



Latest Trends in Opioid-Related Deaths in Ontario

1991 to 2015

**The Ontario Drug Policy Research Network
April 2017**



About the ODPRN

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's core principles are quality, relevance, and timeliness. We conduct research to determine real-world drug utilization, safety, effectiveness, and costs of drugs in Ontario, and have developed partnerships that allow us to engage in cross-provincial comparisons of drug safety and utilization.

We are funded to conduct pharmacoepidemiologic and drug policy research as part of an initiative to provide evidence to inform policy at the Ontario Ministry of Health and Long-Term Care (MOHLTC). As such, the ODPRN works closely with the Ontario Public Drug Programs (OPDP), MOHLTC and other stakeholders to select key priority areas and topics for analysis.

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Key Points

- In 2015, 734 people died of an opioid-related cause, averaging to approximately 2 people every day. The rate of opioid-related deaths has increased almost 4-fold (285%) over the past 25 years.
- Over 80% of all opioid-related deaths in 2015 were accidental. The manner of death differed considerably by age group as almost 60% of accidental deaths occurred among youth and younger adults (15 to 44 years), whereas nearly 80% of suicide deaths occurred among older adults (45 years and older).
- Prior to 2012, oxycodone was the opioid most commonly involved in opioid-related deaths. However, after the introduction of a tamper-deterrent formulation, oxycodone involvement in these deaths decreased, and other opioids became increasingly involved. In particular, fentanyl involvement increased by 548% between 2006 and 2015 and is now the opioid most commonly involved in opioid-related deaths. Hydromorphone involvement also increased by 232% over this time to become the second most commonly involved opioid. Despite small numbers overall, heroin involvement in opioid-related deaths has increased by 975% over this same period.
- It is common for opioid-related deaths to also involve other substances. Benzodiazepines were present in half, and cocaine was present in one-third of opioid-related deaths.
- On average, individuals who died of an opioid-related cause in 2015 were male, middle aged, and living in lower income urban settings.

Background

Opioid analgesics are widely prescribed for the treatment of pain. However, the rate of opioid prescribing and the number of deaths related to opioids have increased dramatically over the last two decades in Ontario, highlighting safety concerns around these commonly prescribed analgesics.^{1,2} Furthermore, the impact of this problem is even more pronounced among younger adults, with premature deaths related to opioids resulting in an extraordinary burden of potential years of life lost. In 2010, nearly one out of every eight deaths among individuals aged 25 to 34 years involved an opioid, demonstrating the public health importance of opioid use.²

The ODPRN has worked over the past several years to capture and report trends in opioid-related deaths in Ontario to provide policy-makers and other stakeholders with information on emerging patterns of opioid overdose and death. This information was

initially published in a November 2014 report and an accompanying manuscript containing analyses of opioid-related deaths up to December 31, 2010.^{2,3}

With the introduction of policies designed to address opioid prescribing practices that may be contributing to this problem, the reported rise in illicit fentanyl availability, and changes to formulation and availability of prescription opioids, current data are needed to understand the trends in opioid-related deaths, the types of opioids most commonly involved in deaths, and the characteristics of the people involved.

Objective

This report describes trends in opioid-related deaths, the opioids involved in each death, and the characteristics of individuals who died of an opioid-related cause in Ontario up to the end of 2015.

Methods

Setting

We conducted a cross-sectional study among individuals who died of opioid-related causes between January 1991 and December 2015 using data obtained from the Office of the Chief Coroner for Ontario (OCCO). Deaths were deemed to be opioid-related by the coroner if post-mortem toxicological analysis revealed opioid concentrations sufficiently high enough to cause death, or if a combination of drugs (including at least one opioid at clinically significant levels) contributed to death. This method has been used in previous studies in this area.^{2,4-7}

Data Sources

Detailed information regarding opioid-related deaths was abstracted from records of all deaths involving drugs or alcohol from the OCCO. In Ontario, all deaths that are sudden and unexpected, or unnatural are investigated by the OCCO to ascertain cause and manner of death. We used the Ontario Health Insurance Plan Registered Persons Database (RPDB) to determine the demographic characteristics (including age, gender, location of residence, and neighbourhood income quintile) of all Ontarians who died of opioid-related causes in 2015. These datasets were linked using unique, encoded identifiers and analyzed at the ICES.

