 M	Acetaminophen, aripiprazole, melatonin	HPT	Yes	No	NAC, IV fluids
23 F	Diphenhydramine, methamphetamine	VD, QRS, DLM	No	Unknown	$NaHCO_3$, intubation, IV fluids
23 M	Bupropion, citalopram	HT, CNS	Yes	Yes	Lipid resuscitation, vasopressors, intubation
25 F	Oxycodone, methadone, carisoprodol, alprazolam	HT, BC, ALI, CNS, MA, AG, HPT, PLT, AKI, RBM	Yes	Unknown	NAC, $NaHCO_3$, vasopressors, antiarrhythmics, glucose, continuous renal replacement, intubation, IV fluids
29 F	Acetaminophen	HT, TC, CNS, MA, AG, HPT, CPT, AKI,	Yes	No	NAC, vasopressors
29 F	Cocaine, carbon monoxide	RD, CNS, MA	Yes	Yes	None listed
31 F	Acetaminophen	HT, TC, VD, RD, CNS, MA, AG, HPT, HYS, CPT, WBC, AKI	Yes	No	NAC, $NaHCO_3$, vitamin K, vasopressors, antiarrhythmics, benzodiazepines, continuous renal replacement, CPR, intubation, IV fluids, transfusion
31 F	Smoke, cyanide, carbon monoxide	HT, VD	Yes	Yes	Hydroxocobalamin, hyperbaric O_2
31 M	Heroin, doxylamine	SZ	Yes	No	Benzodiazepines, intubation
32 F	Quetiapine, oxycodone, heroin, methamphetamine	HT, BC, BP, VD, QTc, QRS, ALI, RD, CNS, MA, AG, HYS, AKI, RBM	Yes	Yes	Lipid resuscitation, NAC, naloxone, $NaHCO_3$, vasopressors, charcoal, CPR, intubation, IV fluids, therapeutic hypothermia
32 M	Acetaminophen, brodifacoum, aspirin	HT, CNS, RFX, HPT, PNC, CPT, AKI, PLT	Yes	Yes	NAC, vitamin K, vasopressors, continuous renal replacement, intubation, IV fluids
35 M	Cyclobenzaprine, hydroxyzine	HT, BC, ALI, CNS, MA	Yes	Unknown	Calcium, NAC, $NaHCO_3$, CPR, intubation, IV fluids, pacemaker
43 F	Propranolol, tizanidine, metformin	HT, RD, CNS, AKI	Yes	No	Insulin-euglycemic therapy, NAC, vasopressors, benzodiazepines, neuromuscular blockers, opioids, intubation, IV fluids
44 F	Acetaminophen, aspirin	RD, CNS, HPT, AKI	Yes	Yes	NAC, naloxone, $NaHCO_3$, vasopressors, continuous renal replacement, intubation, IV fluids, therapeutic hypothermia
45 M	Clonazepam, methadone, gabapentin	HT, TC, BC, RD, CNS	No	Unknown	Vasopressors, antiarrhythmics, CPR, intubation, IV fluids, therapeutic hypothermia
48 M	Verapamil, carvedilol, levetiracetam, lisinopril, atazanavir	BC, RD, CNS, AG, AKI	Unknown	Unknown	Atropine, glucagon, lipid resuscitation, vasopressors, CPR, IV fluids
51 M	Acetaminophen, ethanol	HT, TC, HGY, MA, AG, HPT, PNC, GIB, WBC, PLT, AKI	Unknown	Unknown	NAC, vasopressors, intubation, IV fluids
52 F	Metoprolol, amlodipine	HT, BC, VD, CNS	No	Unknown	Atropine, insulin-euglycemic therapy, vasopressors, antiarrhythmics, glucose, CPR, cardioversion, intubation, IV fluids, pacemaker
54 F	Fentanyl, oxycodone	None listed	Unknown	Unknown	Naloxone, bronchodilators, steroids,
55 F		HTN, ALI, AGT, CNS	Unknown	Unknown	Flumazenil, naloxone, physostigmine

