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Characteristics of Substance-Related Toxicity Deaths in Ontario

Stimulant, Opioid, Benzodiazepine, and Alcohol-Related Deaths

A Report By
The Ontario Drug Policy Research Network
and Public Health Ontario

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Background

Alcohol and drug toxicities continue to be a significant public health concern both in Canada and globally.[1, 2] Coinciding with the COVID-19 pandemic emergency starting in March 2020, deaths due to accidental alcohol and drug toxicities increased 37% from 2020 to 2021 in Canada, with a disproportionate number occurring among younger populations.[1] These deaths were mostly attributable to opioid poisonings where fentanyl – primarily from the unregulated drug supply – directly contributed to the death.[3, 4] Although opioids were directly responsible for the vast majority of alcohol and drug toxicity deaths across Canada, there has been increasing attention on the harms caused by other substances, either alone or in combination with opioids.[1, 3-5] In British Columbia, stimulants, alcohol, and benzodiazepines were the top three non-opioid drugs involved in drug toxicity deaths caused by unregulated substances from 2019 to 2022.[4] Further, alcohol-attributable fatalities (including alcohol-induced chronic and acute conditions) have increased 18% from 2020 to 2021 in Canada, the largest year-over-year change seen in the last 20 years.[1] Similar increases have been observed in the United States in recent years.[5] Benzodiazepine and stimulant toxicities have also been on the rise in Canada[3, 6] and the United States.[7, 8]

Polysubstance use and the adulteration of drug supplies can complicate healthcare responses, particularly when multiple sedating substances are used together, contributing to increasing fatalities in the Canadian population.[9] Importantly, the use of multiple substances has been associated with worse outcomes compared to people who use only one substance, including an increased risk for toxicity-related morbidity and mortality and reduced effectiveness of toxicity-reversing agents such as naloxone, which only reverses the effects of opioids.[6, 10] In Ontario, the high prevalence of polysubstance contributions to opioid toxicity deaths has been reported, with stimulants being the most commonly identified substance in recent years, contributing to half of all accidental opioid toxicity deaths.[11] Although less commonly involved in opioid-related deaths, co-use of opioids with sedatives or respiratory depressants, such as benzodiazepines, is increasingly common as these substances have entered the unregulated fentanyl supply, are especially complex to treat, and are associated with long-term negative health effects and high fatality rates.[6, 10, 12, 13]

In Ontario, detailed data on fatal substance-related toxicities have largely been restricted to opioid toxicity deaths, with limited data available on the relative frequency of toxicity deaths attributable to alcohol, benzodiazepines, and stimulants, and the frequency of polysubstance use among these deaths. Given signals of increasing death rates due to alcohol and other drugs in Canada, there is a need for reporting of trends in toxicity deaths due to alcohol, stimulants, and benzodiazepines, either alone or in combination with other substances, including opioids. Therefore, this report describes trends and circumstances surrounding fatal substance-related toxicities broadly in Ontario, combining data on deaths due to alcohol, stimulants, benzodiazepines, and opioids.

Methods

Setting

We conducted a descriptive cross-sectional study to describe trends and characteristics among people who died from an alcohol, stimulant, benzodiazepine, or opioid toxicity in Ontario, Canada. We defined a substance-related death as an acute toxicity death that was accidental and resulted from the direct contribution of the consumed substance, regardless of how the substance was obtained.

Data Sources

We obtained all data from ICES, an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement.[14] To capture data on opioid toxicity deaths, we used the Drug and Drug/Alcohol Related Death Database (DDARD), which contains records from coronial investigations completed by the Office of the Chief Coroner/Ontario Forensic Pathology Service. To exclude potential heroin metabolites from post-mortem toxicology, we removed the indication of morphine (a heroin metabolite) and flagged as heroin in instances where there was a presence of both morphine and 6-monoacetylmorphine (6-MAM).

To capture data on alcohol, stimulant, and benzodiazepine toxicity deaths, we used a newly derived database which includes information on deaths that occurred between January 1st, 2018 and December 31st 2021 in Ontario. This novel database was created using data from the Office of the Chief Coroner of Ontario as a supplement to the opioid-related death data already housed at ICES in the DDARD, and only includes deaths that do not involve opioids as direct contributing factors. A predefined algorithm was used to identify deaths where alcohol, stimulants, and/or benzodiazepines were direct contributors to death, where manner of death was "accident"; death factor was "drug toxicity", "drug and alcohol toxicity" or "alcohol toxicity"; and at least one stimulant, benzodiazepine or alcohol was listed in the cause of death. Note that these deaths are subject to change, as they are based on ongoing investigations.

We combined the Alcohol, Stimulant, and Benzodiazepine-Related Mortality Database with the existing DDARD. The combination of both datasets allowed for the broad assessment of all alcohol, stimulant, benzodiazepine, and opioid-related deaths in Ontario. Substance toxicity deaths in this report reflect those where the above-described substances were determined to be direct contributors to death. Furthermore, due to a lack of clear thresholds to determine whether benzodiazepines in the unregulated drug supply (e.g., etizolam, flualprazolam, flubromazolam) directly contributed to death, we also reported the percentage of opioid toxicity deaths where benzodiazepines were detected (but not necessarily direct contributors to death).

To capture data on sociodemographic characteristics and population denominators, we linked the above datasets to the Registered Persons Database, which includes demographic information on individuals registered under Ontario's universal health insurance plan. Income quintile and rurality were determined using Statistics Canada's standard geographical areas using the Postal Code Conversion File and reference file.

Small cells (N<6) were suppressed according to ICES privacy policies, and ranges were provided as needed to prevent back-calculation of small cells. Stratifications that resulted in a substantial number of small cells were also removed from the report. Datasets were linked using unique encoded identifiers and analyzed at ICES.

Measures

1. Trends

Trends were reported from January 1, 2018 to December 31, 2021. We reported monthly death rates directly attributable to alcohol, stimulants, benzodiazepines, and opioids separately (i.e., groups are not mutually exclusive). Stimulant trends were reported overall and by stimulant type (cocaine, methamphetamine, and amphetamine). We also reported monthly death rates where one, two, or three or more substances directly contributed to death, among all substances combined (i.e., alcohol, stimulants, benzodiazepines, and opioids). The percentage of alcohol, benzodiazepine, and stimulant toxicity deaths that also involved an opioid as a direct contributor was also reported, as well as the percentage of opioid toxicity deaths that involved other substances (alcohol, stimulants, or benzodiazepines).

We additionally created mutually exclusive groups representing each combination of the four substances as direct contributors and reported the number and proportion of total substance-related deaths falling into each of these categories in the COVID-19 pandemic and pre-pandemic periods (described below).

2. Characteristics

Using ICES data in the final year of the study period (2021), we reported the following demographic characteristics: age group (<25, 25 to 44, 45 to 64, 65+ years), sex, neighbourhood income quintile, location of residence (urban/rural, Northern/Southern), location of incident, number of substances directly involved in death and the presence of other substances (alcohol, stimulant, benzodiazepine, opioid) directly involved in death. See Appendix A for definitions. We stratified these characteristics by overall substance groupings and by whether the death was caused by one (mono-) or more than one (poly-) substance across substance groupings. Poly-substance deaths are counted in more than one overall substance grouping (e.g., a combined opioid and stimulant death would be captured in both the opioid and stimulant overall categories). For stimulant toxicity deaths, we also stratified by substance type (cocaine [which includes crack cocaine], methamphetamine, amphetamine). For benzodiazepine and opioid toxicity deaths, we also stratified by pharmaceutical vs non-pharmaceutical origin.

Analysis

We reported monthly rates in substance toxicity deaths over time from January 1, 2018 to December 31 2021, adjusted based on the overall Ontario population (per 100,000). For assessing changes in substance combinations over the pandemic, we defined the pre-pandemic and pandemic periods as March 17, 2018 to December 31, 2019 and March 17, 2020 to December 31, 2021, respectively. We used descriptive statistics to describe patterns, and chi-square/Fisher's exact tests to compare percentages where categories were mutually exclusive. To assess whether differences were statistically significant, we employed a significance level of 0.05.

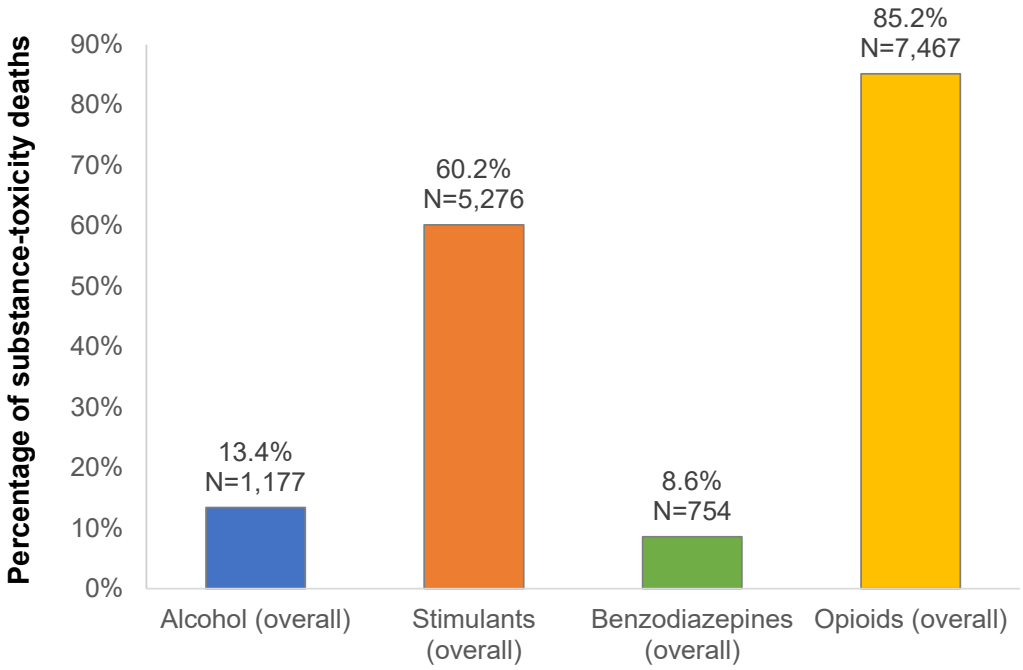
Key Findings

NOTES FOR ALL ANALYSES

- All analyses were restricted to accidental deaths.
- See Appendix B for complete data tables.
- Unless otherwise stated, substance toxicity deaths reflect direct contributors to death; however, other substances detected in post-mortem (but not direct contributors) may be present.
- Substance toxicity deaths may overlap (i.e., belong to more than one substance groupings), unless explicitly stated as a mono-substance death.

Trends and characteristics across overall substance groupings

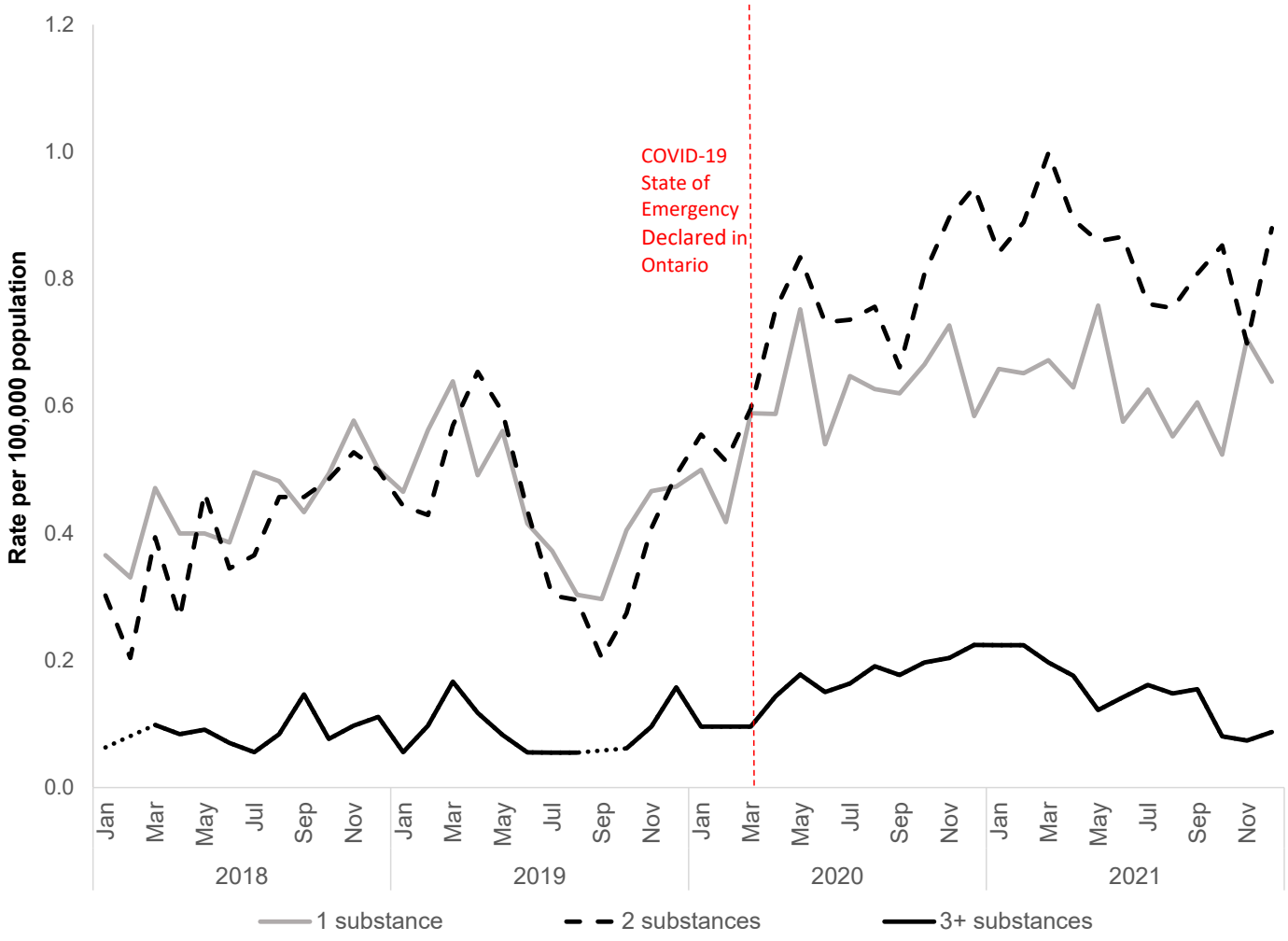
Figure 1. Proportion of substance toxicity deaths directly attributable to individual substances from 2018 to 2021



There were 8,767 accidental substance toxicity deaths from 2018 to 2021 in Ontario that involved alcohol, stimulants, benzodiazepines, and/or opioids. Overall, substance toxicity deaths nearly doubled from 1,586 in 2018 to 2,886 in 2021 in Ontario (data not shown).

Among these 8,767 individuals who died, 85.2% of deaths involved opioids (N=7,467), 60.2% involved stimulants (N=5,276), 13.4% involved alcohol (N=1,177), and 8.6% involved benzodiazepines (N=754). The median age at death was 40 years (IQR: 32-52 years) and 74.6% (N=6,544) were male. When location of incident was known (N=7,921), three-quarters of incidents occurred in a private residence (74.8%, N=5,924).

Figure 2. Toxicity death rates (per 100,000 population) stratified by number of substances directly involved†



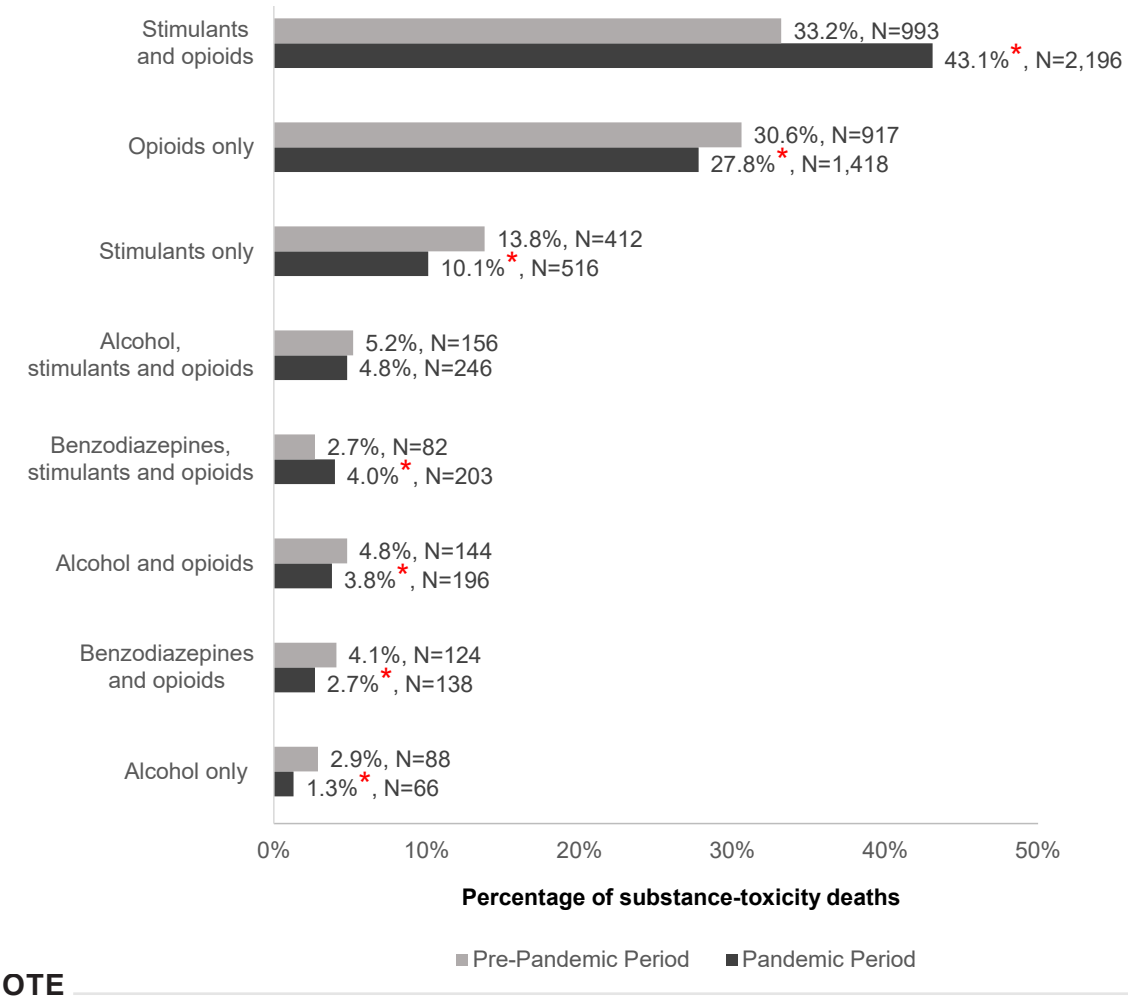
NOTE

- Dotted lines for three or more substances indicate cell suppression to preserve anonymity (i.e., N<6).
- †Counts of substances are restricted to broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).

Generally, there was a similar trend in deaths involving one and two substance groups, with those involving three or more substance groups being less common. After the COVID-19 State of Emergency however, deaths involving two substances surpassed those involving only one substance.

From January 2018 to December 2021, the monthly number of deaths involving one substance doubled (N=52 to 95, 0.4 to 0.6 per 100,000 population), and the number of deaths involving two substances tripled (N=43 to 131, 0.3 to 0.9 per 100,000 population). The increase in deaths involving two substance groups was likely driven by rising deaths involving a combination of opioids and stimulants (see figure below). The monthly number of deaths involving three or more substance groups also increased across the study period, although to a lesser degree (N=9 to 13, 0.06 to 0.09 per 100,000 population).