Study Drugs

Opioids: Codeine, methadone, oxycodone, fentanyl, hydromorphone, heroin, morphine, other opioids (hydrocodone, meperidine, propoxyphene, pentazocine, anileridine, tramadol, buprenorphine, oxymorphone), undetermined.

Other drugs: Cocaine, gammahydroxybutyrate (GHB), benzodiazepines, tricyclic antidepressants, other antidepressants, antipsychotics, antihistamines, stimulants, tetrahydrocannabinol (THC; cannabis).

Analysis

Opioid-Related Deaths

We calculated the rate of opioid-related deaths annually, adjusting for the population of Ontario using estimates obtained from Statistics Canada. In 2015, there were 16 suspected opioid-related deaths where the coroner's investigation was not yet closed and 4 confirmed opioid-related deaths where details of the investigation were not available to us at the time of conducting the analysis. Therefore, these cases are included in our total counts of opioid-related deaths in 2015, but are not included in more detailed analyses described below. Furthermore, we reported trends in the absolute number of opioid-related deaths by age group and type of opioid involved in deaths, stratifying opioid involvement into each of the categories described above. In this analysis, deaths involving multiple opioids may be represented in multiple categories related to the specific opioids involved. For example, if a death involved both methadone and oxycodone, it would be represented in counts of methadone-involved deaths and oxycodone-involved deaths.

Characteristics of Individuals Dying of Opioid Overdose

We explored the demographic characteristics of 714 of the 734 (97%) individuals who died of an opioid-related cause in 2015, where data was available. This includes age at death, sex, rural/urban location of residence, and neighbourhood income quintile (1 = lowest income to 5 = highest income based on average household income, in region defined using an individual's postal code). Furthermore, details regarding the circumstances of the opioid-related deaths were captured, including manner of death (accidental, suicide, undetermined), number of opioids involved in death (single vs. multiple), types of opioids identified on post-mortem toxicology, and other drugs identified on post-mortem toxicology (see list of specific drugs above).

Deaths by Age, Sex, & Manner of Death

We reported the distribution of opioid-related deaths by age group and sex among those deaths determined to be suicides and those determined

to be accidental. Age groups were defined as ≤14, 15-24, 25 to 34, 35 to 44, 45 to 54, 55 to 64 and ≥65 years. We also reported the proportion of accidental opioid-related deaths that occurred in each age group and sex. This was then replicated to determine the proportion of all opioid-related deaths deemed to be suicides that occur in each age group and sex.

Findings

Rate of Opioid-Related Deaths

The annual rate of opioid-related deaths has increased 285% from 1991 to 2015, rising from 14 deaths per million (144 deaths) to 53 deaths per million (734 deaths) over this time (Figure 1). By 2015, there was 1 death for every 18,797 people living in the province, and on average 2 people died of an opioid-related cause every day. The total number of opioid-related deaths in 2014 (N=676) far exceeded the number of people killed

in motor vehicle collisions in Ontario that same year (N=481).⁸

In 1991, the majority of opioid-related deaths (65.3%) occurred among individuals aged 25 to 44 years (Figure 1). However, over the subsequent 25 years, there has been a considerable increase in the number of opioid-related deaths among other age groups, particularly those aged 45 to 64 years, who now represent 43% of all opioid-related deaths in Ontario (rising from only 19% of deaths in 1991). Opioid-related deaths among the elderly (aged 65 and older) and children (aged 0 to 14) remained low throughout our study period (34 deaths among elderly in 2015, 5% of all opioid-related deaths; ≤5 deaths annually among children over entire study period).