Table 32 (continued)

Age/gender[a]	Agents involved	Clinical findings	Life Support Withdrawn	Brain Death Confirmed	Treatment[b]
	Propofol, hydromorphone, midazolam, quetiapine, fluoxetine				
56 F	Hydroxychloroquine, hydrocodone, acetaminophen, clonazepam, levodopa/carbidopa	HT, CNS	Yes	Unknown	NAC
65 F	Propafenone, clonazepam	None listed	Unknown	Unknown	None listed
71 M	Oxycodone, acetaminophen	AP, RD, CNS, MA, AG, AKI	Yes	No	NAC, $NaHCO_3$, intubation, IV fluids
76 F	Acetaminophen, butalbital	HT, TC, QTc, RD, CNS, MA, AG, HPT, GIB, CPT, WBC, RBM	Yes	No	Naloxone, vasopressors, glucose
78 F	Rivaroxaban, clopidogrel	CNS	Yes	No	Factor replacement, bronchodilators, benzodiazepines, opioids, intubation, IV fluids
79 M	Digoxin, atenolol, carvedilol, furosemide	HT, BC, VD, MA, AKI	No	Yes	Digoxin Fab, vasopressors

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

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

[a] Age in years unless otherwise stated

[b] Pharmacological and nonpharmacological support as reported by a medical toxicologist

(86.4 % with no agent), the consulting/attending medical toxicologist determined that the patient did not have a toxicological exposure (7 cases), or it was unclear/unknown (12 cases); therefore, no agent information was entered. In the remaining three cases, the data was either missing or coded as "unknown agent" by the clinician.

In 57 cases (64 %), life support was withdrawn; among this latter subset, actual brain death was confirmed in 24 cases (42.1 %).

Adverse Drug Reactions

In 2014, 410 Registry cases (4.5 %) reported the involvement of an adverse drug reaction (ADR). During 2014, Registry data fields were expanded to include a separate field to identify ADRs from among the reasons for a toxicological consultation. A total of 194 drugs or substances were mentioned at least once with the aid of this additional indicator field. Table 33 lists the 16 most frequently encountered drugs associated with ADRs (single and multiple drug exposure). The overall findings are similar to the ADR summary from the 2013 Registry report [5]. Lithium remains the most frequently cited drug associated with ADRs. Likewise, the most frequently encountered agent classes (non-opioid analgesics, sedative-hypnotics, opioids) are relatively underrepresented in Table 33, with psychiatric medications (antipsychotics 14.6 %, antidepressants 19.3 %) and cardiovascular medications (17.6 %) cited more frequently. The relative pattern changes somewhat if only single drug exposure events are considered (259 or 63.2 % of all ADRs). Lithium (13.5 %), digoxin (9.3 %), and phenytoin and valproic acid (both <5 %) are the four most common individual medications, with cardiovascular (15.8 %), lithium (13.5 %), anticonvulsants (10.8 %), and antipsychotics (8.9 %) as the most common classes.

Table 33 Most common drugs associated with ADRs

	N (%)[a]
Lithium	45 (11.0)
Digoxin	29 (7.1)
Valproic acid	16 (3.9)
Phenytoin	14 (3.4)
Quetiapine	12 (2.9)
Citalopram	11 (2.7)
Tramadol	11 (2.7)
Bupropion	10 (2.4)
Risperidone	10 (2.4)
Trazodone	10 (2.4)
Aripiprazole	8 (2.0)
Fentanyl	8 (2.0)
Glipizide	8 (2.0)
Methadone	8 (2.0)
Metoprolol	8 (2.0)
Sertraline	8 (2.0)
Total	216 (36.4)

[a] Percentages are out of the total number of all drugs reported involved in adverse drug reactions (ADRs); 410 ADRs, with 593 individual agents; 4.5 % of registry cases in 2014 reported as a ADR

Treatment

Specific treatment was rendered in 62.3 %, with 5715 Registry cases reporting more than one treatment modality. There were a total of 2962 instances of antidote administration, accounting for 51.8 % of all treatments reported; 4.2 % of all Registry cases received more than one antidotal therapy for a given event. *N*-acetylcysteine and naloxone/nalmefene collectively comprised over half of all antidotal treatment (Table 34). With the exception of sodium bicarbonate, all other antidotes were used relatively infrequently, with each individual drug accounting for less than 10 % of antidote administrations. Antivenom usage was uncommon, being given in only 197 (2.1 %) of all Registry cases, with polyvalent anti-Crotalidae Fab accounting for a large majority of antivenom treatments (93.4 %) (Table 35).