Figure 3. Proportion of substance toxicity deaths directly attributable to each mono- or polysubstance during the COVID-19 pandemic and pre-pandemic periods†

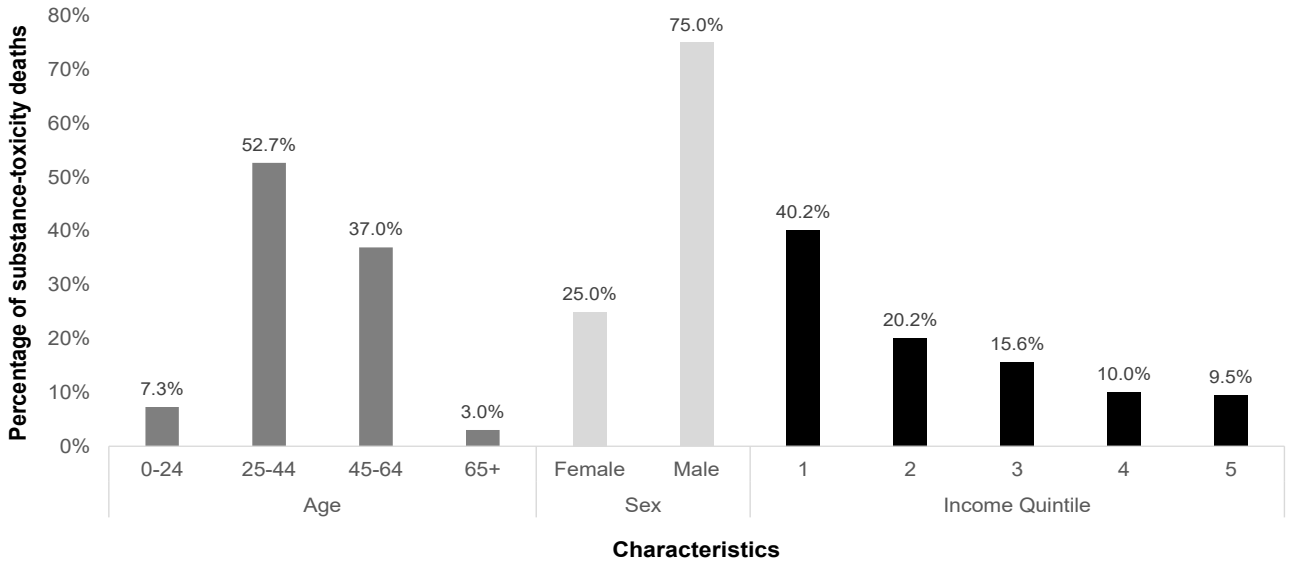


NOTE

- All categories are mutually exclusive.
- All substance combination categories <1% during both the pre-pandemic and pandemic periods were omitted from the figure.
- Red asterisk indicates statistically significant difference between pre-pandemic and pandemic periods ($p<0.05$).
- Benzodiazepines were detected in 62.4% of deaths directly caused by opioids alone.
- † Pre-COVID-19 period: March 17, 2018 to December 31, 2019. COVID-19 period: March 17, 2020 to December 31, 2021.

Stimulants and opioids, either alone or in combination, directly contributed to the majority of substance-related deaths both before and during the COVID-19 pandemic period (81.0%, N=4,130 in the pandemic period). In the pandemic period, the combination of stimulants and opioids as direct contributors made up the highest proportion and number of substance-related deaths (43.1%, N=2,196), and exhibited the largest increase between the pre-pandemic and pandemic periods (33.2% to 43.1%, $p<0.001$). Notably, the absolute number of deaths involving both stimulants and opioids more than doubled during the pandemic (N=993 to 2,196). The absolute number of deaths increased for all categories displayed above during the pandemic, with one exception. The number and proportion of deaths where only alcohol was directly involved declined during the pandemic (from N=88 to 66 deaths; 2.9% to 1.3%; $p<0.001$), although the number of deaths involving alcohol with other substances (e.g., stimulants and opioids) increased over this time.

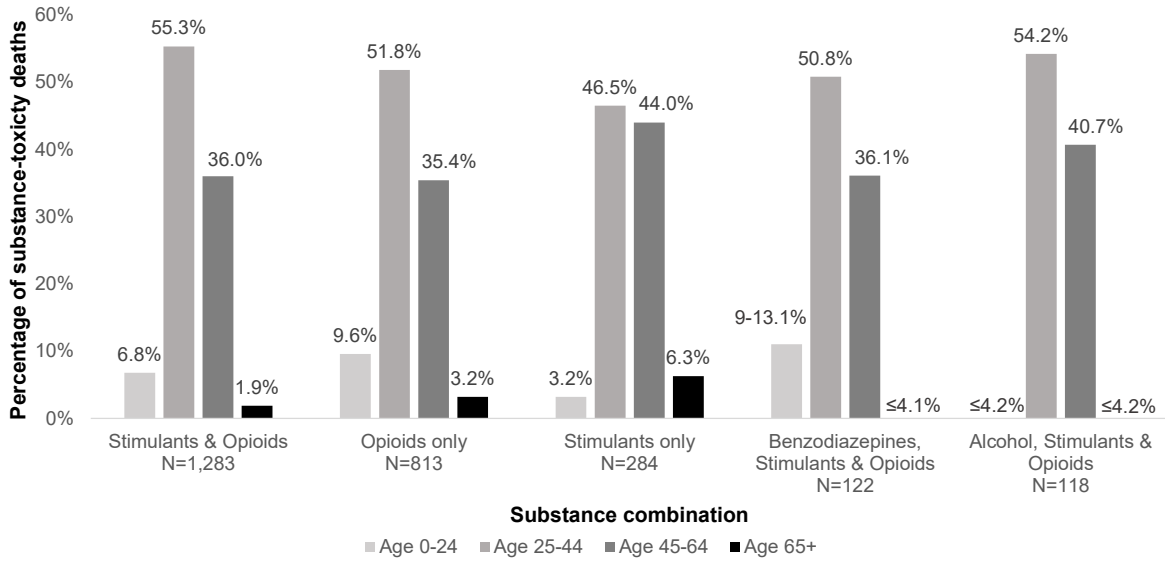
Figure 4. Proportion of substance toxicity deaths in 2021, by age, sex and neighbourhood income quintile in 2021



Overall, the highest proportion of individuals who died from an alcohol-, benzodiazepine-, opioid- and/or stimulant toxicity death were between the ages of 25 to 44 (52.7%), followed by 45 to 64 (37.0%). Only approximately 10% of substance-related deaths occurred in the oldest (65+) and youngest (0-24) age groups, combined. Males comprised three-quarters (75.0%) of all substance-toxicity deaths, and deaths were skewed towards neighbourhoods with the lowest income quintile. When considering geographic location of residence, the rate of substance-toxicity deaths was almost three times higher in Northern Ontario than in Southern Ontario (47.9 vs. 16.9 per 100,000 population, respectively; see Appendix B, Table B1). The rates were similar when stratified by urban vs. rural location of residence (18.5 vs 17.0 per 100,000 population in urban vs. rural areas; see Appendix B, Table B1).

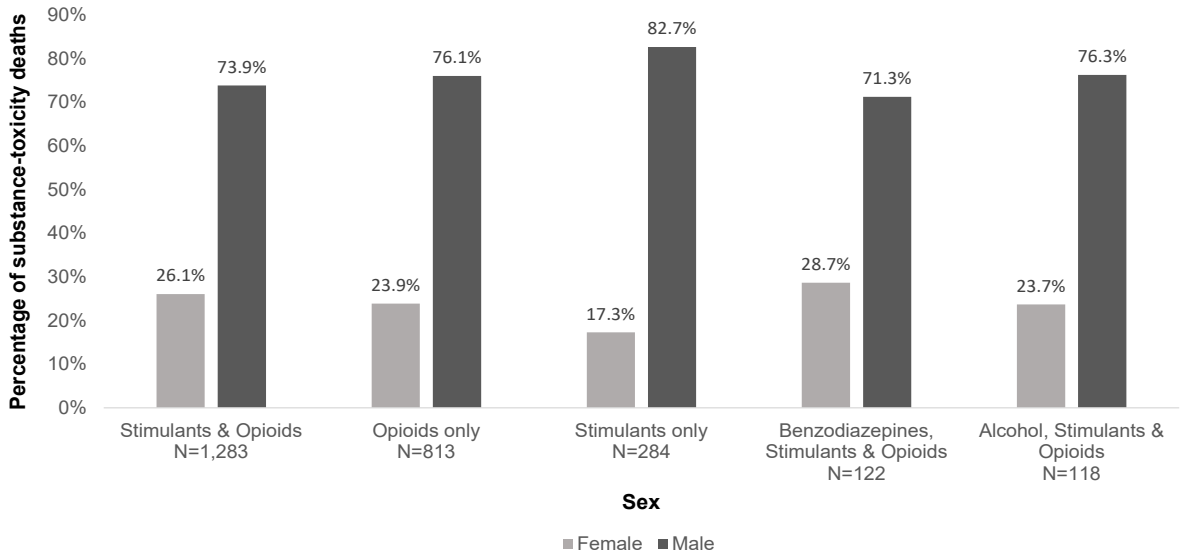
The following 4 figures (Figures 5 to 8) summarize demographic characteristics of substance-related deaths in Ontario in 2021, stratified across the 5 most prevalent substance-combinations (as presented in Figure 3 above). Altogether, they account for 90.7% of substance toxicity deaths that occurred in 2021.

Figure 5. Age distribution of the 5 most common substance toxicity death categories in 2021



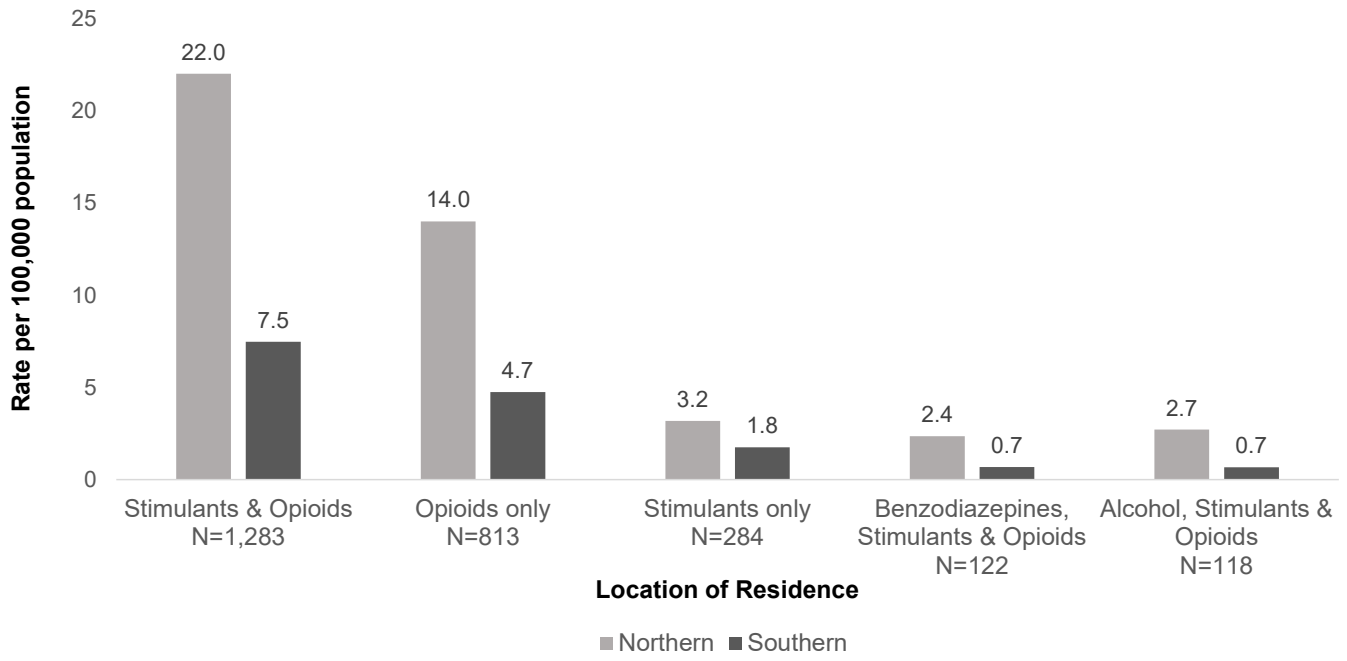
In general, the age distribution was similar across the top 5 substance combination categories, where the highest proportions of substance toxicity deaths were among adults aged 25 to 44 (46.5-55.3%) and 45 to 64 years (35.4-44.0%). In deaths involving stimulant toxicities alone, the age distribution was skewed slightly more towards older individuals than in the other four substance combination categories, all of which involved opioids..

Figure 6. Sex distribution of the 5 most common substance toxicity death categories in 2021



Across all of the top 5 substance combinations, the proportion of deaths were higher among males than females. A similar proportion of toxicity deaths were among males across the 4 substance combinations involving opioids, with males comprising approximately 71.3 to 76.3% of these toxicity deaths. Deaths involving stimulants alone were even more concentrated among males (82.7% male).

Figure 7. Geographic location of residence of the 5 most common substance toxicity death categories in 2021

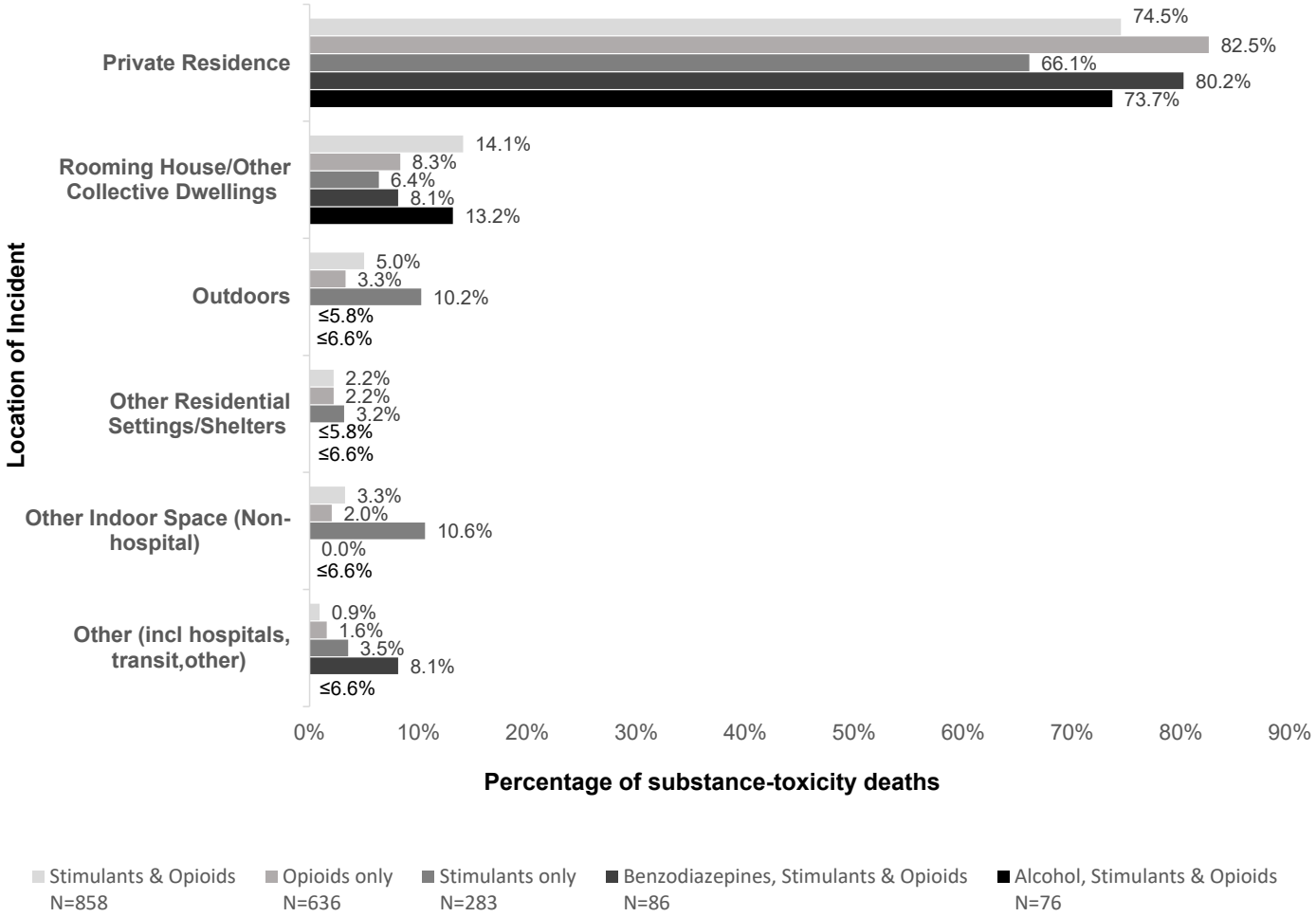


NOTE

Unknown Northern/Southern location ranged from 0.8% to 4.1% across substance combinations.

The rate of substance-related deaths were higher in Northern Ontario across the top 5 substance combinations, although the relative differences between Northern and Southern Ontario differed slightly. Among the 4 substance combinations involving opioids, rates of death in Northern Ontario were approximately three times higher than those observed in Southern Ontario. Although deaths from stimulant toxicity alone were also elevated in Northern Ontario, the difference in rate compared to Southern Ontario was smaller (3.2 vs 1.8 per 100,000 population). Higher substance-related death rates in the North likely reflect disparities in access to substance use treatment and harm reduction programs in more remote parts of the province, as well as the harms resulting from systemic social inequities and intergenerational trauma experienced by First Nations People, which make up a large proportion of Northern Ontario communities.[16, 17] Rates of toxicity deaths were similar between urban and rural areas for all of the top 5 substance categories (Appendix B, Table B1).

Figure 8. Location of incident of the 5 most common substance toxicity death categories in 2021



NOTE

Unknown location of incident was excluded from the denominator. Incident location was unknown in 0.4% of the stimulants only toxicity deaths, and ranged between 21.8 and 33.1% of cases for the other 4 substance combinations (all involving opioids).

Where reported or known, most substance toxicity events occurred in private residences across all of the top 5 substance combinations, although the proportion of deaths in private residences was lower in deaths involving only stimulants (66.1%) compared to the other 4 substance combinations (73.7-82.5%). For the 4 substance combinations containing opioids, rooming houses or other collective dwellings were the next most common location of toxicity incident (8.1-14.1%). Among deaths involving stimulants alone, toxicity incidents were much more likely to occur in non-hospital indoor spaces (10.6%) and outdoors (10.2%) compared to deaths from other substance combinations (see Appendix B, Table B1).

Alcohol toxicity deaths

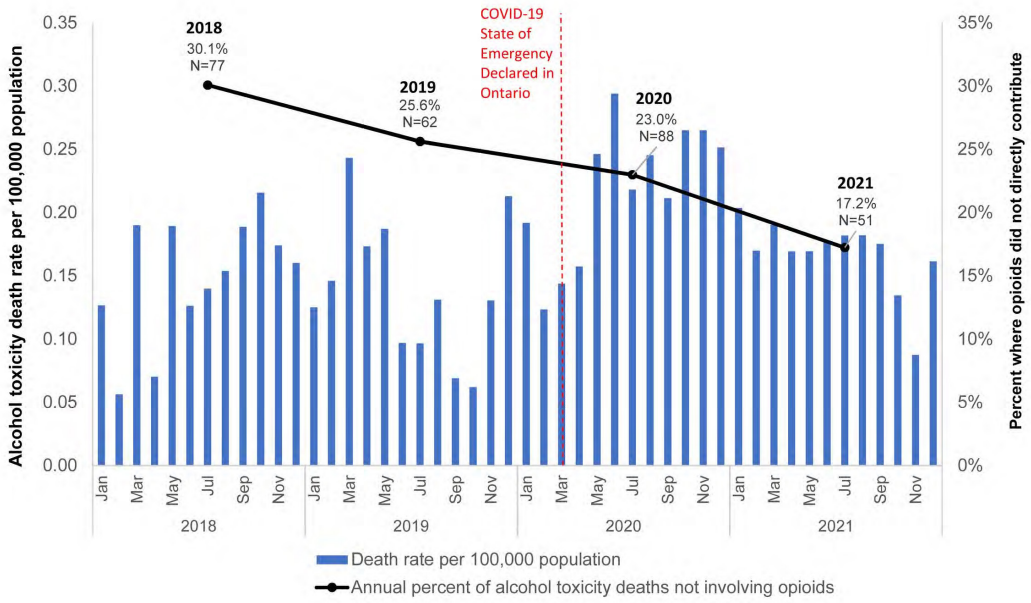
Trends & characteristics

SUMMARY

16% Increase in the number of alcohol toxicities from 2018 to 2021

13% of all substance-related deaths from 2018 to 2021 **involved alcohol** as a direct contributor to death

296 Alcohol toxicity **deaths** in 2021



Alcohol Toxicity Deaths in 2021

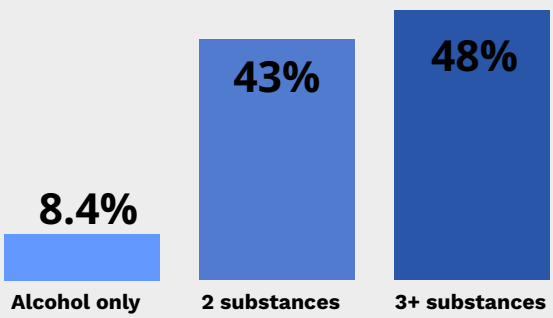
92% of deaths had **other substances** directly contribute to death

83% involved **opioids**

10% involved **benzodiazepines**

52% involved **stimulants**

*Proportion of deaths by **number of substances** directly contributing to death*