In 2005, oxycodone became the opioid involved in the highest number of opioid-related deaths in Ontario, reaching a high of 233 deaths in 2010 (41% of all opioid-related deaths that year; Figure 2). However, since this time, oxycodone involvement has declined considerably, reaching 173 deaths

Figure 1: Trends in Opioid-Related Deaths by Year and Age Groups in Ontario, 1991 to 2015

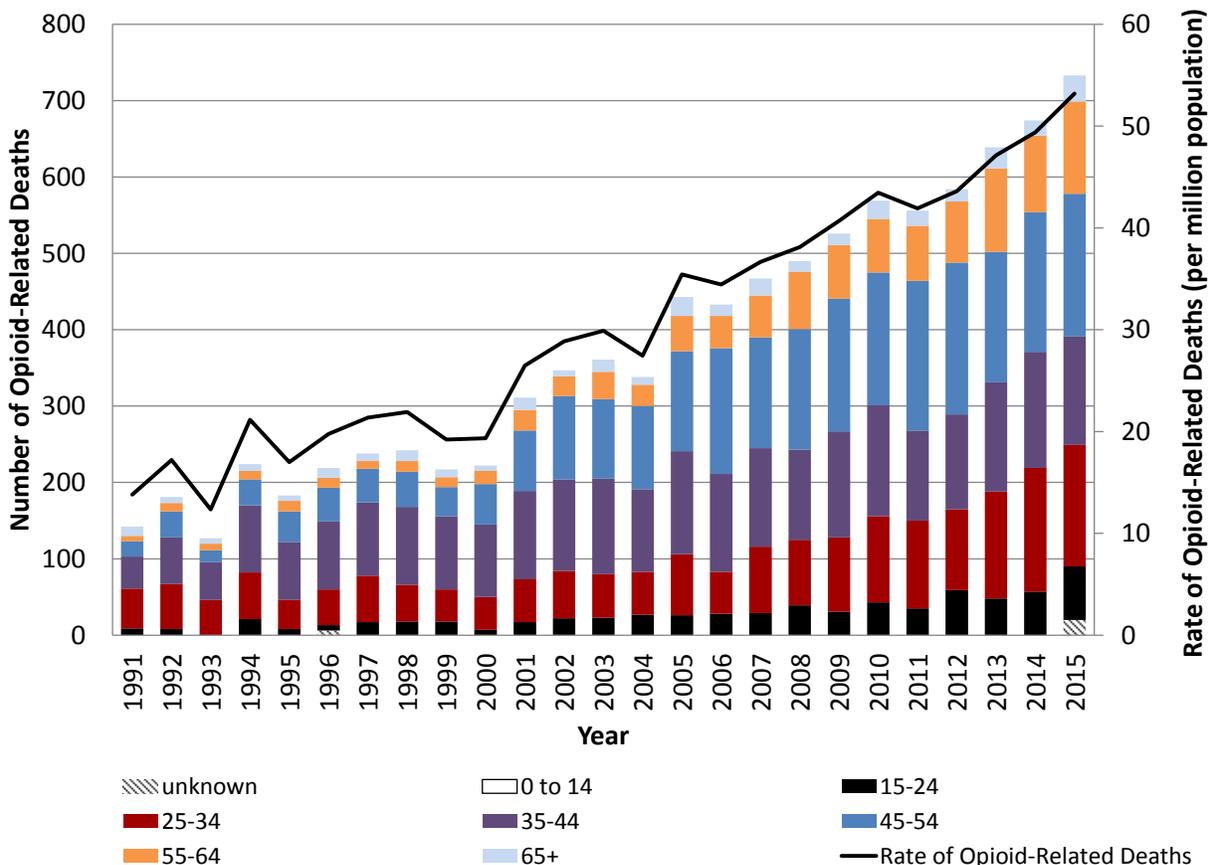
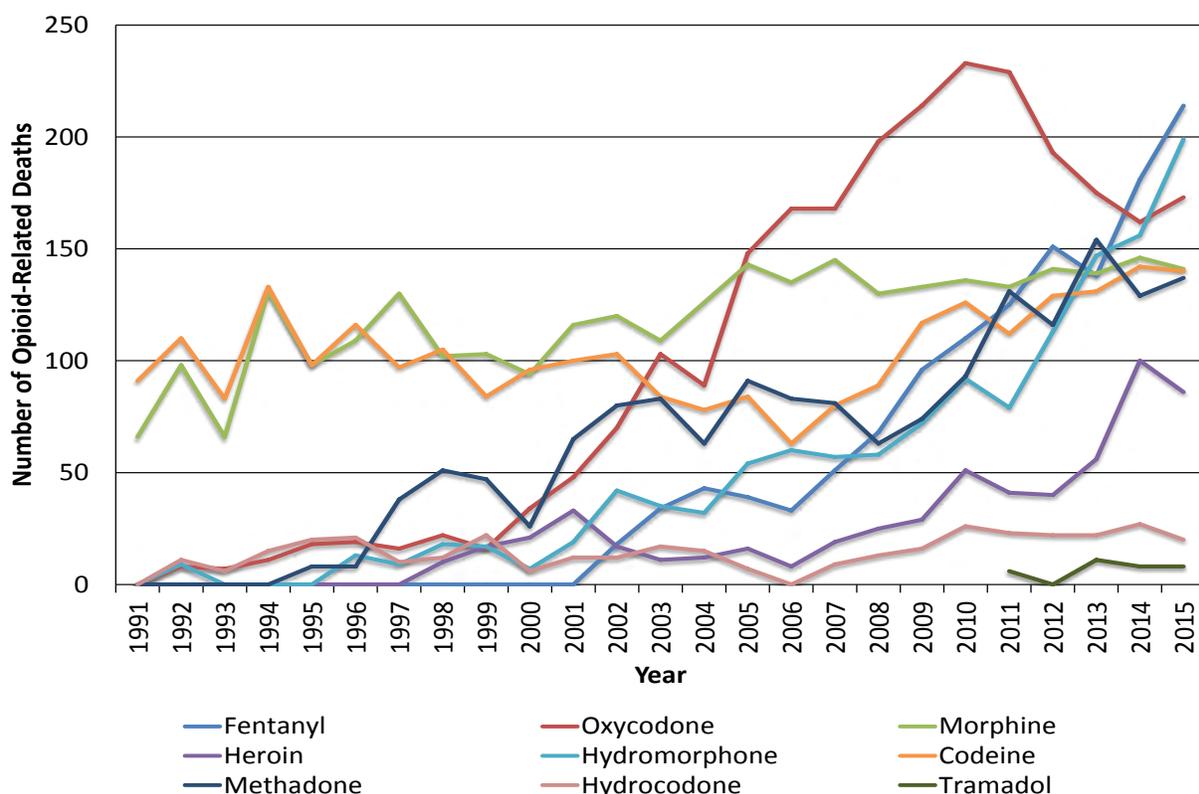