In the case of pharmacological support, 5.2 % of the Registry cases indicated that more than one form was used for the given toxic event (Table 36). Benzodiazepines and opioids were utilized most frequently, combining for approximately two thirds of all treatments rendered. There were 2867 nonpharmacological therapies given, with 5.8 % of cases receiving more than one treatment modality (Table 37). Intravenous fluid resuscitation and mechanical ventilation management accounted for a large majority of treatments, 67.6 and 27.8 %, respectively. The remaining non-pharmacological supportive care each accounted for less than 2 % of treatments rendered. Chelation was reported for only 21 Registry cases, with 2 receiving multiple chelation modalities. Dimercaptosuccinic acid (DMSA) and ethylenediaminetetraacetic acid (EDTA) accounted for 18 of the 23 chelation therapies reported (Table 38).

There were 409 recorded decontamination therapies across 372 cases, indicating that 37 cases received multiple treatments (Table 39). Activated charcoal was the most frequently reported decontamination modality applied (79.5 %). There were 245 separate uses of enhanced elimination techniques, with only 0.3 % of all registry cases receiving multiple forms of enhanced elimination (Table 40). Renal replacement therapy, either hemodialysis or continuous renal replacement (e.g., CVVH), accounted for 70.6 % of enhanced elimination therapy.

Table 34 Antidotal therapy

	N (%)[a]
N-acetylcysteine	921 (31.1)
Naloxone/nalmefene	605 (20.4)
Sodium bicarbonate	322 (10.9)
Physostigmine	156 (5.3)
Thiamine	119 (4.0)
Fomepizole	90 (3.0)
Flumazenil	81 (2.7)
Glucagon	80 (2.7)
Calcium	77 (2.6)
Folate	74 (2.5)
Octreotide	67 (2.3)
Atropine	51 (1.7)
Cyproheptadine	49 (1.7)
Vitamin K	45 (1.5)
Insulin-euglycemic therapy	41 (1.4)
L-Carnitine	38 (1.3)
Fab for digoxin	35 (1.2)
Lipid resuscitation	33 (1.1)
Pyridoxine	17 (0.6)
Bromocriptine	12 (0.4)
Dantrolene	11 (0.4)
Hydroxocobalamin	11 (0.4)
2-PAM	7 (0.2)
Anticoagulant reversal therapy	4 (0.1)
Thiosulfate	4 (0.1)
Ethanol	3 (0.1)
Coagulation factor replacement	3 (0.1)
Methylene blue	3 (0.1)
Nitrites	3 (0.1)
Total	2962 (100)

[a] Percentages are out of the total number of antidotes administered (2962); 4.2 % of registry cases received more than one antidote

Discussion

This report of the ACMT ToxIC Registry serves as an overview of cases involving medical toxicology consultations reported in 2014. In its fifth year, the Registry continues to grow in both the number of reported cases and participating institutions (Fig. 1, Tables 1 and 2). In 2014, many of the observed percentages of type of consultation, reason for consultation, as well as general agent class reported remain similar to those found in prior years [2–5]. Intentional pharmaceutical exposure remains the most frequent cause of consultations, with analgesics, sedative-hypnotic agents, opioids, and antidepressants continuing to constitute the most frequently encountered agent classes.

However, the rank order based on relative proportion of these classes has varied somewhat over the 5-year period.