Demographics

73% of deaths occurred among **males**

The median age at death was **41 years**

74%* of deaths occurred in a **private residence**

Alcohol toxicity death rates were **3x higher** in **Northern** vs **Southern Ontario**

Deaths rates were **similar** in **rural** vs **urban** residences

Rural

1.8 deaths per 100,000 people

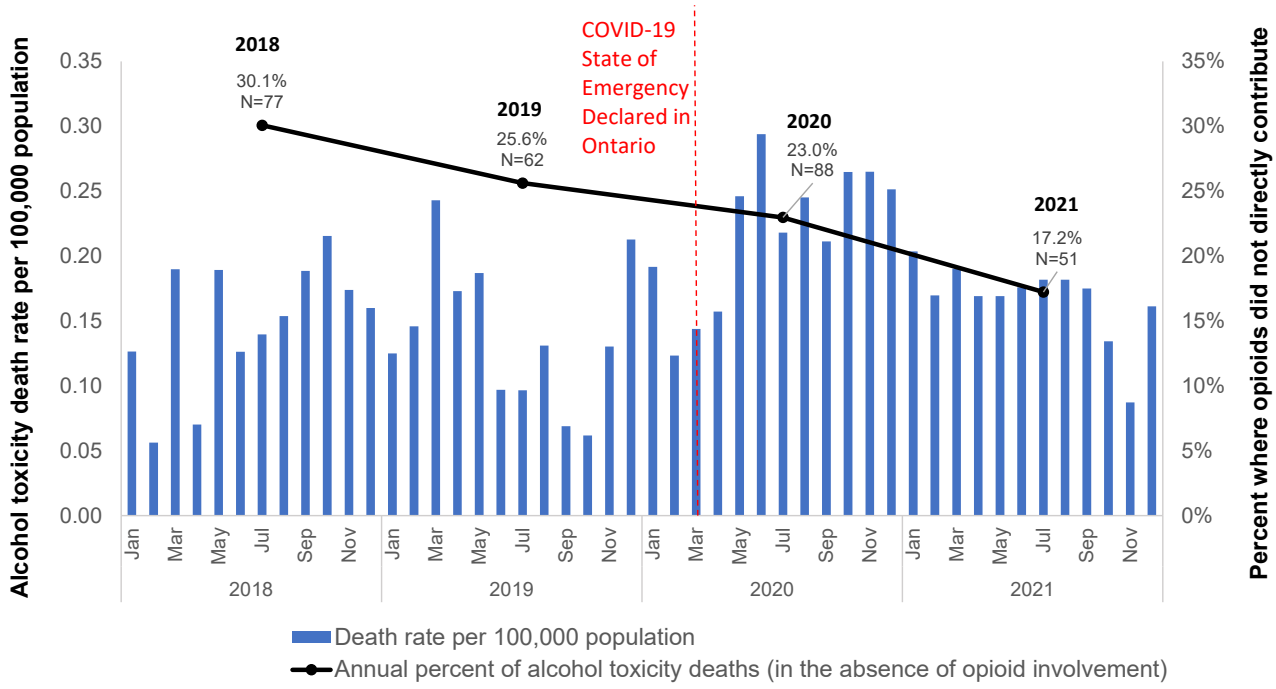
Urban

1.9 deaths per 100,000 people

*This proportion is among cases where location of incident was known

Detailed Analyses on Trends and Characteristics of Alcohol Toxicity Deaths

Figure 9. Alcohol toxicity death trends from 2018 to 2021



Alcohol toxicity deaths increased 15.6% from 256 in 2018 to 296 in 2021. When only considering alcohol toxicity deaths without the involvement of opioids, deaths reached a maximum of 88 in 2020, then fell to 51 in 2021. The proportion of alcohol toxicity deaths in the absence of opioid involvement decreased steadily from 30.1% in 2018 to 17.2% in 2021.

Figure 10. Proportion of toxicity deaths directly attributable to alcohol in 2021, by number of substance groups directly contributing to death†

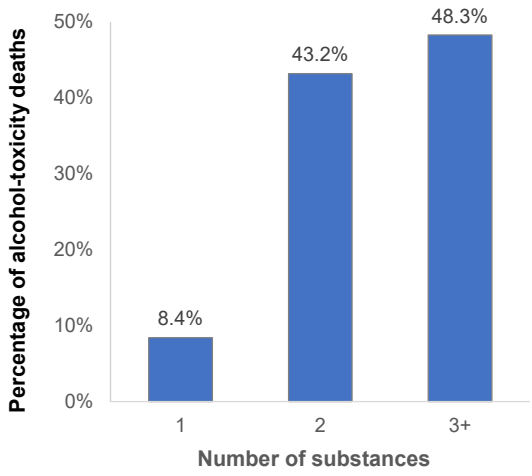
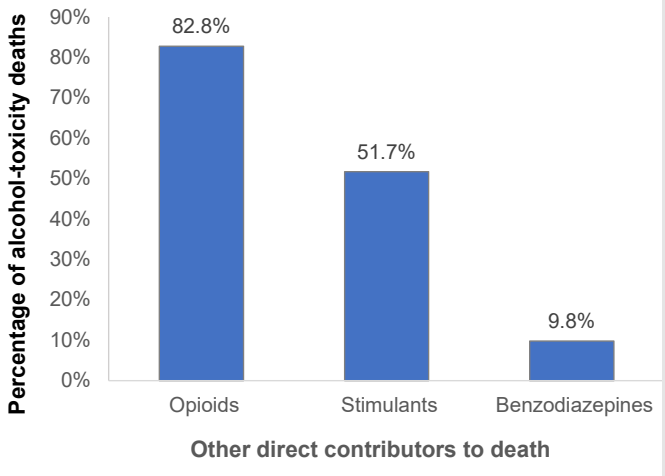


Figure 11. Proportion of toxicity deaths directly attributable to alcohol in 2021, by other substances directly contributing to death



NOTE

† Number of substances represent broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).

Alcohol toxicity deaths most often involved other substance groups (2 substances, 43.2%, N=128; 3+ substances, 48.3%, N=143) and rarely involved only alcohol (8.4%, N=25). Opioids were the most common co-contributor to alcohol toxicity death (82.8%, N=245), followed by stimulants (51.7%, N=153). One in ten (N=29) alcohol toxicity deaths involved benzodiazepines as a direct contributor.

Table 1. Descriptive characteristics, toxicity deaths directly attributable to alcohol in 2021, by mono versus polysubstance

	Alcohol only	Alcohol + other substances
Total deaths (N)	25	271
Age, median (IQR)	49 (37-54)	41 (34-52)
Age category (N, %)		
0 to 44	12 (48.0%)	156 (57.6%)
45+	13 (52.0%)	115 (42.4%)
Sex (N, %)		
Female	7 (28.0%)	73 (26.9%)
Male	18 (72.0%)	198 (73.1%)

NOTE

Column categories are mutually exclusive. There were no statistically significant differences between alcohol only vs alcohol plus other substances for any of the characteristics reported ($p<0.05$). Categories were combined where there were small counts. Reporting of income, location of residence, and incident location across strata were not included due to small cell counts. See previous figures or Appendix B, Table B2 for characteristics reported for alcohol (overall).

Among overall alcohol toxicity deaths, the median age at death was 41 years (IQR: 34-52 years) and 73.0% (N=216) of deaths occurred among males. Overall, alcohol toxicity death rates were three times higher in Northern vs Southern Ontario (5.5 vs 1.7 deaths per 100,000, N=47 vs 243), with similar rates across urban (1.9 deaths per 100,000, N=255) and rural (1.8 per 100,000, N=28) residences. When considering location of incident, 74.2% (N=155 of 209) of alcohol toxicity deaths occurred in a private residence (where location of incident was known).

Although not statistically significant, median age was nearly one decade older among those who died from alcohol toxicity (49 years, IQR: 37-54) compared to alcohol plus other substances (41 years, IQR: 34-52, p=0.15), while sex did not differ (72.0% vs 73.1% male, p=0.91). Findings for sex were consistent with overall deaths due to alcohol.

Stimulant toxicity deaths

Trends & characteristics

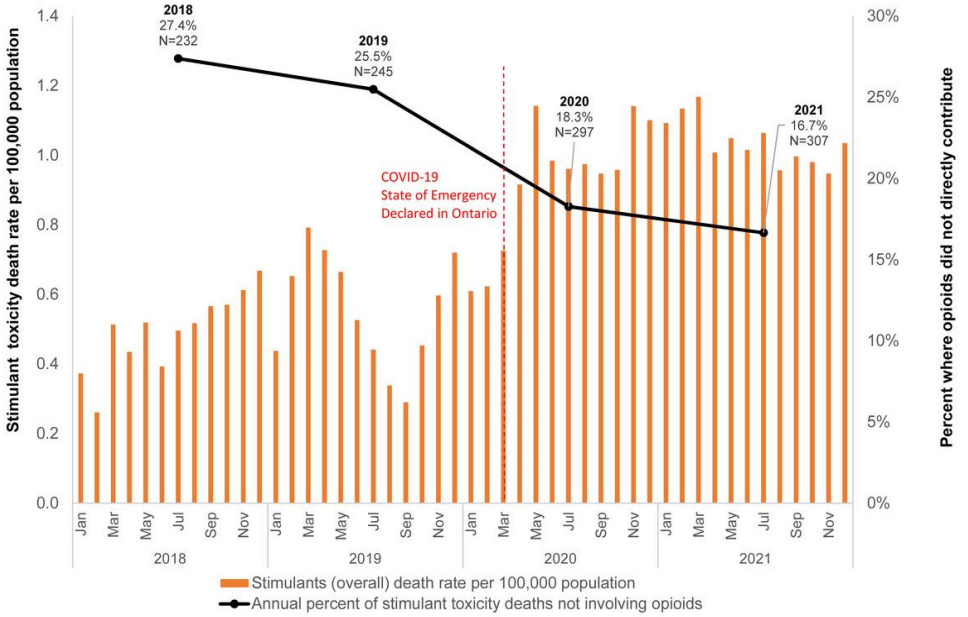
SUMMARY

2x Increase in the number of stimulant toxicity deaths from 2018 to 2021

60% of all substance-related deaths from 2018 to 2021 **involved stimulants** as a direct contributor to death

1843 Stimulant toxicity **deaths** in 2021

- **68%** Cocaine
- **48%** Methamphetamine
- **17%** Both cocaine and methamphetamine
- **7%** Amphetamine

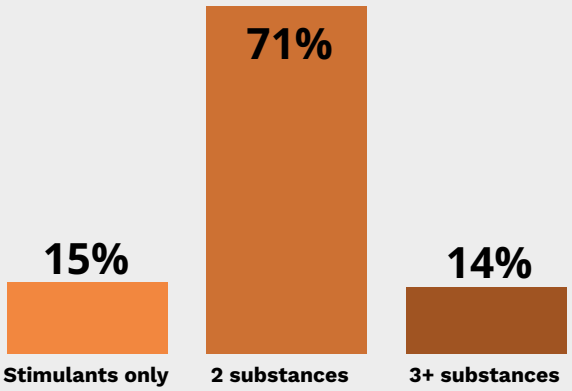


Stimulant Toxicity Deaths in 2021

85% of deaths had **other substances** directly contribute to death

- **83%** involved **opioids**
- **8%** involved **benzodiazepines**
- **8%** involved **alcohol**

*Proportion of stimulant-related deaths by **number of substances** directly contributing to death*



Demographics

75% of deaths occurred among **males**

The median age at death was **40 years**

73%* of deaths occurred in a **private residence**

Death rates for **cocaine** and **methamphetamine** were **3x higher** in **Northern** vs. **Southern Ontario**

Deaths rates were **similar** in **rural** vs **urban** residences

Rural

11 stimulant deaths per 100,000 people

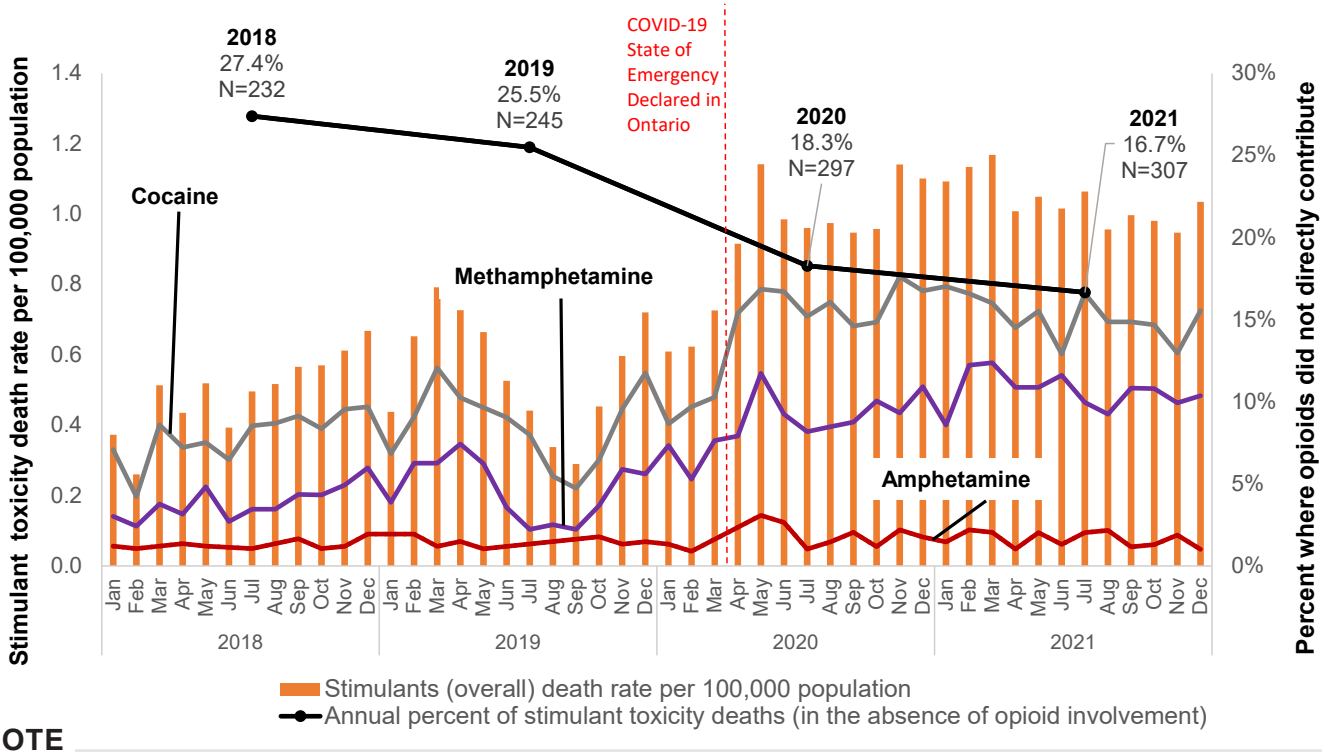
Urban

12 stimulant deaths per 100,000 people

*This proportion is among cases where location of incident was known

Detailed Analyses on Trends and Characteristics of Stimulant Toxicity Deaths

Figure 12. Stimulant toxicity death trends from 2018 to 2021

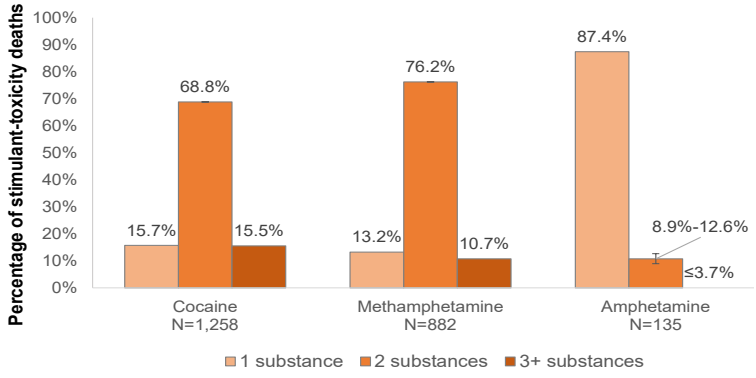


NOTE

Dotted lines for amphetamine indicate suppressed data due to small cell counts (i.e., N<6).

Stimulant toxicity deaths increased two-fold from 847 in 2018 to 1,843 in 2021. These increases were attributable to increases in deaths involving cocaine and methamphetamine, which made up 68.3% (N=1,258) and 47.9% (N=882) of stimulant toxicity deaths in 2021 respectively. Considering only stimulant toxicity deaths without the involvement of opioids, deaths gradually increased from 232 in 2018 to 307 in 2021. The proportion of stimulant toxicity deaths in the absence of opioid involvement decreased steadily from 27.4% in 2018 to 16.7% in 2021.

Figure 13. Proportion of toxicity deaths directly attributable to stimulant types in 2021, by number of substance groups directly contributing to death†

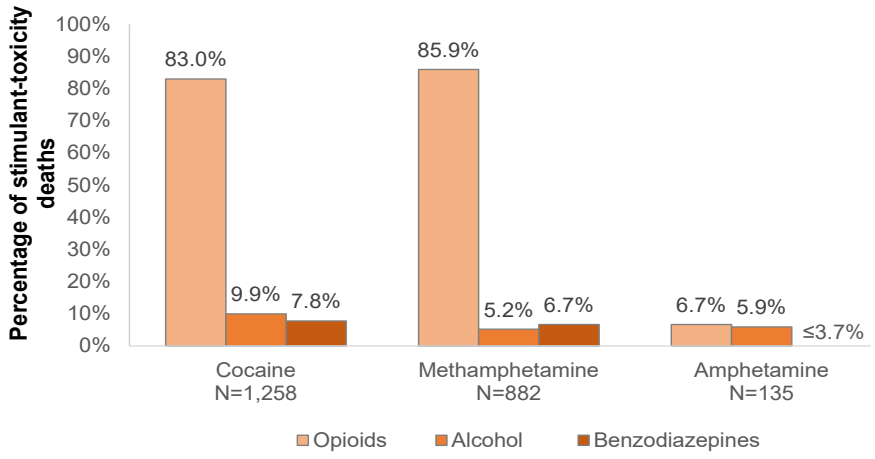


Overall, stimulant toxicity deaths most often involved two substance groups (70.8%, N=1,304), and less commonly involved only stimulants (15.4%, N=284) or three or more substance groups (13.8%, N=255; see Table 2 below). Similarly, cocaine and methamphetamine deaths often involved one additional non-stimulant substance group (cocaine: 68.8%, N=866; methamphetamine: 76.2%, N=672), whereas amphetamine toxicity deaths most often involved only stimulants (87.4%, N=118).

NOTE

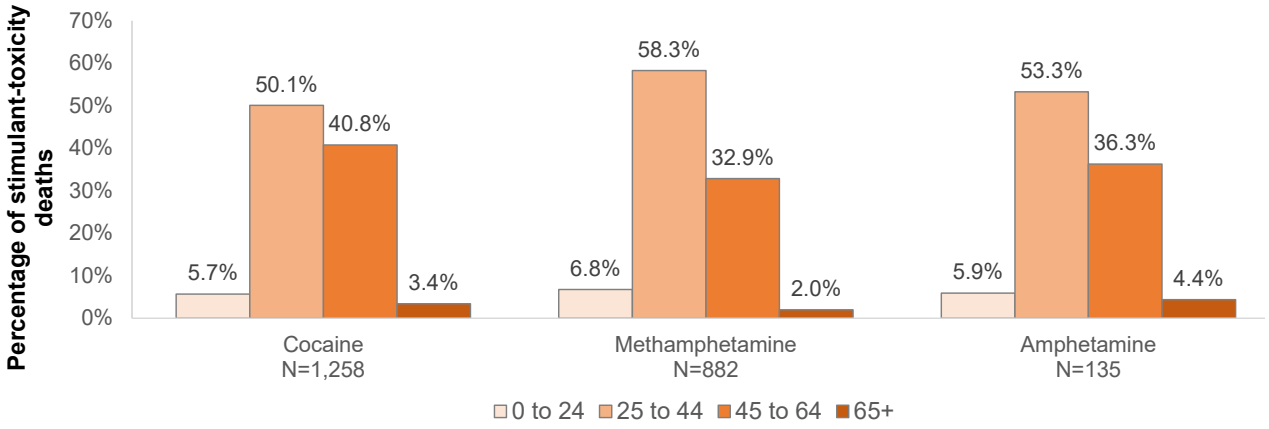
† Number of substances represent broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).