Figure 2: Trend in Opioid-Related Deaths in Ontario by Type of Opioid Involved, 1991 to 2015



Note: 20 deaths from 2015 where details on specific opioid involvement was unavailable are not reported in this figure.

by 2015. Between 2006 and 2015, fentanyl involvement in opioid-related deaths increased 548%, and in 2014 fentanyl surpassed oxycodone to become the opioid most commonly involved in these deaths (reaching 214 fentanyl-involved deaths by 2015). Hydromorphone involvement also quickly increased over this time (232% increase), and was the second most common opioid involved in opioid-related deaths with 199 hydromorphone-involved deaths in 2015. Despite a lower overall prevalence, heroin-involved deaths rose 975% between 2006 and 2015, contributing to 86 opioid-related deaths in the last year of the study period. The majority of this rise occurred between 2012 and 2015, when heroin-involved deaths more than doubled.

Characteristics of Individuals Dying of an Opioid Overdose

On average, two-thirds of individuals who died of an opioid-related cause in 2015 were male (66%), and the average age at time of death was 43 years (Table 1). Over half of individuals who died resided

Table 1: Characteristics of Individuals Dying of an Opioid Overdose in Ontario in 2015

Characteristic	Number of Deaths (N=714)
Age (Mean (SD))	43 (14)
Male	472 (66%)
Income Quintile	
1 (lowest income)	244 (34%)
2	121 (17%)
3	127 (18%)
4	106 (15%)
5 (highest income)	82 (11%)
Missing	34 (5%)
Rural Location of Residence	72 (10%)
Missing	30 (4%)
Manner of Death	
Accidental	592 (83%)
Suicide	87 (12%)
Undetermined/Other	35 (5%)

in a low income neighbourhood (51% in income quintile 1 or 2), one-quarter resided in high income neighbourhoods (26% in income quintile 4 or 5), and the majority lived in an urban setting (86%).