Table 35 Antivenom therapy

	N (%)[a]
Polyvalent anti-Crotalidae Fab fragments	184 (93.4)
Spider antivenom	6 (3.0)
Other snake antivenom	4 (2.0)
Scorpion antivenom	3 (1.5)
Total	197 (100)

[a] Percentages are out of the total number of antivenom treatments administered (197)

Table 36 Supportive care—pharmacological

	N (%)[a]
Benzodiazepines	1624 (7.1)
Opioids	261 (9.2)
Vasopressors	239 (8.4)
Antipsychotics	186 (6.5)
Glucose (concentration>5 %)	165 (5.8)
Anticonvulsants	78 (2.7)
Neuromuscular blockers	66 (2.3)
Albuterol (or other bronchodilator)	63 (2.2)
Corticosteroids	49 (1.7)
Antiarrhythmics	42 (1.5)
Antihypertensives	35 (1.2)
Beta blockers	27(0.9)
Vasodilators	8 (0.3)
Total	2843 (100)

[a] Percentages are out of the total number of treatments administered (2843); 5.2 % of registry cases received more than one form of pharmacological treatment

Table 37 Supportive care—non-pharmacological

	N (%)[a]
IV fluid resuscitation	1937 (67.6)
Intubation/ventilatory management	796 (27.8)
CPR	40 (1.4)
Hyperbaric oxygen	21 (0.7)
Transfusion	21 (0.7)
Pacemaker	15 (0.5)
Therapeutic hypothermia	13 (0.5)
Cardioversion	11 (0.4)
ECMO	7 (0.2)
Organ transplantation	4 (0.1)
Aortic balloon pump	1 (0.0)
Bypass	1 (0.0)
Total	2867 (100)

CPR cardiopulmonary resuscitation, *ECMO* extracorporeal membrane oxygenation

[a] Percentages are out of the total number of treatments administered (2867); 5.8 % of registry cases received more than one form of nonpharmacological treatment

Table 38 Chelation therapy

	N (%)[a]
DMSA	11 (47.8)
EDTA	7 (30.4)
Dimercaprol (BAL)	4 (17.4)
Deferoxamine	1 (4.3)
Total	23 (100)

DMSA dimercaptosuccinic acid, *EDTA* ethylenediamine-tetraacetic acid

[a] Percentages are out of the total number of chelation treatments administered (23)

Table 40 Enhanced elimination

	N (%)[a]
Hemodialysis (toxin removal)	74 (30.2)
Urinary alkalinization	56 (22.9)
Hemodialysis (other indication)	50 (20.4)
Continuous renal replacement therapy	49 (20.0)
Multiple-dose activation charcoal	14 (5.7)
Exchange transfusion	2 (0.8)
Total	245 (100)

[a] Percentages are out of the total number of treatments administered (245); 27 registry cases received more than one form of enhanced elimination

As the number of data years collected increase, the ability to observe real changes or trends will continue to improve. The degree to which this variability reflects an actual change in the affected populations' exposure (or type of use) versus operational or other characteristic changes in the participating institutions cannot be determined from a single broad, descriptive review based on single variables. The Registry data can be used to identify more refined areas for hypothesis generation, and provide starting points for initiating additional observation or clinical research by specific type of encounter, agent, or treatment.

As a nonpopulation-based surveillance system, the ToxIC Registry is unable to produce a weighted rate based on either total population covered, or total poisoning/clinical cases for a given medical catchment or geographic area. The Registry nonetheless provides a standardized and detailed view of the relative occurrence in the type of poisonings and other clinical encounters due to both acute and chronic toxic exposures severe enough to require clinical intervention from a medical toxicologist. This feature provides an opportunity to identify changes in exposure, as well as clinical care and practice over time, for the most severe, subset of poisoning cases. However, in order to utilize such data obtained through any disease and clinical surveillance system requires vigilance in the specific data collected, primarily through design of the data collection tool and quality improvement activities.