Figure 14. Proportion of toxicity deaths directly attributable to stimulant types in 2021, by other substances directly contributing to death



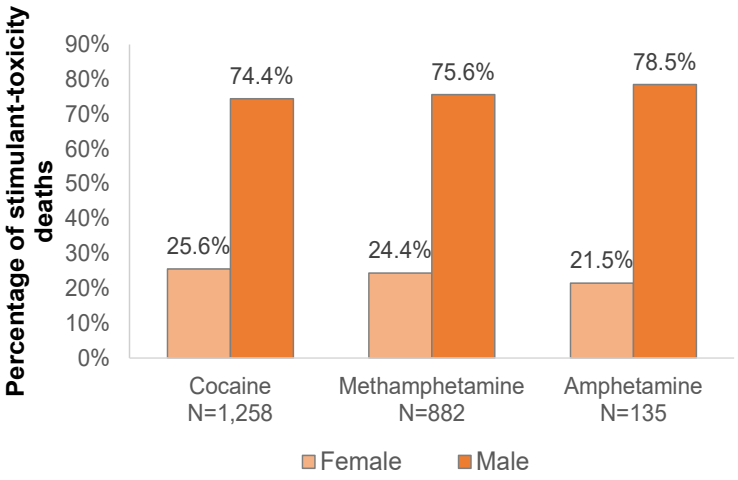
Overall, opioids were the most frequent co-contributors in stimulant toxicity death (83.3%, N=1,536), and there was a low involvement of alcohol (8.3%, N=153) or benzodiazepines (7.5%, N=138) as direct co-contributors to death (see Table 2 below). Similarly, cocaine and methamphetamine deaths most often involved opioids (cocaine: 83.0%, N=1,044; methamphetamine: 85.9%, N=758). Benzodiazepines and alcohol were rare as co-contributors to death across all stimulant types (<10% across all stimulant types).

Figure 15. Proportion of toxicity deaths directly attributable to stimulant types in 2021, by age



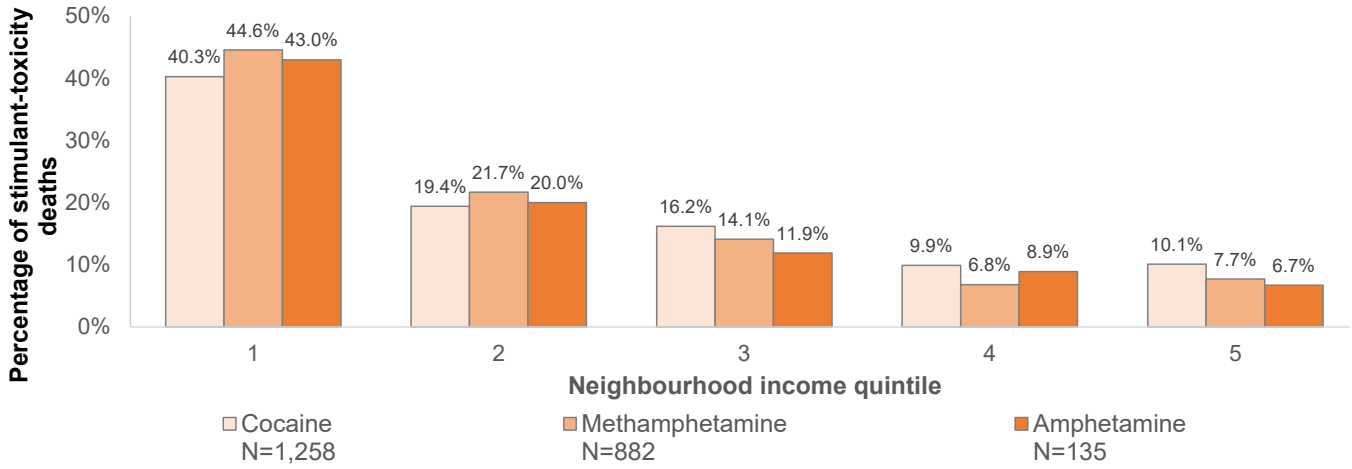
The age distribution across stimulant types was reflective of overall deaths due to stimulants (See Appendix B, Table B2). Age differences were present across stimulant types, with most stimulant deaths occurring among those aged 25 to 44 (50.1-58.3%), followed by 45 to 64 years (32.9-40.8%). There was a higher proportion of methamphetamine deaths occurring in the 25 to 44 year age group (methamphetamine, 58.3%, N=514) compared to 45 to 64 years (methamphetamine, 32.9%, N=290), while cocaine deaths were more evenly distributed across these two age groups (25 to 44 years, 50.1%, N=630; 45 to 64 years, 40.8%, N=513).

Figure 16. Proportion of toxicity deaths directly attributable to stimulant types in 2021, by sex



Overall, 75.0% (N=1,383) of stimulant toxicity deaths occurred among males. Consistent across stimulant types, there was a higher proportion of stimulant deaths occurring in males (74.4-78.5%) vs females (21.5-25.6%).

Figure 17. Proportion of toxicity deaths directly attributable to stimulant types in 2021, by neighbourhood income quintile

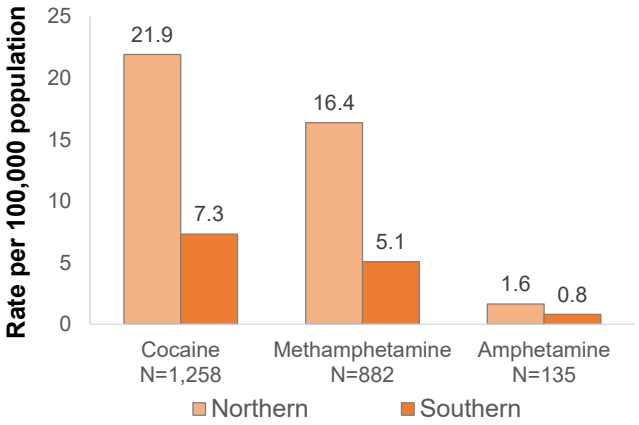


NOTE

- Unknown income was 4.1%, 5.2%, and 9.6% for cocaine, methamphetamine, and amphetamine, respectively.
- Neighbourhood income quintile is sorted from lowest (Q1) to highest (Q5) income.

An income gradient was seen across stimulant types, with the highest concentration of stimulant-toxicity deaths observed among those living in neighbourhoods with lowest income quintile (Q1: 40.3-44.6% of deaths) and the lowest concentration in the highest income quintiles (Q4 and Q5: 6.7-10.1%). Income differences across stimulant types were minimal and consistent with findings for overall stimulants (Q1: 41.8% and Q5: 9.4%; see Appendix B, Table B2).

Figure 18. Population-adjusted toxicity death rates directly attributable to stimulant types in 2021, by location of residence

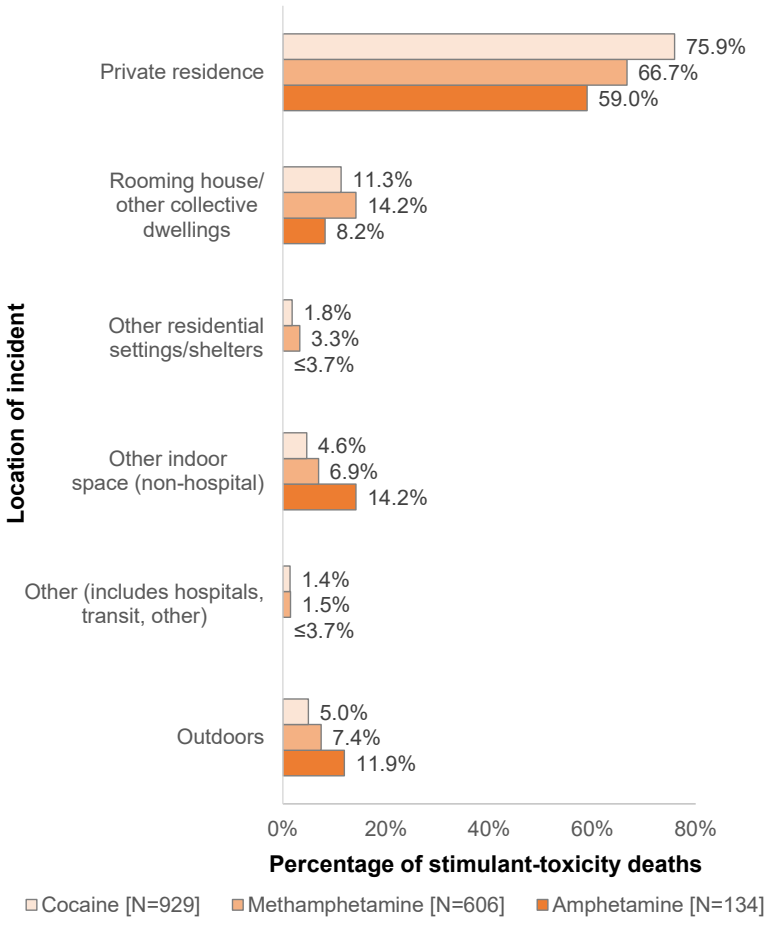


NOTE

Unknown urban/rural was 4.1%, 5.2% and 9.6% for cocaine, methamphetamine, and amphetamine, respectively. Unknown Northern/Southern was 2.3%, 2.2%, and 3.7% for cocaine, methamphetamine, and amphetamine, respectively.

Overall, stimulant toxicity death rates were three times higher in Northern (31.2 deaths per 100,000, N=265) vs Southern (10.8 deaths per 100,000, N=1,533) Ontario, and similar across urban (11.8 deaths per 100,000, N=1,588) and rural (11.0 deaths per 100,000, N=169) location of residence (see Table 3 below). Higher death rates in Northern (vs Southern) Ontario were observed across all stimulant types (1.6-21.9 per 100,000 vs 0.8-7.3 per 100,000). Death rates for cocaine and methamphetamine were three times higher in the North. Death rates were similar across stimulant types for urban vs rural residence locations, with slightly lower cocaine deaths rates in rural (vs urban) locations (6.9 vs 8.1 per 100,000; N=107 vs 1,100; data not shown).

Figure 19. Proportion of toxicity deaths directly attributable to stimulant types in 2021, by location of incident



NOTE

Unknown location of incident was excluded from the denominator in this figure, given that unknown location of incident differed by stimulant type. Incident location was unknown in 26.2%, 31.3%, and 0.7% of cases for cocaine, methamphetamine, and amphetamine, respectively.

Overall, 73.0% (N=973 of 1,333) of stimulant toxicity deaths occurred in a private residence (where location of incident was known; see Appendix B, Table B2). Compared to cocaine (75.9%, N=705), there was a lower proportion of methamphetamine (66.7%, N=404) and amphetamine (59.0%, N=79) deaths that occurred in private residences, and a higher proportion that occurred in other indoor spaces (non-hospital) (cocaine: 4.6%, N=43; methamphetamine: 6.9%, N=42; amphetamine: 14.2%, N=19) and outdoors (5.0%, N=46; 7.4%, N=45; 11.9%, N=16). There was a slightly higher proportion of methamphetamine deaths that occurred in rooming houses/other collective dwellings (14.2%, N=86) compared to cocaine (11.3%, N=105) and amphetamine (8.2%, N=11).

Table 2. Descriptive characteristics, toxicity deaths directly attributable to stimulants in 2021, by mono versus polysubstance

	Stimulants (overall)	Stimulant only	Stimulants + other substances	Stat. sig.
Total deaths (N)	1,843	284	1,559	
Age, median (IQR)	40 (33-51)	45 (35-56)	40 (32-50)	*
Age category (N, %)				
0 to 24	114 (6.2%)	9 (3.2%)	105 (6.7%)	*
25 to 44	989 (53.7%)	132 (46.5%)	857 (55.0%)	*
45 to 64	688 (37.3%)	125 (44.0%)	563 (36.1%)	*
65+	52 (2.8%)	18 (6.3%)	34 (2.2%)	*
Sex (N, %)				
Female	460 (25.0%)	49 (17.3%)	411 (26.4%)	*
Male	1,383 (75.0%)	235 (82.7%)	1,148 (73.6%)	*
Income quintile (N, %)				
1	770 (41.8%)	110 (38.7%)	660 (42.3%)	
2	371 (20.1%)	61 (21.5%)	310 (19.9%)	
3	280 (15.2%)	44 (15.5%)	236 (15.1%)	
4	162 (8.8%)	29 (10.2%)	133 (8.5%)	
5	173 (9.4%)	26 (9.2%)	147 (9.4%)	
Unknown	87 (4.7%)	14 (4.9%)	73 (4.7%)	
Location of incident among cases where location of incident was known (N, %)				
Known location of incident	1,333	283	1,050	
Private residence	973 (73.0%)	187 (66.1%)	786 (74.9%)	*
Rooming house/other collective dwellings	157 (11.8%)	18 (6.4%)	139 (13.2%)	*
Other residential settings/shelters	33 (2.5%)	9 (3.2%)	24 (2.3%)	
Other indoor space (non-hospital)	71 (5.3%)	30 (10.6%)	41 (3.9%)	*
Other (includes hospitals, transit, other)	20 (1.5%)	10 (3.5%)	10 (1.0%)	*
Outdoors	79 (5.9%)	29 (10.2%)	50 (4.8%)	*
Unknown location of incident (N, %)	510 (27.7%)	1 (0.4%)	509 (32.6%)	*
Number of substance groups involved in death (N, %)				
1	284 (15.4%)	284 (100.0%)	0 (0.0%)	N/A
2	1,304 (70.8%)	0 (0.0%)	1,304 (83.6%)	N/A
3+	255 (13.8%)	0 (0.0%)	255 (16.4%)	N/A
Other substances contributing to death (N, %)				
Opioids	1,536 (83.3%)	0 (0.0%)	1,536 (98.5%)	N/A
Alcohol	153 (8.3%)	0 (0.0%)	153 (9.8%)	N/A
Benzodiazepines	138 (7.5%)	0 (0.0%)	138 (8.9%)	N/A
Stimulant types (N, %)				
Cocaine	1,258 (68.3%)	197 (69.4%)	1,061 (68.1%)	
Methamphetamine	882 (47.9%)	116 (40.8%)	766 (49.1%)	*
Amphetamine	135 (7.3%)	118 (41.5%)	17 (1.1%)	*
Other stimulants	14 (0.8%)	0 (0.0%)	14 (0.9%)	

NOTE

Column categories are mutually exclusive for stimulant only versus stimulants plus other substances. Other stimulants includes all other stimulants other than cocaine, methamphetamine and amphetamine, such as non-pharmaceutical stimulants ephedrine and methylenedioxymethamphetamine (MDMA) and pharmaceutical stimulants methylphenidate and pseudoephedrine. Categories

may include other substances as detected in post-mortem, although only direct contributors are reflected. Red asterisk indicates statistically significant (stat. sig) difference between stimulant only and stimulants plus other substances ($p<0.05$). Number of substances represent broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).

The majority (84.6%) of stimulant toxicity deaths were attributable to stimulants plus other substances. Overall, the median age at stimulant toxicity death was 40 years (IQR: 33-51 years), and was higher among those who died from only stimulants (45 years, IQR: 35-56) compared to stimulants plus other substances (40 years, IQR: 32-50, $p<0.001$). The proportion of males who died from stimulant toxicity only (82.7%) was higher compared to the proportion of males who died due to stimulants plus other substances (73.6%, $p=0.001$).

Most stimulant only deaths were caused by cocaine (69.4%; N=197), followed by amphetamines (41.5%; N=118) and methamphetamines (40.8%; N=116). The proportion of deaths where methamphetamines were direct contributors was higher among those whose deaths involved both stimulants and other substances compared to those where only stimulants were involved (49.1% vs 40.8%, $p=0.01$). More stimulant-related polysubstance deaths occurred in private residences (74.9% vs 66.1%, $p=0.003$) and rooming houses/other collective dwellings (13.2% vs 6.4%, $p=0.001$), and less occurred in other indoor spaces (3.9% vs 10.6%, $p<0.001$), other (1.0% vs 3.5%, $p=0.004$) and outdoor settings (4.8% vs 10.2%, $p<0.001$), compared to stimulant only deaths.

Table 3. Location of residence, toxicity deaths directly attributable to stimulants in 2021, by mono versus polysubstance

	Stimulants (overall)	Stimulant only	Stimulants + other substances
Total deaths (N)	1,843	284	1,559
Urban/rural location of residence (N, rate per 100,000)			
Urban	1,588 (11.8)	246 (1.8)	1,342 (9.9)
Rural	169 (11.0)	24 (1.6)	145 (9.4)
Unknown	86	14	72
Northern/Southern location of residence (N, rate per 100,000)			
Northern	265 (31.2)	27 (3.2)	238 (28.0)
Southern	1,533 (10.8)	250 (1.8)	1,283 (9.0)
Unknown	45	7	38

NOTE

Column categories are mutually exclusive for stimulant only versus stimulants plus other substances. Categories may include other substances as detected in post-mortem, although only direct contributors are reflected.

Deaths due to only stimulants were 1.8 times higher in Northern Ontario (vs South; 3.2 vs 1.8 per 100,000), while deaths due to stimulants plus other substances were 3.1 times higher in the North (28.0 vs 9.0 per 100,000). Deaths due to stimulants only (1.8 vs 1.6 per 100,000) and stimulants plus other substances (9.9 vs 9.4 per 100,000) was slightly higher in urban (vs rural) locations of residence.

Benzodiazepine toxicity deaths

Trends & characteristics

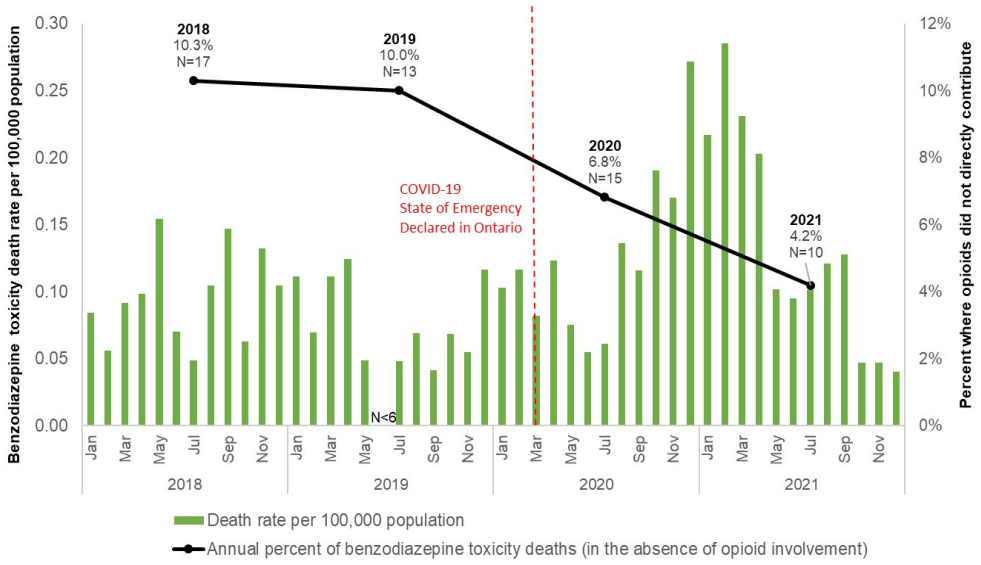
SUMMARY

45% **increase** in the number of benzodiazepine toxicity deaths from 2018 to 2021

9% of all substance-related deaths from 2018 to 2021 **involved benzodiazepine** as a direct contributor to death

239 benzodiazepine toxicity **deaths** in 2021

↳ **82%** were caused by **non-pharmaceutical** benzodiazepines



Benzodiazepine Toxicity Deaths in 2021

It is very rare to die from benzodiazepine toxicity alone

>98% of deaths had **other substances** directly contribute to death

- **96%** involved **opioids**
- **12%** involved **alcohol**
- **58%** involved **stimulants**

*Proportion of deaths by **number of substances** directly contributing to death*

Non-pharmaceutical benzodiazepines N = 197

- **34%** — **1 - 2 substances**
- **66%** — **3+ substances**

Pharmaceutical benzodiazepines N = 42

- **60%** — **1 - 2 substances**
- **41%** — **3+ substances**

Demographics

68% of deaths occurred among **males**

The median age at death was **40 years**

78%* of deaths occurred in a **private residence**

Death rates for **non-pharmaceutical** benzodiazepines were **2.3x** **higher** in **Northern** vs. **Southern Ontario**

Death rates for **pharmaceutical** benzodiazepines were **7x** **higher** in **Northern** vs. **Southern Ontario**