In 2015, over half of all opioid-related deaths involved a single opioid (58%), with the most common opioids involved being fentanyl (28%), hydromorphone (21%), and methadone (20%; **Table 2**). When multiple opioids were involved at

Table 2: Characteristics of Drugs Involved in Fatal Opioid Overdoses in Ontario in 2015

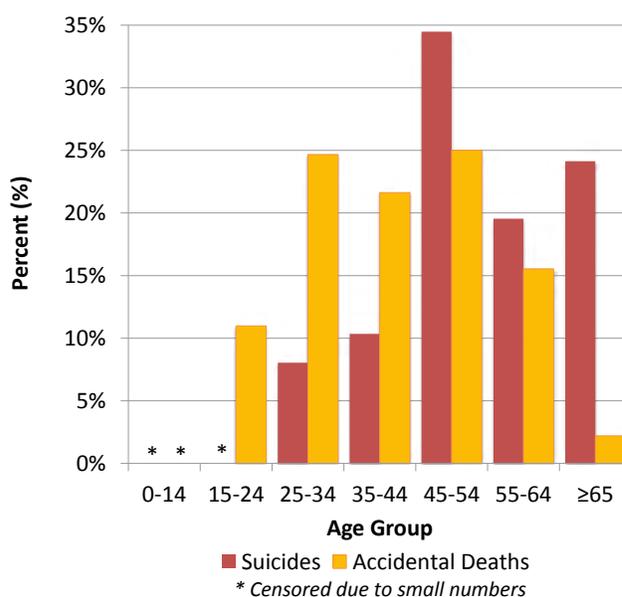
Characteristic	Number of Deaths (N=714)
Single Opioid Involved	415 (58%)
Fentanyl	114 (16%)
Oxycodone	66 (9%)
Morphine (no heroin)	36 (5%)
Heroin	22 (3%)
Hydromorphone	88 (12%)
Codeine	7 (1%)
Methadone	82 (11%)
Multiple Opioids Involved	295 (41%)
Fentanyl	100 (14%)
Oxycodone	107 (15%)
Morphine (no heroin)	105 (15%)
Heroin	64 (9%)
Hydromorphone	111 (16%)
Codeine	133 (19%)
Methadone	55 (8%)
Other Opioids	67 (9%)
Unknown Number of Opioids Involved	4 (1%)
Other Drugs Involved	
Cocaine	230 (32%)
Cocaine and Fentanyl	94 (13%)
GHB	6 (1%)
Benzodiazepines	363 (51%)
Antipsychotics	98 (14%)
Antihistamines	125 (18%)
Stimulants	157 (22%)
THC	26 (4%)
Tricyclic Antidepressants	65 (9%)
Other Antidepressants	270 (38%)

time of death, codeine (45%), oxycodone (36%), hydromorphone (38%) and fentanyl (34%) were the drugs most commonly identified on post-mortem toxicology. This may be due in part to widespread use of codeine and oxycodone combination products (e.g. Percocet and Tylenol 3) in Ontario. Finally, opioid-related deaths often involved other drugs (both legal and illicit) that could have contributed to these deaths. This included over half of individuals having a benzodiazepine (51%), and nearly one-third (32%) having cocaine or its metabolite identified in post-mortem toxicology.

Deaths by Age Group, Sex and Manner of Death

Over 80% of all opioid-related deaths in 2015 were accidental (83%, N=592). There was a considerable difference in the distribution of deaths by age group when comparing accidental and suicide deaths (**Figure 3**). In particular, nearly 80% of the 87 deaths determined to be suicides occurred in those aged 45 and older, with one-quarter (24%) of these deaths occurring among people older than 65. In contrast, almost 60% of accidental deaths occurred among individuals aged 15 to 44 years, with one-quarter of accidental deaths (25%) occurring among