Table 39 Decontamination

	N (%)[a]
Activated charcoal	325 (79.5)
Whole bowel irrigation	46 (11.2)
Gastric lavage	23 (5.6)
External irrigation	15 (3.7)
Total	409 (100)

[a] Percentages are out of the total number of treatments administered (409); 37 registry cases received more than one form of decontamination

Reporting bias is a potential limitation of any database dependent on voluntary reporting. However, all participating sites agree, as a condition of participation, that all of their consultations will be entered into the Registry, thus minimizing such bias. In the initial years of the Registry, data quality had been the responsibility of the participating sites, which could lead to missing, inconsistent, or unclear data capable of leading to underreporting. In 2014, the ToxIC Registry initiated a centralized quality assurance review of Registry data, to help reduce issues such as incorrectly coded or absent data fields. The degree of detail concerning therapy was also variable. While it is likely that many fatality cases received certain aspects of critical care, such as intubation or IV fluids, documentation of therapy was relatively minimal in some cases. With the initiation of a more centralized quality improvement program, the ToxIC Registry will work toward reducing issues such as incorrectly coded or absent data fields, and programming changes to help differentiate missing/skipped data fields from "not applicable/none." This has now been applied in several areas including clinical signs and symptoms, treatment, and outcome (death) with the aim to improve case completeness and data quality in future years.

In addition, while it may be inferred from the type of treatment rendered (Tables 34, 35, 36, 37, 38, 39, and 40), the Registry lacks a mechanism to directly describe the relative severity of toxicity (aside from fatality) in any specific case. Currently, a study is underway, and data is being collected, aimed at designing a severity scoring system for ToxIC. Furthermore, by not being population-based, the ToxIC Registry has a specific ascertainment bias, which is present by design. The key inclusion criterion for entry into the Registry is the consultation by a medical toxicologist. Thus, Registry cases represent patients for whom there was a concern for significant toxicity. Cases of no, or mild, toxicity are likely to be underrepresented.

In response to data from earlier years, several changes were initiated in 2014 including improved demographic information on race and ethnicity to better identify subgroups

potentially at higher risk or specific toxic encounters. Unfortunately, this variable was initiated mid-year with limited detailed response, with a large proportion of participating institutions indicating "Unknown" for the two variables: 32.8 % race and 29.5 % ethnicity (Table 4). In order to provide consistent and useful information, the Registry will need to continue to actively inform and follow up with sites to improve the data quality on this important social indicator.

Another 2014 data change focused on refining the information collected on events related to intentional pharmaceutical use (52.4 % cases in 2014), specifically by adding an additional information requirement to detail the presence of attempt at self-harm in any intentional exposure. This information was provided for the majority of relevant cases (Table 7), therefore enabling future study into agent type, treatment provided, and patient outcome in cases of self-harm with suicidal intent.

Also in 2014, concerns around another type of pharmaceutical exposure, specifically adverse drug reactions (ADRs), continue. Over the year, 410 events were identified as ADRs, and another 175 as adverse drug events (ADEs), 4.5 and 1.9 %, respectively (data not presented). However, concerns persist to the relative completeness of the data field. In the future, the Registry will include more stringent data entry requirements, including that each case must be documented as an ADR (undesirable effect medication at a normal dose) or a medication error, in order to submit a case to the Registry. Additional question subfields related to type of event (e.g., exaggeration, continuing action, etc.), or error (e.g., administering, dosing, dispensing error, etc.), type of intervention, and strength of causality are now required. By better elucidating ADR-related events, the Registry aims to recreate a large, detailed case set for more effective descriptive analysis and to determine the relative engagement, and influence of, medical toxicologists in these cases.

Fatality data has also been expanded to include the withdrawal of care in poisoning cases. Information regarding withdrawal of care collected in this and future Registry reports will help increase understanding of a controversial issue for a subset of severe poisoning and other exposure events [8].

Conclusions

The majority of cases requiring medical toxicology consultation in 2014 involved intentional or unintentional exposure to pharmaceutical products. Non-opioid analgesics, sedative-hypnotic agents, and opioids remain the most commonly encountered agent classes. Though nearly two thirds of patients required some form of medical treatment, fatalities were uncommon.

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