Deaths rates were **similar** in **rural** vs **urban** residences

Rural
1.2 deaths per 100,000 people

Urban
1.5 deaths per 100,000 people

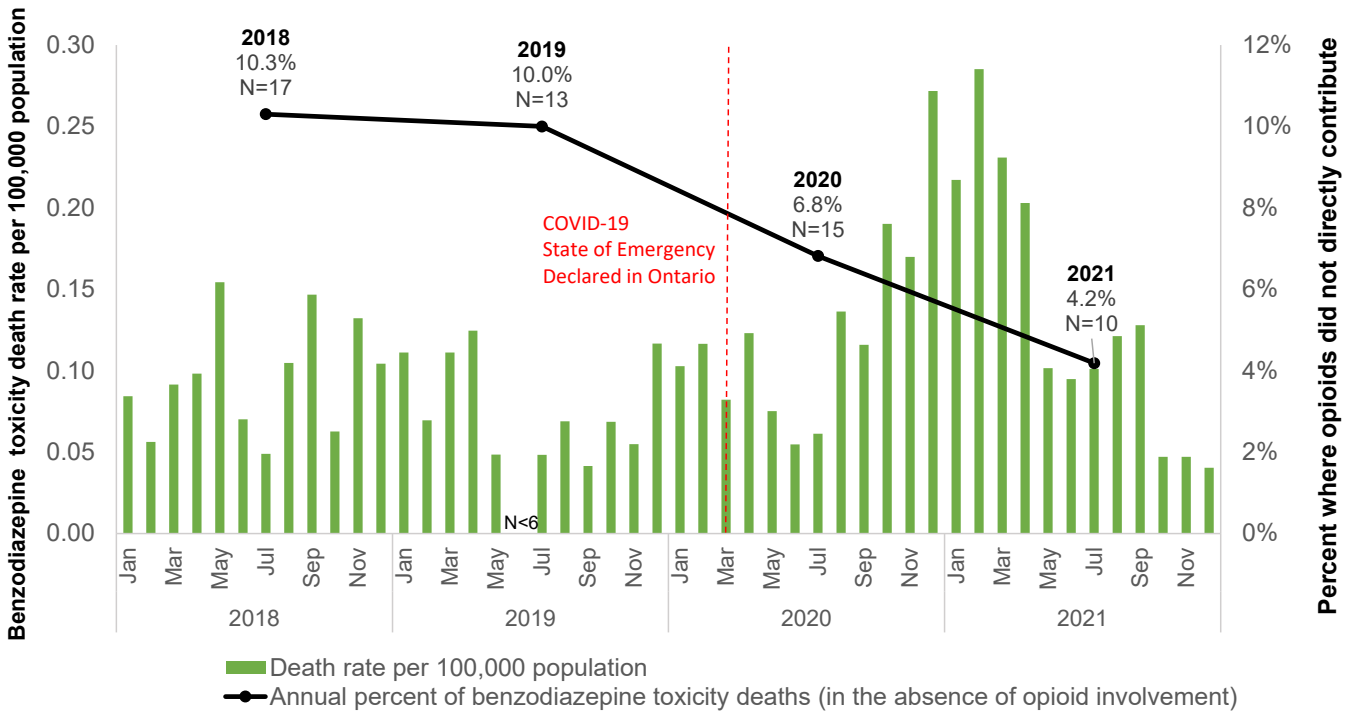
*This proportion is among cases where location of incident was known

Detailed Analyses on Trends and Characteristics of Benzodiazepine Toxicity Deaths

NOTE

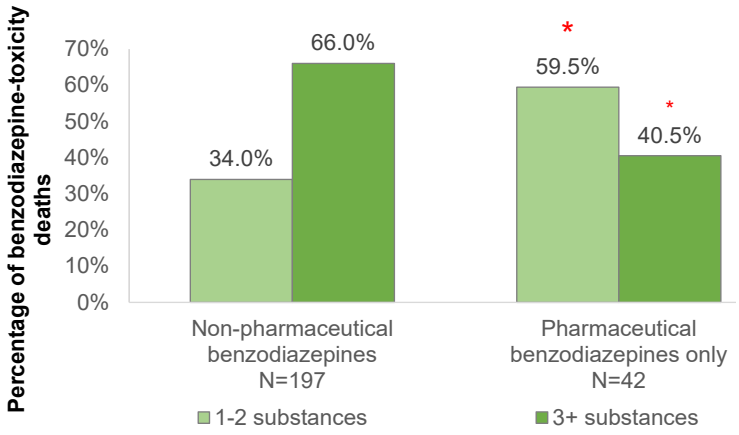
- In order to create mutually exclusive subgroups according to the source of benzodiazepine, we categorized deaths as pharmaceutical benzodiazepine-related deaths if they involved only pharmaceutical benzodiazepines. Cases where non-pharmaceutical benzodiazepines alone or a combination of pharmaceutical and non-pharmaceutical benzodiazepines (N=10) contributed to death were categorized as non-pharmaceutical benzodiazepine deaths.
- Stratification according to single substance vs polysubstance deaths was not included due to very small frequency of deaths involving benzodiazepines without other substances (N<6).
- Reporting of location of incident across pharmaceutical and non-pharmaceutical benzodiazepines was not included due to small counts. See Appendix B, Table B2 for location of incident for benzodiazepine (overall).
- See Appendix A for the definition and list of pharmaceutical and non-pharmaceutical benzodiazepines.
- Red asterisk indicates statistically significant (stat. sig) difference (p<0.05) between pharmaceutical and non-pharmaceutical benzodiazepines.

Figure 20. Benzodiazepine-only toxicity death trends from 2018 to 2021



Overall benzodiazepine toxicity deaths rarely involved only benzodiazepines (≤2.1%, N<6) and most often involved other substance groups (data not shown). Benzodiazepine toxicity deaths increased 44.8% from 165 in 2018 to 239 in 2021. In 2021, non-pharmaceutical benzodiazepines were involved in 82.4% (N=197) of all benzodiazepine toxicity deaths. Importantly, benzodiazepine deaths in the absence of other substances are exceedingly rare. Specifically, Only 17 (10.3%) benzodiazepine deaths in 2018 did not involve opioids, which fell to 10 (4.2%) by 2021.

Figure 21. Proportion of toxicity deaths directly attributable to benzodiazepine types in 2021, by number of substance groups directly contributing to death†



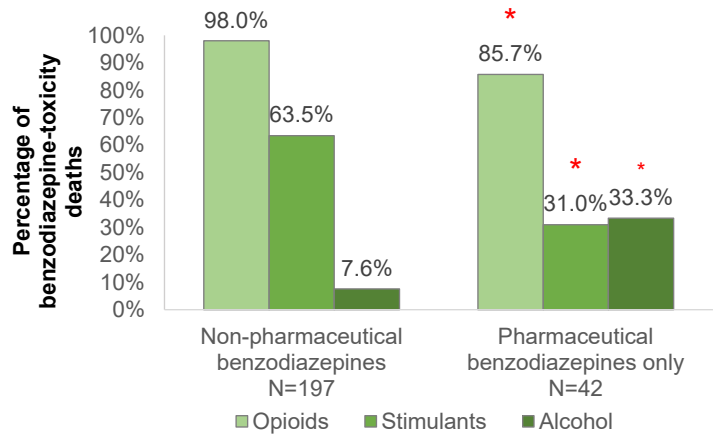
NOTE

- Categories were combined due to small cell counts.
- †Number of substances represent broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).

Most benzodiazepine toxicity deaths involved three or more substances (61.5%, N=147), followed by two substances (36.4-38.5%, N=87-92; data not shown)

Most deaths involving non-pharmaceutical benzodiazepines involved three or more substance groups (66.0%, N=130), while most deaths involving pharmaceutical benzodiazepines involved one or two substances (59.5%, N=25). There were significant differences in the number of substance groups involved in non-pharmaceutical vs pharmaceutical benzodiazepine deaths (p=0.003 for both 1-2 and 3+ substances).

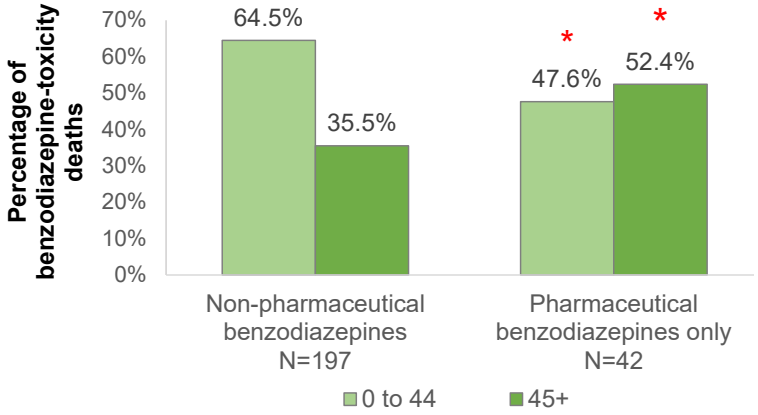
Figure 22. Proportion of toxicity deaths directly attributable to benzodiazepine types in 2021, by other substances directly contributing to death



Overall, most (95.8%, N=229) benzodiazepine attributable deaths were co-attributed to opioids, and over half (57.7%, N=138) also had stimulants directly contribute (data not shown). Alcohol directly contributed to 12.1% (N=29) of benzodiazepine deaths (data not shown).

Among non-pharmaceutical benzodiazepine deaths, 98.0% (N=193) involved opioids and two-thirds involved stimulants (N=125). Alcohol was less common, directly contributing to 7.6% (N=15) of non-pharmaceutical benzodiazepine deaths. Similar to non-pharmaceutical benzodiazepine deaths, most deaths from pharmaceutical benzodiazepines involved opioids; however, opioids directly contributed less frequently (85.7% vs 98.0%, N=36 vs 193, p<0.001) and stimulants also contributed less frequently (31.0% vs 63.5%, N=13 vs 125, p<0.001). Alcohol, on the other hand, directly contributed more frequently in deaths involving pharmaceutical benzodiazepines (1 in 3 deaths, N=14) compared to non-pharmaceutical benzodiazepines (7.6%, N=15, p<0.001).

Figure 23. Proportion of toxicity deaths directly attributable to benzodiazepine types in 2021, by age

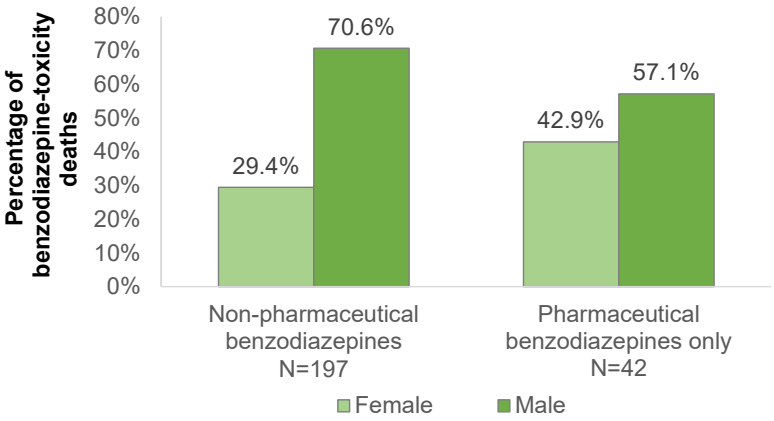


NOTE

Categories were combined due to small cell counts.

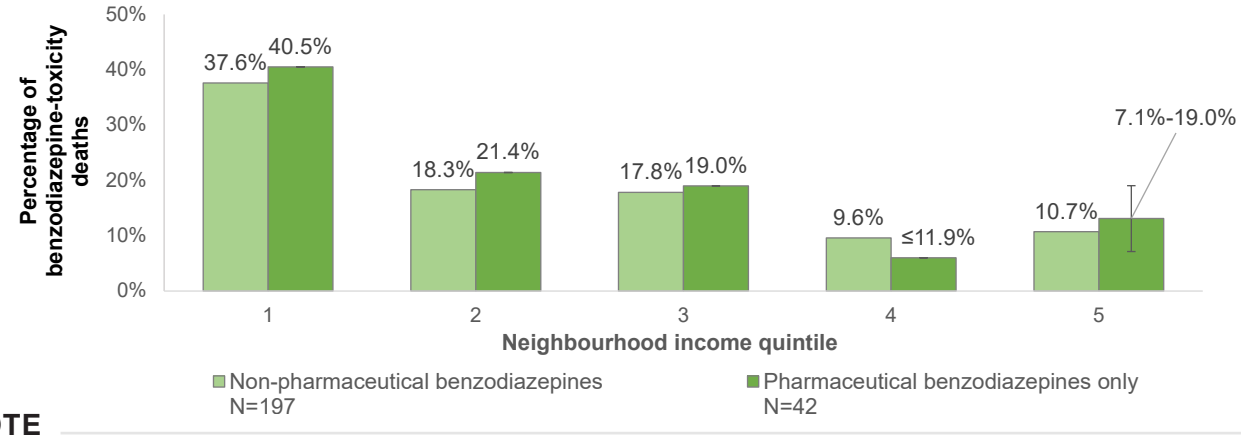
For overall benzodiazepines, the median age at death was 40 years (IQR: 31-55 years; data not shown). The median age involving pharmaceutical benzodiazepines only was older (46 years, IQR: 35-56) than deaths involving non-pharmaceutical benzodiazepines (39 years, IQR: 31-50, p=0.02; data not shown). Most non-pharmaceutical benzodiazepine deaths occurred among those aged 0 to 44 years (64.5%, N=127), while the age distribution among pharmaceutical benzodiazepine deaths was distributed more evenly among those aged 0 to 44 years (47.6%, N=20) and aged 45 years and older (52.4%, N=22). A higher proportion of non-pharmaceutical (p=0.04) and pharmaceutical benzodiazepine deaths (p=0.04) occurred in the younger and older age groups, respectively. Nonetheless, the absolute number of deaths involving non-pharmaceutical (vs pharmaceutical) benzodiazepines was consistently higher across both age groups (see Appendix B, Table B4).

Figure 24. Proportion of toxicity deaths directly attributable to benzodiazepine types in 2021, by sex



Overall, 68.2% (N=163) of benzodiazepine toxicity deaths occurred among males (see see Appendix B, Table B2). Sex differences were larger for deaths caused by non-pharmaceutical benzodiazepines (males vs females; 70.6% vs 29.4%, N=139 vs 58) compared to pharmaceutical benzodiazepines (57.1% vs 42.9%, N=24 vs 18). The sex distribution; however, was not significantly different across benzodiazepine type (p=0.09). Overall, more deaths were attributable to non-pharmaceutical (vs pharmaceutical) benzodiazepines for both males and females (see Appendix B, Table B4).

Figure 25. Proportion of toxicity deaths directly attributable to benzodiazepine types in 2021, by neighbourhood income quintile

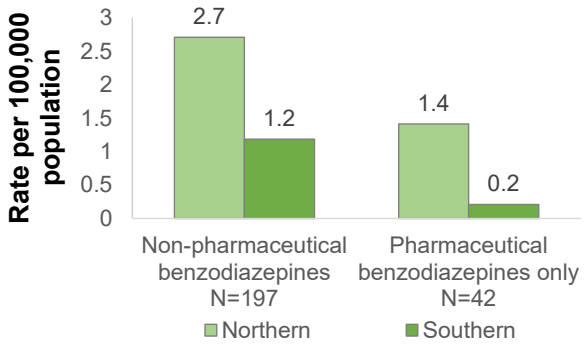


NOTE

- Unknown income was 6.1% for non-pharmaceutical benzodiazepines and 0.0% for pharmaceutical benzodiazepines
- Neighbourhood income quintile is sorted from lowest (Q1) to highest (Q5) income.

An income gradient was seen across pharmaceutical and non-pharmaceutical benzodiazepine toxicity deaths, with the highest concentration observed among those living in neighbourhoods with lowest income quintile (Q1: 37.6-40.5%) and lower concentrations in the higher income quintiles (Q4-Q5: 7.1-19.0%). Income differences across pharmaceutical vs non-pharmaceutical benzodiazepines were non-significant (p>0.05 for all comparisons). Overall, more deaths were attributable to non-pharmaceutical (vs pharmaceutical) benzodiazepines across all income quintiles (see Appendix B, Table B4).

Figure 26. Population-adjusted toxicity death rates directly attributable to benzodiazepine types in 2021, by location of residence



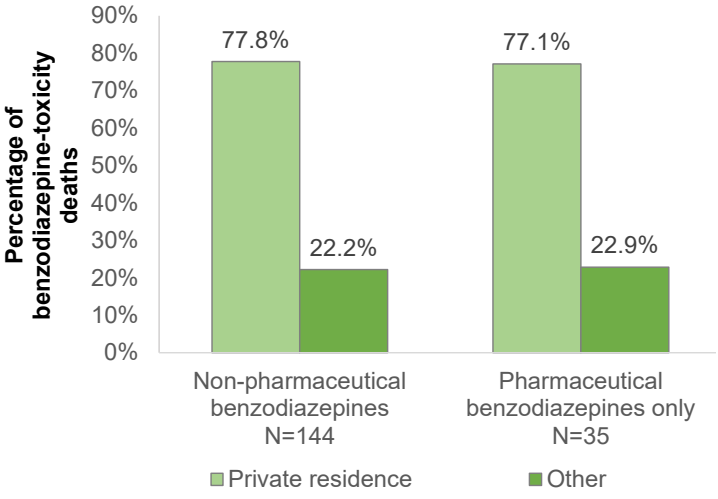
NOTE

For non-pharmaceutical benzodiazepine deaths, unknown urban/rural and Northern/Southern was 6.1% and 2.5%, respectively.

Overall, benzodiazepine toxicity death rates were three times higher in Northern (4.1 deaths per 100,000, N=35) vs Southern Ontario (1.4 deaths per 100,000, N=199; see Appendix B, Table B2), and were similar across rural (1.2 deaths per 100,000, N=18) vs urban (1.5 deaths per 100,000, N=209) locations of residence (data not shown).

Death rates due to non-pharmaceutical (vs pharmaceutical) benzodiazepines were consistently higher across urban/rural and Northern/Southern locations. There were substantially higher death rates in Northern (vs Southern) Ontario across non-pharmaceutical (2.7 vs 1.2 per 100,000, N=23 vs 169) and pharmaceutical benzodiazepine deaths (1.4 vs 0.2 per 100,000, N=12 vs 30). The death rates for non-pharmaceutical benzodiazepines were about 2.3 times higher in the North (vs South), while pharmaceutical benzodiazepine deaths rates were about 7 times higher in the North. Death rates were similar across urban vs rural residence locations, with slightly lower non-pharmaceutical and pharmaceutical benzodiazepine death rates among those residing in rural (non-pharmaceutical: 0.9 per 100,000, N=14; pharmaceutical: ≤0.3 per 100,000, N<6) vs urban residences (non-pharmaceutical: 1.3 per 100,000, N=171; pharmaceutical: 0.27-0.31 per 100,000, N=37-42).

Figure 27. Proportion of toxicity deaths directly attributable to benzodiazepine types in 2021, by location of incident



NOTE

Unknown location of incident was excluded from the denominator in this figure, given that unknown location of incident differed by benzodiazepine type. Incident location was unknown in 26.9% and 16.7% of cases for non-pharmaceutical and pharmaceutical benzodiazepine deaths, respectively.

Overall, 77.7% (N=139 of 179) of benzodiazepine deaths occurred in a private residence (where location of incident was known; see Appendix B, Table B2). Similarly, the highest proportion of stimulant-toxicity deaths where location was reported or known occurred in private residences across non-pharmaceutical (77.8%, N=112) and pharmaceutical benzodiazepine deaths (77.1%, N=27). Location of incident did not differ by pharmaceutical vs non-pharmaceutical benzodiazepine ($p>0.05$ for both comparisons). Overall, more deaths were attributable to non-pharmaceutical (vs pharmaceutical) benzodiazepines among those whose incident took place in a private residence or other setting (see Appendix B, Table B4).