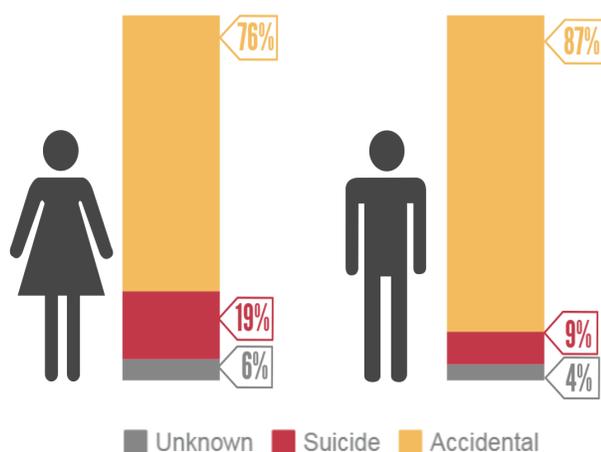
Figure 3: Distribution of Opioid-Related Deaths by Age Group, Stratified by Manner of Death in 2015



young adults (25 to 34 years), and only 2% of accidental deaths occurring among those aged 65 and older.

There were considerable differences in manner of opioid-related deaths between men and women. Overall, approximately half of deaths determined to be suicides were among women (45 of 87; 52%). While only 9% of deaths in men were determined to be suicides by the investigating coroner, nearly 1 in 5 (19%) opioid-related deaths among women were deemed to be suicides (**Figure 4**).

Figure 4: Percentage of Deaths by Manner among Men and Women in 2015



Discussion

In this analysis of all opioid-related deaths occurring in the province of Ontario over the past 25 years, we found that the rate of these deaths has continued to climb, despite the introduction of policies and programs designed to address this issue. Furthermore, these deaths are increasingly occurring among all ages, income brackets, and in both sexes, highlighting the pervasiveness of this public health problem.

Opioid Involvement

The introduction of a tamper-deterrent formulation of long-acting oxycodone in 2012 appears to have shifted opioid involvement in opioid-related deaths.

In particular, oxycodone involvement in opioid-related deaths fell 24% from 229 deaths in 2011 to 173 deaths in 2015. Despite this, there has been no overall reduction in the rate of opioid-related deaths, and instead a rapid increase in this rate since 2012. This appears to be driven by rising involvement of other opioids such as fentanyl, hydromorphone and heroin in deaths between 2012 and 2015. This illustrates the persistent nature of this issue and suggests that the introduction of a tamper-deterrent opioid formulation will have limited impact on related adverse events. Instead, the introduction of tamper-deterrent long-acting oxycodone appears to have driven shifts in the types of opioids that are used towards alternatives (both illicit and prescribed) that do not have these tamper-deterrent properties. Although we are unable to determine the relative contributions of illicit and prescribed opioids to this issue, recent advances in linking prescribing data from the Narcotics Monitoring System (NMS) to patient outcome data will help facilitate these analyses in the future.



We found that nearly 60% of opioid-related deaths involved a single opioid, and that fentanyl, methadone and hydromorphone were the opioids most often contributing to these deaths. These findings are likely reflective of a number of drug-related factors, which may include the high potency of these drugs, the emergence of illicit fentanyl in some jurisdictions in Canada, and the potential for relapse among people with opioid use disorder who are treated with methadone. Furthermore, studies have shown that hydromorphone prescribing partially replaced long-acting oxycodone upon the introduction of a tamper-deterrent form (and subsequent restrictions on public drug formularies)⁹. Therefore, rising hydromorphone involvement in

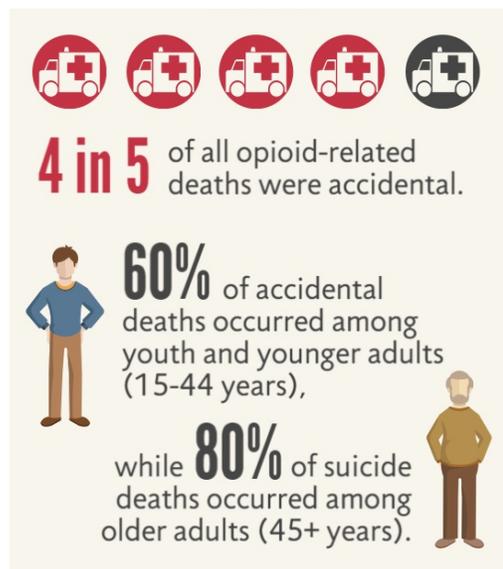
deaths could be partly attributable to dosing errors (either by patient or prescriber) when switching from oxycodone to hydromorphone, which is approximately 3 times more potent than oxycodone.

The high degree of concomitant use of opioids with other central nervous system (CNS) depressants merits discussion. For example, half of all opioid-related deaths also involved a benzodiazepine, 18% involved antihistamines, and 9% involved a tricyclic antidepressant. Not only does this suggest a high level of mental health comorbidity in this population, but given the body of research confirming a clinically important interaction between opioids and CNS depressants^{10,11}, these findings are of considerable concern. In particular, this suggests that dangerous combinations of medications contribute frequently to accidental fatal opioid overdoses. Furthermore, almost one-third of opioid-related deaths also had cocaine present on post-mortem toxicology, and 40% of deaths where cocaine was present also involved fentanyl. This may be indicative of the concerning practice of combining cocaine with illicitly produced fentanyl (which is relatively inexpensive) to extend the drug supply¹² and suggests that growing use of illicit fentanyl is having an important impact on public safety in Ontario.

Manner of Death

Overall, 4 in 5 opioid-related deaths in Ontario in 2015 were accidental, highlighting the avoidable nature of these deaths. However, there is considerable variation in manner of death by sex and age. The clustering of deaths deemed to be suicides among older age groups appears more pronounced among opioid-related deaths compared with the general population. In our study, we found that over 80% of opioid-involved suicides occurred among people aged 45 and older, compared to just over half (58%) of all suicides in Canada in 2013.¹³ Furthermore, although men are generally more likely to commit suicide¹³, in our study, approximately half of all suicides were among women. This may be explained in part by a higher prevalence of drug overdose suicide deaths among women compared to men.¹⁴ In contrast, accidental deaths were largely clustered among youth and young adults,

with only 2% of accidental deaths occurring among people aged 65 and older and almost two-thirds of accidental deaths occurring among people aged 15 to 44 years. These demographic variations in manner of death suggest that programs and policies must be tailored to identify and address the specific needs of men, women, young adults and the elderly.



Limitations

The following limitations must be considered in interpreting these findings. First, these findings are reliant on records of death investigations conducted by the Office of the Chief Coroner of Ontario, and therefore the cause and manner of death are based on the determination of the investigating coroner and examining pathologist. However, it is anticipated that these data are of high validity given the number of factors that are considered by the investigating coroner and pathologist, and the fact that we had access to findings from post-mortem toxicology to determine opioids involved in deaths. Second, we are unable to stratify fentanyl-involved deaths according to those involving illicit (i.e. diverted or illicitly produced) vs. prescribed fentanyl, and therefore cannot determine the extent to which illicit fentanyl has contributed to the recent rise in opioid-related deaths. Third, we have reported all opioids and other drugs present on post-mortem toxicology analysis at time of deaths deemed to be opioid-related. Therefore, while present at time of death, the drug involvement reported here may or may not have actually contributed to the death according to

the coroner's investigation. For example, while an antidepressant may have been present on post-mortem toxicology, it was not necessarily cited as a contributing factor in the opioid-related death. Fourth, we were unable to determine the extent of alcohol involvement in opioid-related deaths. Finally, details on opioid involvement, manner of death and demographics were not available for 20 opioid-related deaths occurring in 2015. However, this represents <3% of the opioid-related deaths in that year, and therefore are unlikely to change the conclusions reported here.

Conclusions

In general, the rate of opioid-related deaths continues to rise in Ontario; however the types of opioids involved has changed considerably over the past 8 years, as oxycodone is replaced by drugs like fentanyl and hydromorphone. The high prevalence of accidental deaths in Ontario, the young age at which these deaths are occurring, and the large shifts in the types of drugs involved highlights the need for ongoing monitoring of these trends and engagement with drug users and harm reduction workers to determine how best to target programs and policies that can help to prevent these deaths. Finally, the emergence of heroin-involved deaths in recent years suggests that more work must be done to understand whether these trends are reflective of policies restricting access to prescription opioids leading to higher use of illicit opioids that are more easily accessed, an increasing prevalence of the dangerous practice of mixing heroin with illicit fentanyl powder, or other factors.

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