Opioid toxicity deaths

Trends & characteristics

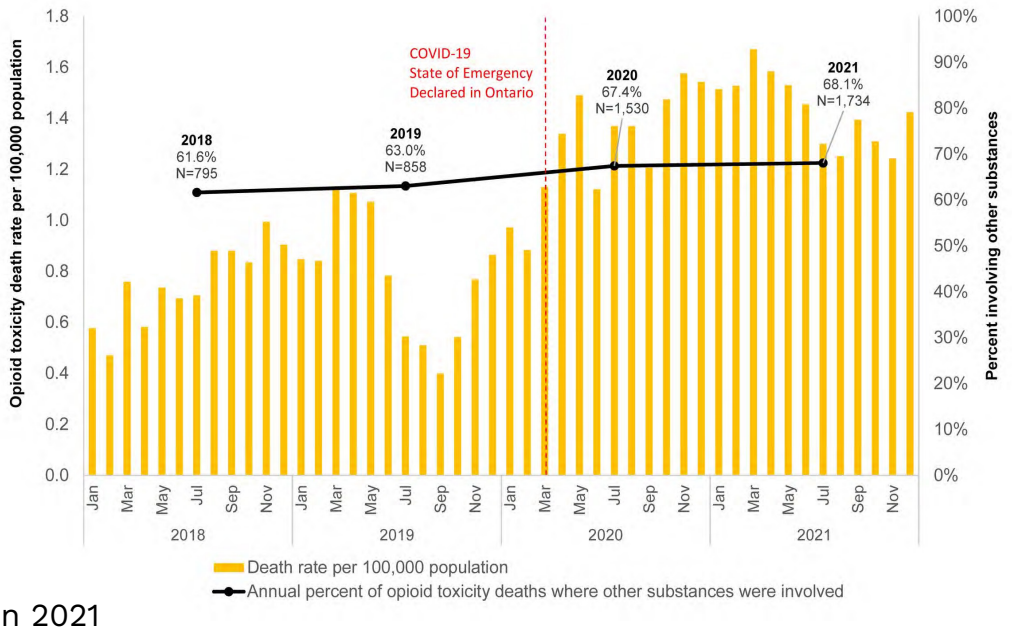
SUMMARY

2x Increase in the number of opioid toxicity deaths from 2018 to 2021

85% of all substance-related deaths from 2018 to 2021 **involved opioids** as a direct contributor to death

2547 Opioid toxicity **deaths** in 2021

↳ **90%** were caused by **non-pharmaceutical** opioids



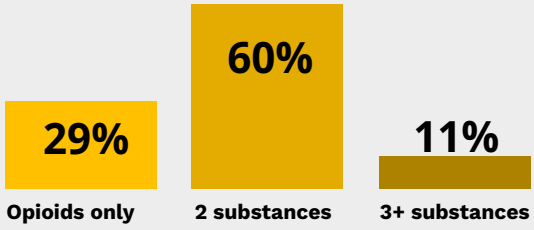
Opioid Toxicity Deaths in 2021

68% of deaths had **other substances** directly contribute to death

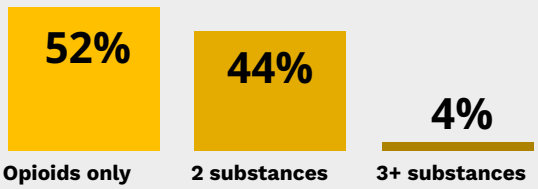
- **10%** involved **alcohol**
- **9%** involved **benzodiazepines**
- **60%** involved **stimulants**

*Proportion of deaths by **number of substances** directly contributing to death*

Non-pharmaceutical opioids N = 2,303



Pharmaceutical opioids only N = 204



Demographics

74% of deaths occurred among **males**

The median age at death was **40 years**

78%* of deaths occurred in a **private residence**

Death rates for **non-pharmaceutical** and **pharmaceutical** opioids were **3x higher** in **Northern** vs. **Southern Ontario**

Deaths rates were **similar** in **rural** vs **urban** residences

Rural

15 deaths per 100,000 people

Urban

16 deaths per 100,000 people

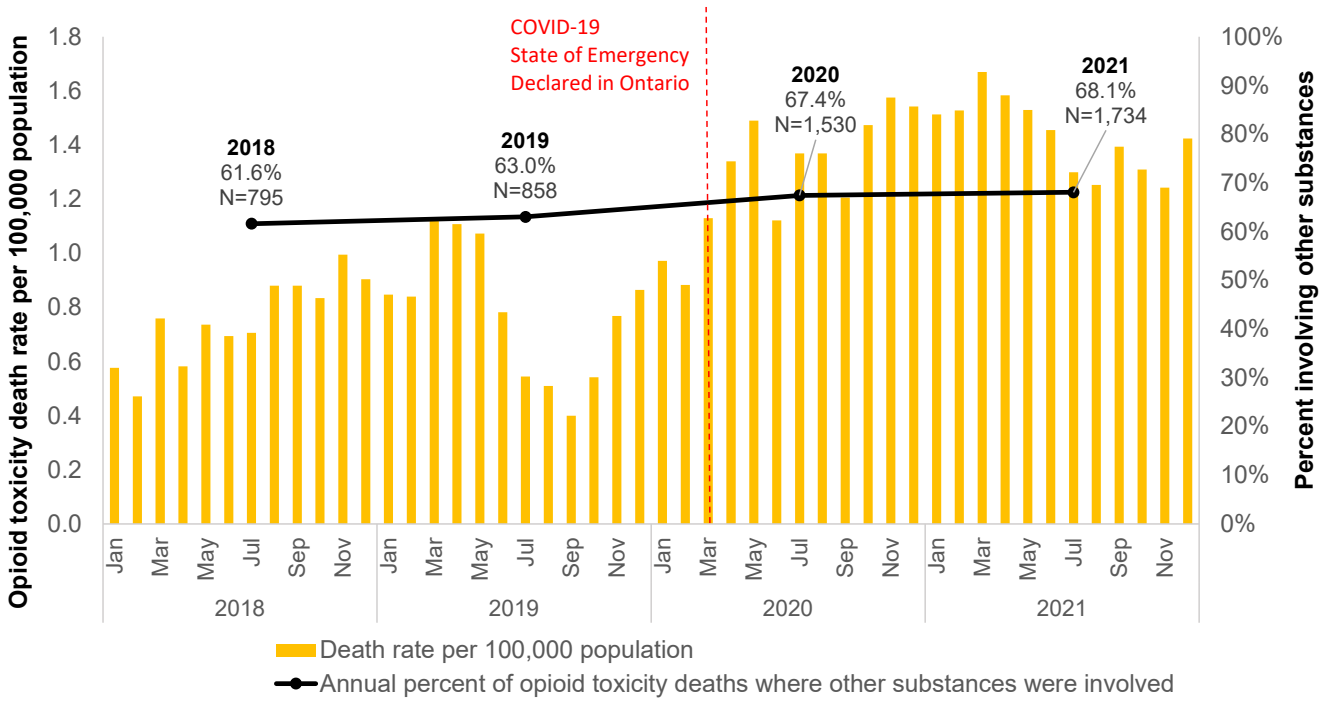
*This proportion is among cases where location of incident was known

Detailed Analyses on Trends and Characteristics of Opioid Toxicity Deaths

NOTE

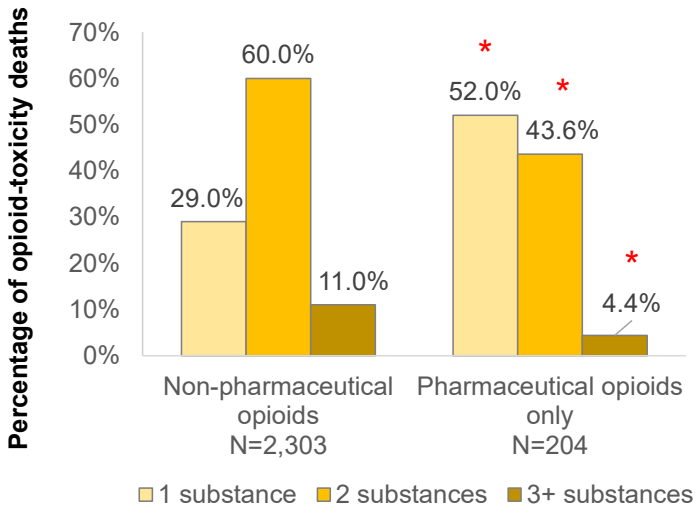
- The pharmaceutical opioid only category does not include non-pharmaceutical opioids, while non-pharmaceutical opioids includes deaths involving both pharmaceutical and non-pharmaceutical opioids (N=272).
- See Appendix A for the definition and list of pharmaceutical and non-pharmaceutical opioids.
- Red asterisk indicates statistically significant (stat. sig) difference (p<0.05) between pharmaceutical and non-pharmaceutical opioids in figures.

Figure 28. Opioid toxicity death trends from 2018 to 2021



Opioid toxicity deaths increased two-fold from 1,290 in 2018 to 2,547 in 2021. The majority of opioid toxicity deaths were caused by non-pharmaceutical opioids in 2021 (90.4%, N=2,303). When only considering opioid toxicity deaths that involved other substances, deaths increased from 795 in 2018 to 1,734 in 2021. The proportion of opioid toxicity deaths that directly involved other substances increased from 61.6% in 2018 to 68.1% in 2021.

Figure 29. Proportion of toxicity deaths directly attributable to opioid types in 2021, by number of substance groups directly contributing to death†



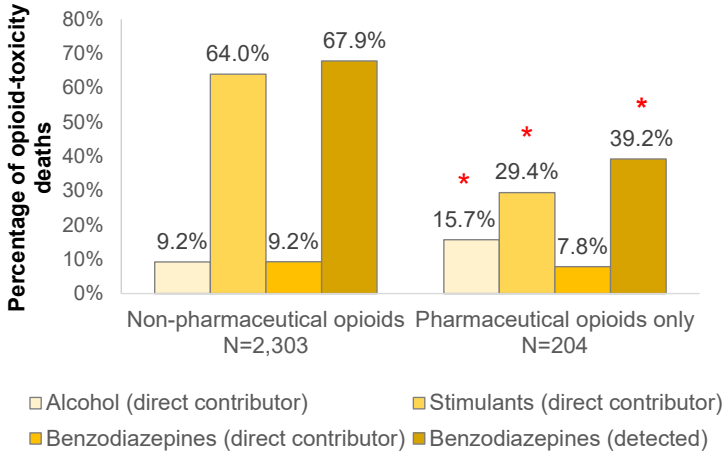
NOTE

† Number of substances represent broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).

Opioid toxicity deaths most often involved two substance groups (57.8%, N=1,471), followed by opioids as the sole contributor in nearly one-third of deaths (31.9%, N=813; see Table 4 below).

Similarly, most deaths involving non-pharmaceutical opioids involved two substance groups (60.0%, N=1,381), followed by only opioids (29.0%, N=669), while deaths involving pharmaceutical opioids were split more evenly between only opioids (52.0%, N=106) and two substances (43.6%, N=89). The presence of two substance groups leading to death was proportionally higher for non-pharmaceutical vs pharmaceutical opioid deaths (60.0% vs 43.6%, p<0.001), while the presence of only one substance was proportionally higher for pharmaceutical opioid deaths (52.0% vs 29.0%, p<0.001). The presence of three or more substance groups was rarer among deaths involving only pharmaceutical opioids (4.4%, N=9) vs non-pharmaceutical opioids (11.0%, N=253, p=0.003).

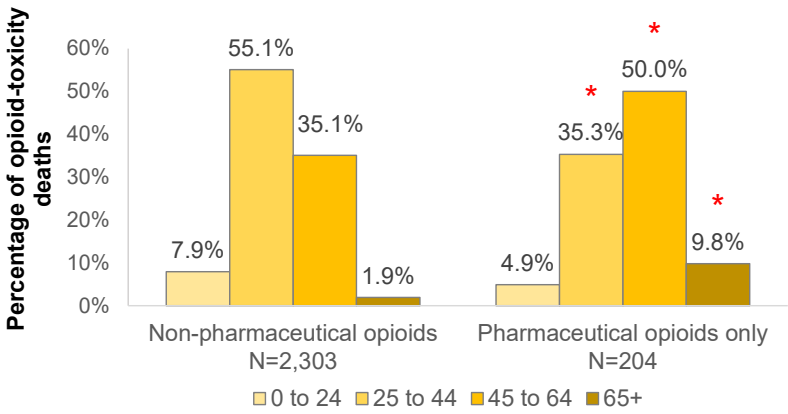
Figure 30. Proportion of toxicity deaths directly attributable to opioid types in 2021, by other substances directly contributing to death



Most overall opioid toxicity deaths were co-attributed to stimulants (60.3%, N=1,536), while alcohol and benzodiazepines were co-contributors in 9.6% (N=245) and 9.0% (N=229) of cases, respectively (see Table 4 below). Benzodiazepines were detected in 65.1% (N=1,658) of overall opioid toxicity deaths (see Table 4 below).

Similarly, most deaths due to non-pharmaceutical opioids were co-attributed to stimulants (64.0%, N=1,474) and had benzodiazepines detected (67.9%, N=1,563). Stimulants were also the most prevalent contributor to pharmaceutical opioid deaths, although at a much lower degree compared to non-pharmaceutical opioids (29.4%, N=60; p<0.001). A higher proportion of pharmaceutical opioid deaths (vs non-pharmaceutical opioid deaths) were co-attributed to alcohol (15.7% vs 9.2%; N=32 vs 212; p=0.003). Although there were no significant differences in the proportion of deaths involving benzodiazepines across non-pharmaceutical vs pharmaceutical opioid deaths (9.2% vs 7.8%; N=213 vs 16; p=0.5), there was a significantly higher proportion of benzodiazepines detected in non-pharmaceutical vs pharmaceutical opioid deaths (67.9% vs 39.2%, N=1,563 vs 80).

Figure 31. Proportion of toxicity deaths directly attributable to opioid types in 2021, by age



Most deaths due to pharmaceutical or non-pharmaceutical opioids occurred in the middle age groups (25 to 64 years). Age differences were apparent, with deaths due to non-pharmaceutical opioids skewed towards the younger age groups, and deaths due to pharmaceutical opioids skewed towards the older age groups. Non-pharmaceutical opioid deaths were higher than pharmaceutical opioid deaths among those aged <25 years (7.9% vs 4.9%, N=183 vs 10, p=0.1) and 25 to 44 years (55.1% vs 35.3%, N=1,269 vs 72, p<0.001), whereas pharmaceutical opioids were proportionally higher in the older age groups (45 to 64 years: 50.0% vs 35.1%, N=102 vs 808, p<0.001; 65+ years: 9.8% vs 1.9%, N=20 vs 43, p<0.001). Nonetheless, the absolute number of deaths involving non-pharmaceutical (vs pharmaceutical) opioids was consistently higher across all age groups (see Appendix B, Table B5).

Figure 32. Proportion of toxicity deaths directly attributable to opioid types in 2021, by sex

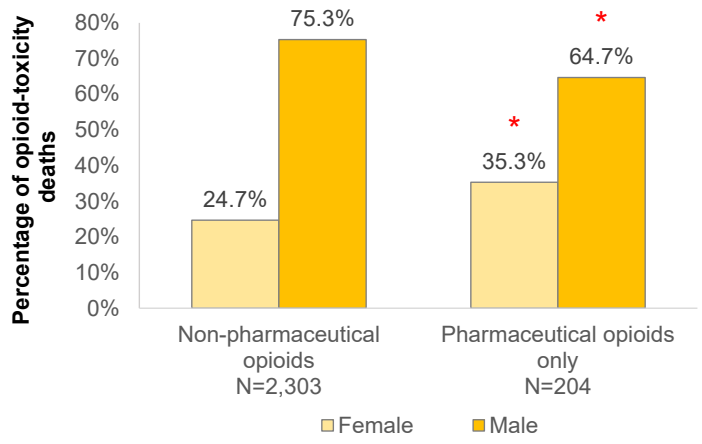


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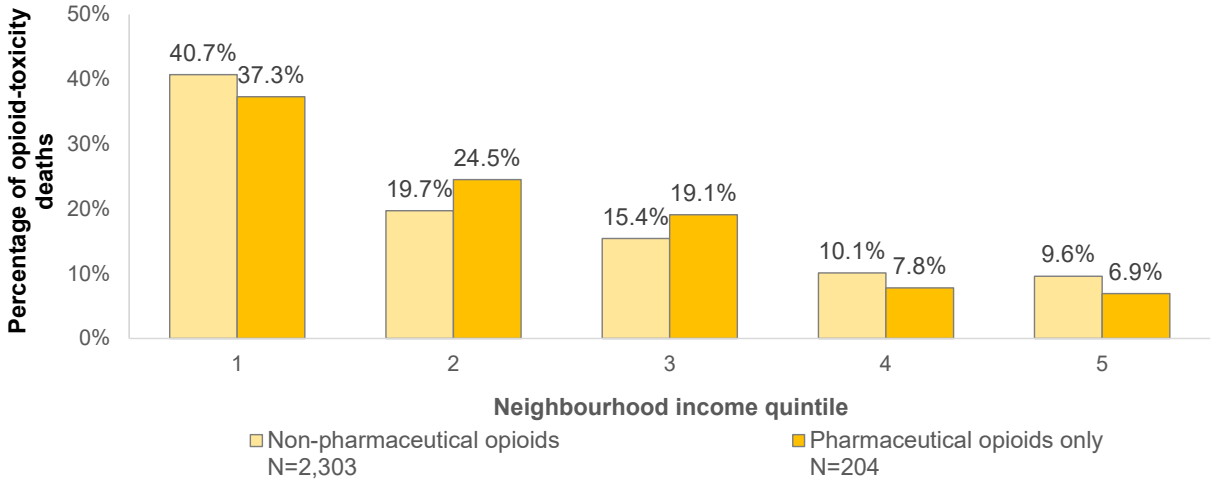
Figure 33. Proportion of toxicity deaths directly attributable to opioid types in 2021, by neighbourhood income quintile

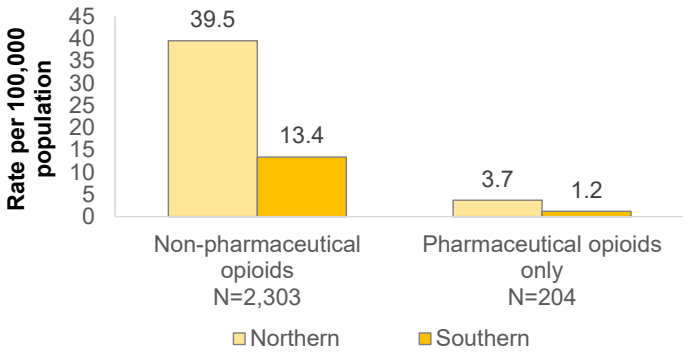


NOTE

- Unknown income was 4.6% and 4.4% for non-pharmaceutical and pharmaceutical opioids, respectively.
- Neighbourhood income quintile is sorted from lowest (Q1) to highest (Q5) income.

An income gradient was seen across non-pharmaceutical and pharmaceutical opioid toxicity deaths, with the highest concentration observed among those living in neighbourhoods with lowest income quintile (37.3-40.7%) and the lowest concentrations in the highest income quintile (6.9-9.6%). Income differences across pharmaceutical vs non-pharmaceutical opioids were non-significant (p>0.05 across all income categories). Overall, more deaths were attributable to non-pharmaceutical (vs pharmaceutical) opioids across income quintiles (see Appendix B, Table B5).

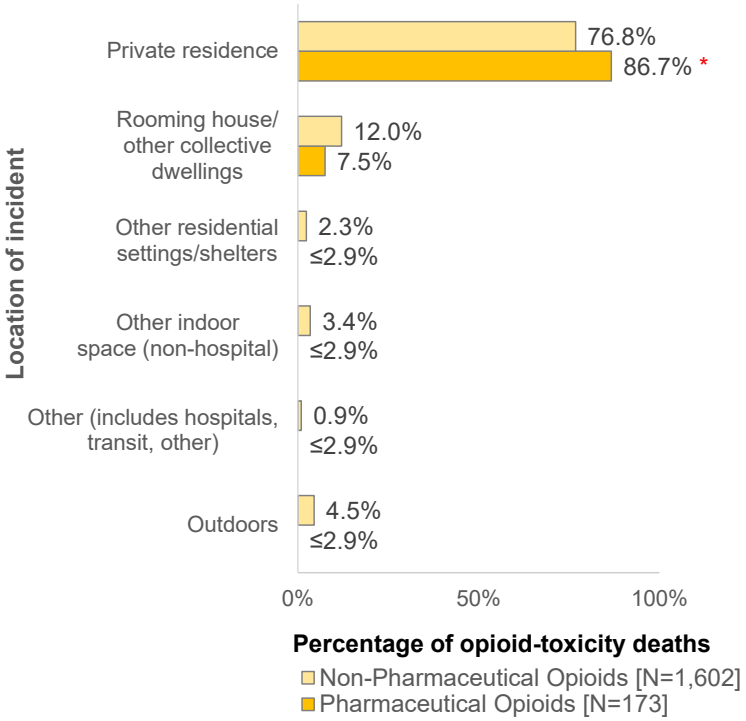
Figure 34. Population-adjusted toxicity death rates directly attributable to opioid types in 2021, by location of residence



Overall opioid toxicity death rates were three times higher in Northern (43.7 deaths per 100,000, N=371) vs Southern Ontario (14.9 deaths per 100,000, N=2,116), and similar across rural (15.0 deaths per 100,000, N=231) vs urban (16.3 deaths per 100,000, N=2,203) location of residence (see Table 5 below).

Death rates due to non-pharmaceutical (vs pharmaceutical) opioids only were consistently higher across urban/rural and Northern/Southern locations. There were substantially higher rates in Northern (vs Southern) Ontario for non-pharmaceutical (39.5 vs 13.4 per 100,000, N=335 vs 1,912) and pharmaceutical opioid deaths (3.7 vs 1.2 per 100,000, N=31 vs 169). The death rates for non-pharmaceutical and pharmaceutical opioids were both about three times higher in the North (vs South). In contrast, death rates did not differ across urban vs rural residence locations, with similar non-pharmaceutical and pharmaceutical opioid deaths rates among those residing in rural (non-pharmaceutical: 13.1 per 100,000, N=202; pharmaceutical: 1.8 per 100,000, N=28) vs urban residences (non-pharmaceutical: 14.8 per 100,000, N=1,996; pharmaceutical: 1.2 per 100,000, N=168; data not shown).

Figure 35. Proportion of toxicity deaths directly attributable to opioid types in 2021, by location of incident



NOTE

Unknown location of incident was excluded from the denominator in this figure, given that unknown location of incident differed by opioid type. Incident location was unknown in 30.4% and 15.2% of cases for non-pharmaceutical and pharmaceutical opioids, respectively. P-values were not reported for small cells (N<6) or ranges.

Overall, 77.5% (N=1,401 of 1,807) of opioid toxicity deaths occurred in a private residence (where location of incident was known; see Table 4). The proportion of deaths occurring in private residences was higher when pharmaceutical opioids were involved (86.7%, N=150) compared to non-pharmaceutical opioids (76.8%, N=1,230, p<0.001). A slightly higher proportion of deaths due to non-pharmaceutical (vs pharmaceutical) opioids occurred in rooming houses/other collective dwellings (12.0% vs 7.5%, N=193 vs 13, p=0.08) and outdoors (4.5% vs ≤2.9%, N=72 vs <6). Overall, more deaths were attributable to non-pharmaceutical (vs pharmaceutical) opioids across incident location (see Appendix B, Table B5).

Table 4. Descriptive characteristics, toxicity deaths directly attributable to opioids in 2021, by mono versus polysubstance

	Opioid (overall)	Opioid only	Opioid + other substances	Stat. sig.
Total deaths (N)	2,547	813	734	
Age, median (IQR)	40 (32-51)	40 (31-52)	40 (32-51)	
Age category (N, %)				
0 to 24	200 (7.9%)	78 (9.6%)	122 (7.0%)	*
25 to 44	1,361 (53.4%)	421 (51.8%)	940 (54.2%)	
45 to 64	922 (36.2%)	288 (35.4%)	634 (36.6%)	
65+	64 (2.5%)	26 (3.2%)	38 (2.2%)	
Sex (N, %)				
Female	652 (25.6%)	194 (23.9%)	458 (26.4%)	
Male	1,895 (74.4%)	619 (76.1%)	1,276 (73.6%)	
Income quintile (N, %)				
1	1,027 (40.3%)	304 (37.4%)	723 (41.7%)	*
2	514 (20.2%)	168 (20.7%)	346 (20.0%)	
3	398 (15.6%)	123 (15.1%)	275 (15.9%)	
4	252 (9.9%)	104 (12.8%)	148 (8.5%)	*
5	242 (9.5%)	82 (10.1%)	160 (9.2%)	
Unknown	114 (4.5%)	32 (3.9%)	82 (4.7%)	
Location of incident among cases where location of incident was known (N, %)				
Known location of incident	1,807	636	1,171	
Private residence	1,401 (77.5%)	525 (82.5%)	876 (74.8%)	*
Rooming house/other collective dwellings	206 (11.4%)	53 (8.3%)	153 (13.1%)	*
Other residential settings/shelters	42 (2.3%)	14 (2.2%)	28 (2.4%)	
Other indoor space (non-hospital)	61 (3.4%)	13 (2.0%)	48 (4.1%)	*
Other (includes hospitals, transit, other)	19 (1.1%)	10 (1.6%)	9 (0.8%)	
Outdoors	78 (4.3%)	21 (3.3%)	57 (4.9%)	
Unknown location of incident (N, %)	740 (29.1%)	177 (21.8%)	563 (32.5%)	*
Number of substance groups involved in death (N, %)				
1	813 (31.9%)	813 (100.0%)	0 (0.0%)	N/A
2	1,471 (57.8%)	0 (0.0%)	1,471 (84.8%)	N/A
3+	263 (10.3%)	0 (0.0%)	263 (15.2%)	N/A
Other substances directly contributing to death (N, %)				
Alcohol	245 (9.6%)	0 (0.0%)	245 (14.1%)	N/A
Stimulants	1,536 (60.3%)	0 (0.0%)	1,536 (88.6%)	N/A
Benzodiazepines	229 (9.0%)	0 (0.0%)	229 (13.2%)	N/A
Benzodiazepines detected in post-mortem (N, %)	1,658 (65.1%)	507 (62.4%)	1,151 (66.4%)	*

NOTE

Column categories for opioid only and opioid plus other substances are mutually exclusive from one another. Only direct contributors are reflected here, although other substances as detected in post-mortem may be included. Red asterisk

indicates statistically significant (stat. sig.) difference between opioid only and opioid plus other substances ($p<0.05$). Number of substances represent broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).

The majority (two-thirds) of opioid toxicity deaths were attributable to other substances. The median age at opioid toxicity death was 40 years (IQR: 32-51 years), which was similar across deaths caused by opioids only (40 years, IQR: 31-52) and opioids plus other substances (40 years, IQR: 32-51). There was a higher proportion of those aged <25 years among those who died from opioid toxicity only compared to opioids plus other substances (9.6% vs 7.0%, p=0.03). Most opioid toxicity deaths occurred among those in the lower income quintiles, with a slightly higher proportion of opioid polysubstance deaths which occurred in the lowest income quintile (41.7%) compared to opioid only deaths (37.4%, p=0.04). Most opioid toxicity deaths occurred in private residences, which was higher among deaths due to only opioids (82.5%) compared to opioids plus other substances (74.8%, p<0.001). Compared to opioid only deaths, opioid deaths that involved other substances more frequently occurred in rooming houses/other collective dwellings (13.1% vs 8.3%, p=0.002) and other non-hospital indoor spaces (4.1% vs 2.0%, p=0.02). Benzodiazepines were detected in most opioid toxicity deaths, with a slightly higher proportion among opioid deaths that involved other substances (66.4%) vs only opioids (62.4%, p=0.047).

Table 5. Descriptive characteristics, toxicity deaths directly attributable to opioids in 2021, by mono versus polysubstance

	Opioid (overall)	Opioid only	Opioid + other substances
Total deaths (N)	2,547	813	1,734
Urban/rural location of residence (N, rate per 100,000)			
Urban	2,203 (16.3)	708 (5.2)	1,495 (11.1)
Rural	231 (15.0)	73 (4.7)	158 (10.3)
Unknown	113	32	81
Northern/Southern location of residence (N, rate per 100,000)			
Northern	371 (43.7)	119 (14.0)	252 (29.7)
Southern	2,116 (14.9)	676 (4.7)	1,440 (10.1)
Unknown	60	18	42

NOTE

Column categories are mutually exclusive from one another. Only direct contributors are reflected here, although other substances as detected in post-mortem may be included.

Death rates due to opioids only or opioids plus other substances were both three times higher in the North vs South (opioids only: 14.0 vs 4.7 per 100,000; opioids plus other substances: 29.7 vs 10.1 per 100,000), while death rates due to opioids only or opioids plus other substances were generally similar across urban vs rural location of residence (opioids only: 5.2 vs 4.7 per 100,000; opioids plus other substances: 11.1 vs 10.3 per 100,000). Death rates were higher across all locations of residence for deaths involving opioids plus other substances compared to only opioids.

Limitations

1. In our analyses of coronial records, we only included confirmed substance-related toxicity deaths which involved either alcohol, stimulants, benzodiazepines, or opioids. Some deaths that may later be determined to be related to alcohol, stimulants, benzodiazepines, or opioids are not included in our study, although we anticipate that this difference is small.
2. A clear threshold to determine whether benzodiazepines in the unregulated drug supply (e.g., etizolam, flualprazolam, flubromazolam) directly contributed to death is lacking. To mitigate this issue, we additionally reported the percentage of opioid toxicity deaths where benzodiazepines were detected (but not necessarily direct contributors to death).
3. Only acute toxicity deaths are included, and not outcomes which occur in the long-term (e.g., chronic conditions caused by substance use) or other acute injuries related to the substance (e.g., vehicle collision resulting from impaired driving). Thus, our report does not fully capture substance-related deaths, which extend beyond acute toxicities.
4. Our analyses of stimulant-related deaths by stimulant type are not mutually exclusive. Therefore, because amphetamines are a metabolite of methamphetamines, our findings specific to amphetamine-related deaths should be interpreted with caution.

Discussion

Substance toxicity deaths in Ontario are high and have grown considerably during the COVID-19 pandemic, reaching unprecedented rates in Ontario. We reported a total of 8,767 accidental substance toxicity deaths over a 4 year period, with the number of deaths nearly doubling from 1,586 in 2018 to 2,886 in 2021 in the province. This equates to 8 deaths every day from substance-related toxicities in Ontario, with this magnitude of deaths far exceeding the number of deaths from motor vehicle collisions in the province in 2021 (N=565), one of the leading causes of accidental deaths.[15] Most of the 8,767 deaths involved opioids (85.2%, N=7,467) or stimulants (60.2%, N=5,276). Deaths where alcohol or benzodiazepines were direct contributors were less common, contributing to 13.4% (N=1,177) and 8.6% (N=754) of deaths, respectively.

Opioid-related deaths doubled over our 4-year study period, aligning with previous observations of these rates doubling every three years in Ontario since 2015.[18] Importantly, there was a high degree of opioid co-involvement in all substance toxicity deaths, which grew over the study period across all substances studied, contributing directly to over 80% of alcohol and stimulant toxicity deaths and over 95% of benzodiazepine toxicity deaths in 2021. In particular, opioids and stimulants in combination with each other made up the highest proportion of toxicity deaths during the COVID-19 pandemic (43.1%) and represented the largest absolute increase in deaths from the pre-pandemic to pandemic period (doubling of deaths from 993 to 2,196). Notably, alcohol (N=25) and benzodiazepine (N<6) toxicity deaths in the absence of other substance co-contributors were especially rare in 2021. Thus, interventions targeted at reducing alcohol and benzodiazepine toxicity should consider the risks of polysubstance use rather than the use of alcohol or benzodiazepines alone.

In general, demographic and geographic characteristics of toxicity deaths were similar across the top 5 substance combinations, which accounted for 90.7% of all substance toxicity deaths captured in 2021. Across all deaths in 2021, most were concentrated among those aged 25 to 44 years (52.7%), males (75.0%), and individuals

residing in lower income quintile neighbourhoods (Q1: 40.2%). Population-adjusted rates of overall substance toxicity deaths in 2021 were close to three times higher in Northern (vs Southern) Ontario, but were similar across urban and rural regions of residence. Higher substance-related death rates in the North likely reflect disparities in access to mental health and substance use treatment as well as harm reduction programs in more remote parts of the province, as well as the harms resulting from systemic social inequities and intergenerational trauma experienced by First Nations People, which make up a large proportion of Northern Ontario communities.[16, 17] Our findings suggest the need for improvement in accessing and integrating services for those who use unregulated substances in Northern Ontario, with particular focus on increased investments into community-led, culturally appropriate responses in these communities.

Stimulant toxicity deaths doubled across the study period, from 847 in 2018 to 1,843 in 2021. Consistent with fatal and non-fatal stimulant toxicity trends previously reported in the United States[8] and Canada[3], stimulant toxicity deaths increased considerably following the start of the COVID-19 pandemic in Ontario, which may be explained by the high prevalence of combined use with opioids and the increasing toxicity of the unregulated opioid supply.[20] Although most stimulant toxicity deaths involved opioids, it is important to also recognize that one in six (N=307) stimulant toxicity deaths occurred without opioid involvement, suggesting the need for responses to stimulant-related harm that are both integrated within opioid responses and also tailored towards individuals who use stimulants alone. Stimulant toxicity deaths most often involved cocaine and/or methamphetamines, and commonly involved other substances (mostly opioids). Individuals who died from cocaine and methamphetamine toxicity were similar in age, sex, and income.

In addition, while most stimulant toxicity deaths occurred in a private residence, those involving cocaine were more concentrated within private residences (75.9%) compared with toxicity deaths involving methamphetamines (66.7% in a private residence). This may reflect different patterns of stimulant access and use among people who are vulnerably housed. With the increasing understanding of methamphetamine use and its relationship with socioeconomic factors, as well as the role of multiple concurrent substances in drug toxicity death more broadly, there is a need for more comprehensive research and strategies to mitigate harms from stimulant use alone, as well as from polysubstance use. Further, more programs, supports and services for people using stimulants in various contexts are needed. Importantly, those who died from a stimulant-only toxicity were slightly older (median: 45 years) than those who died from an opioid-only toxicity (40 years), which aligns with emerging evidence about the cumulative effects of long-term stimulant use that can lead to accumulating harm and risk of toxicity over time.[21] Further characterization of comorbidity and health service utilization in this population should be undertaken to identify opportunities for early intervention. Policies and interventions that support the health of people who use stimulants long-term may be warranted, in addition to identifying risk factors for long-term harms associated with stimulant use.

The majority of benzodiazepine toxicity deaths involved non-pharmaceutical benzodiazepines (82.4%, N=197) in 2021, with only 17.6% of benzodiazepine toxicity deaths (N=42) having pharmaceutical benzodiazepines (without non-pharmaceutical involvement) as direct contributors. Opioids were involved in most deaths involving non-pharmaceutical or pharmaceutical benzodiazepines, with higher opioid (98.0% vs 85.7%, $p<0.001$) and stimulant (63.5% vs 31.0%, $p<0.001$) involvement in non-pharmaceutical benzodiazepine deaths. The high involvement of opioids involved in non-pharmaceutical benzodiazepine deaths (98.0%) requires specific discussion. Evolving evidence in Canada has demonstrated the recent emergence of synthetic benzodiazepines in the unregulated opioid supply,[26] which is reflected in the high proportion of opioid-related deaths where benzodiazepines were detected (65.1%). In particular, community drug checking data from Ontario[27] and British Columbia[28] suggest a substantial degree of benzodiazepine presence in the unregulated opioid supply in recent years. The adulteration of unregulated fentanyl with non-pharmaceutical benzodiazepines is concerning not only given the substantial

risks associated with benzodiazepine and opioid co-use, but also because people who use drugs are often inadvertently consuming benzodiazepines as they are added as adulterants to fentanyl.[26] Benzodiazepine use complicates responses to opioid toxicity and treatment, with opioid-benzodiazepine co-use associated with two-fold higher odds of all-cause mortality[29], increased withdrawal symptoms,[30, 31] and worse retention in OAT compared to those who did not use benzodiazepines.[32] Therefore, effective responses need to address the increased prevalence of benzodiazepines within the unregulated opioid supply, including support for people experiencing withdrawal from benzodiazepines when accessing treatment for OUD.

Although much more uncommon, when they did occur, deaths due to pharmaceutical benzodiazepines were more prevalent among older (45+ years; 52.4% vs 35.5%, p=0.04), female (42.9% vs 29.4%, p=0.09) demographics compared to non-pharmaceutical benzodiazepine deaths, and had more alcohol co-involvement (33.3% vs 7.6%, p<0.001). Opioids were still involved in a large majority of these deaths due to pharmaceutical benzodiazepines (85.7%), even though this proportion was lower than for non-pharmaceutical benzodiazepines (98.0%; p<0.001). These findings may reflect higher prescribing of benzodiazepines among females and older adults in Ontario,[22] as well as the relatively high prevalence of combined use of prescription opioids and benzodiazepines despite known risks[23] – for example, one in four benzodiazepine recipients in Ontario were concurrently receiving an opioid in 2019.[24] Further, our finding that one-third of pharmaceutical benzodiazepine deaths involved alcohol aligns with previous research in the United States where half of those with an alcohol use disorder reported a past prescription for benzodiazepines, and 30% reported benzodiazepine misuse.[25]

Among the 296 alcohol toxicity deaths in Ontario in 2021, deaths caused solely by alcohol were rare (N=25), and generally occurred among a slightly older demographic (median: 49 years, IQR: 37-54 years) compared to deaths where a combination of alcohol and other substances directly contributed to death (median: 41 years, IQR: 34-52 years). This may reflect deaths from acute toxicity resulting from liver damage from long-term alcohol exposure or reduced gastric and liver alcohol dehydrogenase levels in older age, which has been associated with elevated blood alcohol levels.[33, 34] Thus, there is a need to identify and address evolving healthcare needs of people with an alcohol use disorder, especially as they age, to prevent alcohol-related harms. Also, the high percent of alcohol toxicity deaths co-attributed to opioids (82.8%) reflects the high degree of concurrent substance use disorders among people with OUD, and the risks of combined alcohol and opioid use.[35] Improved management and screening of co-occurring substance use disorders may be warranted, as well as the expansion of education, tools and programs to support individuals with complex and co-occurring substance use disorders.

Our findings also stress the need for the adaptation and expansion of consumption and treatment services, healthcare, social services and other supports for people who use drugs across the province. For example, site selection and evaluation plans for consumption and treatment services are currently focused on opioid-related indicators, which highlights the need for responsive approaches that support individuals using other non-opioid substances or multiple substances concurrently.[19] Expansion of services for people who use drugs and tailoring to the current drug context is crucial.

Conclusion

The number of substance toxicity deaths is alarmingly high in Ontario – five times higher than deaths due to motor vehicle collisions in the province – and has grown at an unprecedented rate during the pandemic. Over the past 4 years, substance toxicity deaths have nearly doubled in Ontario, with 8 such deaths occurring on average every day in 2021. The arrival of the COVID-19 pandemic not only led to rising substance-related deaths generally, but to rising polysubstance involvement in deaths, with over 80% of alcohol, stimulant, benzodiazepine deaths also involving opioids. Polysubstance use complicates substance toxicity responses, resulting in higher fatality rates compared to when substances are used alone. Therefore, a high proportion of deaths due to multiple substance toxicity suggests the need for healthcare, community-based and harm reduction interventions which are responsive to multiple concurrent substance use disorders and dependencies. Further, these findings also stress the continued relevance and need for the adaption and expansion of harm reduction programs, including supervised consumption services across Ontario, with a pressing need to consider programs and services in Northern Ontario that address the specific barriers to health and social services that exist in sparsely populated and remote regions. Finally, more research is needed to understand the prevalence of substance-related harms among First Nations People across Ontario to inform investments into First Nations-led, culturally appropriate supports and services.

Contributors

Ontario Drug Policy Research Network

The Ontario Drug Policy Research Network (ODPRN) is a province-wide network of researchers who provide timely, high quality, drug policy relevant research to decision makers. The ODPRN houses the Ontario Opioid Drug Observatory (OODO) which is funded through a grant from the Canadian Institutes of Health Research (CIHR). This observatory aims to measure, assess and evaluate the use of prescription opioids, opioid-related overdoses, and opioid-related drug policy by leveraging large, population-level data sources. For more information, visit odprn.ca.

Public Health Ontario

Public Health Ontario is a Crown corporation dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, frontline health workers and researchers to the best scientific intelligence and knowledge from around the world. Public Health Ontario provides expert scientific and technical support to government, local public health units and health care providers relating to the following:

- communicable and infectious diseases
- infection prevention and control
- environmental and occupational health
- emergency preparedness
- health promotion, chronic disease and injury prevention
- public health laboratory services

Public Health Ontario's work also includes surveillance, epidemiology, research, professional development and knowledge services. For more information, visit **publichealthontario.ca**.

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Disclaimer

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PHO provides scientific and technical advice to Ontario's government, public health organizations and health care providers. This work is guided by the current best available evidence at the time of publication. The application and use of this document is the responsibility of the user. PHO assumes no liability resulting from any such application or use.

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Office of the Chief Coroner – Privacy Statement

Personal information used in developing this report was collected under the authority of the Coroners Act, R.S.O. 1990, C. C.37, as amended. Questions about this collection should be directed to the Chief Coroner, 25 Morton Shulman Avenue, Toronto ON M3M 0B2, Tel.: 416 314-4000 or Toll Free: 1 877 991- 9959.

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Appendix A: Definitions

Substance toxicity death:
An acute intoxication/toxicity death resulting from the direct contribution of consumed substance(s), regardless of how the substance was obtained.

Substance involvement in toxicity deaths:

- **Detected:** Substances detected in toxicology testing, which may or may not have directly contributed to the death.
- **Directly contributing to death:** Substances determined by the pathologist and/or coroner to have directly contributed to the death based on the complete investigative findings, i.e., toxicology findings and the information obtained during the death investigation.

Opioids:
A family of substances that include opioids available through regulated and pharmaceutical sources for the treatment of pain and OUD (e.g., oxycodone, hydromorphone, morphine, methadone) and opioids available primarily through unregulated or non-pharmaceutical markets or sources (e.g., heroin, fentanyl, carfentanil).

Origin of opioids:

- Opioids with **primarily unregulated and non-pharmaceutical origins** include:
  - Heroin, heroin metabolites (morphine where monoacetylmorphine (6-MAM) was also detected), U-47700
  - Fentanyl, fentanyl analogues (including carfentanil)
- Opioids with **primarily regulated and pharmaceutical origins** include:
  - Buprenorphine, codeine, hydrocodone, hydromorphone, methadone, morphine where 6-MAM was not detected, oxycodone, oxymorphone or tramadol. This category may include opioids that were prescribed to the deceased person or that were prescribed to someone else (i.e., diverted).

Benzodiazepines:
A class of sedative and anti-anxiety drugs that are widely prescribed for the treatment of anxiety, sleep disorders (e.g., insomnia), certain forms of epilepsy, and alcohol withdrawal. Currently, 14 different benzodiazepines are approved for use in Canada. Benzodiazepines that are not approved for medical use in Canada, such as etizolam, are increasingly being found in the unregulated drug supply.

Origin of benzodiazepines:

- Benzodiazepines with primarily unregulated and non-pharmaceutical origins:
  - Indicates the presence of benzodiazepines (non-prescription only; exclusively bromazolam, etizolam, flualprazolam, and flubromazolam)
- Benzodiazepines with primarily regulated and pharmaceutical origins:
  - Indicates the presence of benzodiazepines (prescription only; i.e., excluding bromazolam, etizolam, flualprazolam, and flubromazolam)

Stimulants:
A class of drugs used for the treatment of attention-deficit/hyperactivity disorder and sleeping disorders (e.g., narcolepsy). These drugs act on the central nervous system to increase alertness, attention and energy. This category also includes stimulants that are used occasionally and primarily available from the unregulated market, such as cocaine and methamphetamine.

Location of incident:
- **Private residence:** Includes private dwellings.
- Rooming house/other collective dwellings: Includes sober living facilities, boarding houses, halfway houses, rooming houses, etc.
- **Other residential settings/shelters:** Includes shelters, community housing, residential care facilities, etc.
- **Other indoor space (non-hospital):** Includes correctional facilities, custody and hotel/motel/inn.
- **Other** (includes hospital, transit, other)
- **Outdoors:** Includes all outdoor areas.
- **Unknown:** Includes missing, unknown and other categories where there is not sufficient detail to classify (e.g., homeless).

Rural Ontario:
A community with a population of 10,000 people or less, as assigned by Statistics Canada based on the postal code associated with the individual's health card.

Northern Ontario:
North East (13) and North West (14) LHINs. For a map of the various LHINs, click here.

Southern Ontario:
LHINs 1 to 12. For a map of the various LHINs, click here.

Rate:
The frequency with which an event or circumstance occurs per unit of time, population, or other standard of comparison. Example: Based on a rate of 1.5 deaths per 10,000 people, we can expect approximately 15 deaths in a community of 100,000.

Appendix B: Data Tables

Table B1. Descriptive characteristics, overall substance toxicity deaths and top 5 substance combinations in 2021

	All toxicity deaths	Stimulants & Opioids	Opioids only	Stimulants only	Benzodiazepines, Stimulants & Opioids	Alcohol, Stimulants & Opioids
Total deaths (N)	2,886	1,283	813	284	122	118
Age, median (IQR)	40 (32-51)	40 (32-50)	40 (31-52)	45 (35-56)	40 (33-53)	42 (34-52)
Age category (N, %)						
0 to 24	211 (7.3%)	87 (6.8%)	78 (9.6%)	9 (3.2%)	11-16 (9.0%-13.1%)	≤5 (≤4.2%)
25 to 44	1,521 (52.7%)	709 (55.3%)	421 (51.8%)	132 (46.5%)	62 (50.8%)	64 (54.2%)
45 to 64	1,067 (37.0%)	462 (36.0%)	288 (35.4%)	125 (44.0%)	44 (36.1%)	48 (40.7%)
65+	87 (3.0%)	25 (1.9%)	26 (3.2%)	18 (6.3%)	≤5 (≤4.1%)	≤5 (≤4.2%)
Sex (N, %)						
Female	721 (25.0%)	335 (26.1%)	194 (23.9%)	49 (17.3%)	35 (28.7%)	28 (23.7%)
Male	2,165 (75.0%)	948 (73.9%)	619 (76.1%)	235 (82.7%)	87 (71.3%)	90 (76.3%)
Income quintile (N, %)						
1	1,161 (40.2%)	549 (42.8%)	304 (37.4%)	110 (38.7%)	51 (41.8%)	46 (39.0%)
2	582 (20.2%)	255 (19.9%)	168 (20.7%)	61 (21.5%)	22 (18.0%)	28 (23.7%)
3	451 (15.6%)	194 (15.1%)	123 (15.1%)	44 (15.5%)	18 (14.8%)	19 (16.1%)
4	289 (10.0%)	111 (8.7%)	104 (12.8%)	29 (10.2%)	11 (9.0%)	8 (6.8%)
5	273 (9.5%)	115 (9.0%)	82 (10.1%)	26 (9.2%)	11 (9.0%)	13 (11.0%)
Unknown	130 (4.5%)	59 (4.6%)	32 (3.9%)	14 (4.9%)	9 (7.4%)	4 (3.4%)
Urban/Rural location of residence (N, rate per 100,000)						
Urban	2,495 (18.5)	1,103 (8.2)	708 (8.2)	246 (1.8)	106 (0.8)	104 (0.8)
Rural	262 (17.0)	122 (7.9)	73 (7.9)	24 (1.6)	7 (0.5)	10 (0.6)
Unknown	129	58	32	14	9	4
Northern/Southern location of residence (N, rate per 100,000)						
Northern	407 (47.9)	187 (22.0)	119 (14.0)	27 (3.2)	20 (2.4)	23 (2.7)
Southern	2,411 (16.9)	1,064 (7.5)	676 (4.7)	250 (1.8)	97 (0.7)	94 (0.7)
Unknown	68	32	18	7	5	1
Location of incident among cases where location of incident was known (N, %)						
Known location of incident	2144	858	636	283	86	76
Private residence	1,630 (76.0%)	639 (74.5%)	525 (82.5%)	187 (66.1%)	69 (80.2%)	56 (73.7%)
Rooming house/other collective dwellings	226 (10.5%)	121 (14.1%)	53 (8.3%)	18 (6.4%)	7 (8.1%)	10 (13.2%)
Other residential settings/ shelters	52 (2.4%)	19 (2.2%)	14 (2.2%)	9 (3.2%)	≤5 (≤5.8%)	≤5 (≤6.6%)
Other indoor space (non-hospital)	95 (4.4%)	28 (3.3%)	13 (2.0%)	30 (10.6%)	0 (0.0%)	≤5 (≤6.6%)
Other (includes hospitals, transit, other)	31 (1.4%)	8 (0.9%)	10 (1.6%)	10 (3.5%)	7 (8.1%)	≤5 (≤6.6%)
Outdoors	110 (5.1%)	43 (5.0%)	21 (3.3%)	29 (10.2%)	≤5 (≤5.8%)	≤5 (≤6.6%)
Unknown location of incident (N, %)	742 (25.7%)	425 (33.1%)	177 (21.8%)	1 (0.4%)	36 (29.5%)	42 (35.6%)

Table B2. Descriptive characteristics, all substance toxicity deaths in 2021

	Alcohol (overall)	Stimulant (overall)	Benzodiazepine (overall)	Opioid (overall)
Total deaths (N)	296	1,843	239	2,547
Age, median (IQR)	41 (34-52)	40 (33-51)	40 (31-55)	40 (32-51)
Age category (N, %)				
0 to 24	10 (3.4%)	114 (6.2%)	29 (12.1%)	200 (7.9%)
25 to 44	158 (53.4%)	989 (53.7%)	118 (49.4%)	1,361 (53.4%)
45 to 64	116 (39.2%)	688 (37.3%)	83 (34.7%)	922 (36.2%)
65+	12 (4.1%)	52 (2.8%)	9 (3.8%)	64 (2.5%)
Sex (N, %)				
Female	80 (27.0%)	460 (25.0%)	76 (31.8%)	652 (25.6%)
Male	216 (73.0%)	1,383 (75.0%)	163 (68.2%)	1,895 (74.4%)
Income quintile (N, %)				
1	120 (40.5%)	770 (41.8%)	91 (38.1%)	1,027 (40.3%)
2	59 (19.9%)	371 (20.1%)	45 (18.8%)	514 (20.2%)
3	52 (17.6%)	280 (15.2%)	43 (18.0%)	398 (15.6%)
4	26 (8.8%)	162 (8.8%)	20 (8.4%)	252 (9.9%)
5	26 (8.8%)	173 (9.4%)	28 (11.7%)	242 (9.5%)
Unknown	13 (4.4%)	87 (4.7%)	12 (5.0%)	114 (4.5%)
Location of incident among cases where location of incident was known (N, %)				
Known location of incident	209	1,333	179	1,807
Private residence	155 (74.2%)	973 (73.0%)	139 (77.7%)	1,401 (77.5%)
Rooming house/other collective dwellings	22 (10.5%)	157 (11.8%)	15 (8.4%)	206 (11.4%)
Other residential settings/shelters				
Other indoor space (non-hospital)	9 (4.3%)	71 (5.3%)	15 (8.4%)	61 (3.4%)
Other (includes hospitals, transit, other)	≤5 (≤2.4%)	20 (1.5%)	≤5 (≤2.8%)	19 (1.1%)
Outdoors	13 (6.2%)	79 (5.9%)	≤5 (≤2.8%)	78 (4.3%)
Unknown location of incident (N, %)	87 (29.4%)	510 (27.7%)	60 (25.1%)	740 (29.1%)
Number of substance groups involved in death (N, %)				
1	25 (8.4%)	284 (15.4%)	≤5 (≤2.1%)	813 (31.9%)
2	128 (43.2%)	1,304 (70.8%)	87-92 (36.4-38.5%)	1,471 (57.8%)
3+	143 (48.3%)	255 (13.8%)	147 (61.5%)	263 (10.3%)
Other substances contributing to death (N, %)				
Alcohol	296 (100.0%)	153 (8.3%)	29 (12.1%)	245 (9.6%)
Opioids	245 (82.8%)	1,536 (83.3%)	229 (95.8%)	2,547 (100.0%)
Stimulants	153 (51.7%)	1,843 (100.0%)	138 (57.7%)	1,536 (60.3%)
Benzodiazepines	29 (9.8%)	138 (7.5%)	239 (100.0%)	229 (9.0%)
Stimulant types (N, %)				
Cocaine	N/A	1,258 (68.3%)	N/A	N/A
Methamphetamine	N/A	882 (47.9%)	N/A	N/A
Amphetamine	N/A	135 (7.3%)	N/A	N/A
Other stimulants except cocaine, methamphetamine, amphetamine	N/A	14 (0.8%)	N/A	N/A
Benzodiazepines detected in post-mortem (N, %)	N/A	N/A	N/A	1,658 (65.1%)

	Alcohol (overall)	Stimulant (overall)	Benzodiazepine (overall)	Opioid (overall)
Urban/rural location of residence (N, rate per 100,000)				
Urban	255 (1.9)	1,588 (11.8)	209 (1.5)	2,203 (16.3)
Rural	28 (1.8)	169 (11.0)	18 (1.2)	231 (15)
Unknown	13	86	12	113
Northern/Southern location of residence (N, rate per 100,000)				
Northern	47 (5.5)	265 (31.2)	35 (4.1)	371 (43.7)
Southern	243 (1.7)	1,533 (10.8)	199 (1.4)	2,116 (14.9)
Unknown	6	45	5	60

Unknown opioids are not reported (N=45). Only direct contributors are reflected, although other substances as detected may be included. Number of substances represent broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).

Table B3. Descriptive characteristics, stimulant toxicity deaths by type in 2021

	Cocaine	Methamphetamine	Amphetamine
Total deaths (N)	1,258	882	135
Age, median (IQR)	42 (34-53)	39 (32-49)	41 (33-51)
Age category (N, %)			
0 to 24	72 (5.7%)	60 (6.8%)	8 (5.9%)
25 to 44	630 (50.1%)	514 (58.3%)	72 (53.3%)
45 to 64	513 (40.8%)	290 (32.9%)	49 (36.3%)
65+	43 (3.4%)	18 (2.0%)	6 (4.4%)
Sex (N, %)			
Female	322 (25.6%)	215 (24.4%)	29 (21.5%)
Male	936 (74.4%)	667 (75.6%)	106 (78.5%)
Income quintile (N, %)			
1	507 (40.3%)	393 (44.6%)	58 (43.0%)
2	244 (19.4%)	191 (21.7%)	27 (20.0%)
3	204 (16.2%)	124 (14.1%)	16 (11.9%)
4	124 (9.9%)	60 (6.8%)	12 (8.9%)
5	127 (10.1%)	68 (7.7%)	9 (6.7%)
Unknown	52 (4.1%)	46 (5.2%)	13 (9.6%)
Location of incident among cases where location of incident was known (N, %)			
Known location of incident	929	606	134
Private residence	705 (75.9%)	404 (66.7%)	79 (59.0%)
Rooming house/other collective dwellings	105 (11.3%)	86 (14.2%)	11 (8.2%)
Other residential settings/shelters	17 (1.8%)	20 (3.3%)	≤5 (≤3.7%)
Other indoor space (non-hospital)	43 (4.6%)	42 (6.9%)	19 (14.2%)
Other (includes hospitals, transit, other)	13 (1.4%)	9 (1.5%)	≤5 (≤3.7%)
Outdoors	46 (5.0%)	45 (7.4%)	16 (11.9%)
Unknown location of incident (N, %)	329 (26.2%)	276 (31.3%)	1 (0.7%)

	Cocaine	Methamphetamine	Amphetamine
Number of substance groups involved in death (N, %)			
1	197 (15.7%)	116 (13.2%)	118 (87.4%)
2	866 (68.8%)	672 (76.2%)	12-17 (8.9%-12.6%)
3+	195 (15.5%)	94 (10.7%)	≤5 (≤3.7%)
Other substances contributing to death (N, %)			
Opioids	1,044 (83.0%)	758 (85.9%)	9 (6.7%)
Alcohol	125 (9.9%)	46 (5.2%)	8 (5.9%)
Benzodiazepines	98 (7.8%)	59 (6.7%)	≤5 (≤3.7%)
Stimulant types (N, %)			
Cocaine	1258 (100.0%)	318 (36.1%)	45 (33.3%)
Methamphetamine	318 (25.3%)	882 (100.0%)	119 (88.1%)
Amphetamine	45 (3.6%)	119 (13.5%)	135 (100.0%)
Other stimulants except cocaine, methamphetamine, amphetamine	9 (0.7%)	6 (0.7%)	0 (0.0%)
Urban/rural location of residence (N, rate per 100,000)			
Urban	1,100 (8.1)	748 (5.5)	109 (0.8)
Rural	107 (6.9)	88 (5.7)	13 (0.8)
Unknown	51	46	13
Northern/Southern location of residence (N, rate per 100,000)			
Northern	186 (21.9)	139 (16.4)	14 (1.6)
Southern	1,043 (7.3)	724 (5.1)	116 (0.8)
Unknown	29	19	5

Only direct contributors are reflected here, although other substances as detected in post-mortem may be included. Number of substances represent broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).

Table B4. Descriptive characteristics, benzodiazepine toxicity deaths by type in 2021

	Non-pharmaceutical benzodiazepines	Pharmaceutical benzodiazepines only	Stat. sig
Total deaths (N)	197	42	
Age, median (IQR)	39 (31-50)	46 (35-56)	*
Age category (N, %)			
0 to 44	127 (64.5%)	20 (47.6%)	*
45+	70 (35.5%)	22 (52.4%)	*
Sex (N, %)			
Female	58 (29.4%)	18 (42.9%)	
Male	139 (70.6%)	24 (57.1%)	
Income quintile (N, %)			
1	74 (37.6%)	17 (40.5%)	
2	36 (18.3%)	9 (21.4%)	
3	35 (17.8%)	8 (19.0%)	
4	19 (9.6%)	≤5 (≤11.9%)	N/A
5	21 (10.7%)	3-8 (7.1%-19.0%)	
Unknown	12 (6.1%)	0 (0.0%)	

	Non-pharmaceutical benzodiazepines	Pharmaceutical benzodiazepines only	Stat. sig
Location of incident among cases where location of incident was known (N, %)			
Known location of incident	144	35	
Private Residence	112 (77.8%)	27 (77.1%)	
Other	32 (22.2%)	8 (22.9%)	
Unknown location of incident (N, %)	53 (26.9%)	7 (16.7%)	
Number of substance groups involved in death (N, %)			
1 to 2	67 (34.0%)	25 (59.5%)	*
3+	130 (66.0%)	17 (40.5%)	*
Other substances contributing to death (N, %)			
Opioids	193 (98.0%)	36 (85.7%)	*
Alcohol	15 (7.6%)	14 (33.3%)	*
Stimulants	125 (63.5%)	13 (31.0%)	*
Urban/rural location of residence (N, rate per 100,000)			
Urban	171 (1.3)	37-42 (0.27-0.31)	N/A
Rural	14 (0.9)	≤5 (≤0.3)	N/A
Unknown	12	0	N/A
Northern/Southern location of residence (N, rate per 100,000)			
Northern	23 (2.7)	12 (1.4)	N/A
Southern	169 (1.2)	30 (0.2)	N/A
Unknown	5	0	N/A

The pharmaceutical benzodiazepine only category does not include non-pharmaceutical benzodiazepines, while non-pharmaceutical benzodiazepines includes N=10 deaths involving both pharmaceutical and non-pharmaceutical benzodiazepines. Only direct contributors are reflected here, although other substances as detected in post-mortem may be included. Red asterisk indicates statistically significant (stat.sig.) difference between proportions ($p<0.05$). P-values were not computed where N≤5 or for ranges. Number of substances represent broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).

Table B5. Descriptive characteristics, opioid toxicity deaths by type in 2021

	Non-pharmaceutical opioids	Pharmaceutical opioids only	Stat. sig.
Total deaths (N)	2,303	204	
Age, median (IQR)	40 (31-50)	48 (36-58)	*
Age category (N, %)			
0 to 24	183 (7.9%)	10 (4.9%)	
25 to 44	1,269 (55.1%)	72 (35.3%)	*
45 to 64	808 (35.1%)	102 (50.0%)	*
65+	43 (1.9%)	20 (9.8%)	*
Sex (N, %)			
Female	569 (24.7%)	72 (35.3%)	*
Male	1,734 (75.3%)	132 (64.7%)	*
Income quintile (N, %)			
1	938 (40.7%)	76 (37.3%)	
2	453 (19.7%)	50 (24.5%)	
3	354 (15.4%)	39 (19.1%)	

	Non-pharmaceutical opioids	Pharmaceutical opioids only	Stat. sig.
4	232 (10.1%)	16 (7.8%)	
5	221 (9.6%)	14 (6.9%)	
Unknown	105 (4.6%)	9 (4.4%)	
Location of incident among cases where location of incident was known (N, %)			
Known location of incident	1,602	173	
Private residence	1,230 (76.8%)	150 (86.7%)	*
Rooming house/other collective dwellings	193 (12.0%)	13 (7.5%)	
Other residential settings/shelters	37 (2.3%)	≤5 (≤2.9%)	N/A
Other indoor space (non-hospital)	55 (3.4%)	≤5 (≤2.9%)	N/A
Other (includes hospitals, transit, other)	15 (0.9%)	≤5 (≤2.9%)	N/A
Outdoors	72 (4.5%)	≤5 (≤2.9%)	N/A
Unknown location of incident (N, %)	701 (30.4%)	31 (15.2%)	*
Number of substance groups involved in death (N, %)			
1	669 (29.0%)	106 (52.0%)	*
2	1,381 (60.0%)	89 (43.6%)	*
3+	253 (11.0%)	9 (4.4%)	*
Other substances directly contributing to death (N, %)			
Alcohol	212 (9.2%)	32 (15.7%)	*
Stimulants	1,474 (64.0%)	60 (29.4%)	*
Benzodiazepines	213 (9.2%)	16 (7.8%)	
Benzodiazepines detected in post-mortem (N, %)	1,563 (67.9%)	80 (39.2%)	*
Urban/rural location of residence (N, rate per 100,000)			
Urban	1,996 (14.8)	168 (1.2)	N/A
Rural	202 (13.1)	28 (1.8)	N/A
Unknown	105	8	N/A
Northern/Southern location of residence (N, rate per 100,000)			
Northern	335 (39.5)	31 (3.7)	N/A
Southern	1,912 (13.4)	169 (1.2)	N/A
Unknown	56	4	N/A

Unknown opioids are not reported in this table (N=45). The pharmaceutical opioid only category does not include non-pharmaceutical opioids, while non-pharmaceutical opioids includes N=272 deaths involving both pharmaceutical and non-pharmaceutical opioids. Only direct contributors are reflected here, although other substances as detected in post-mortem may be included. Red asterisk indicates statistically significant (stat.sig.) difference between proportions ($p<0.05$). P-values were not computed where N≤5. Number of substances represent broad groupings (i.e., alcohol, stimulant, benzodiazepine, or opioid).