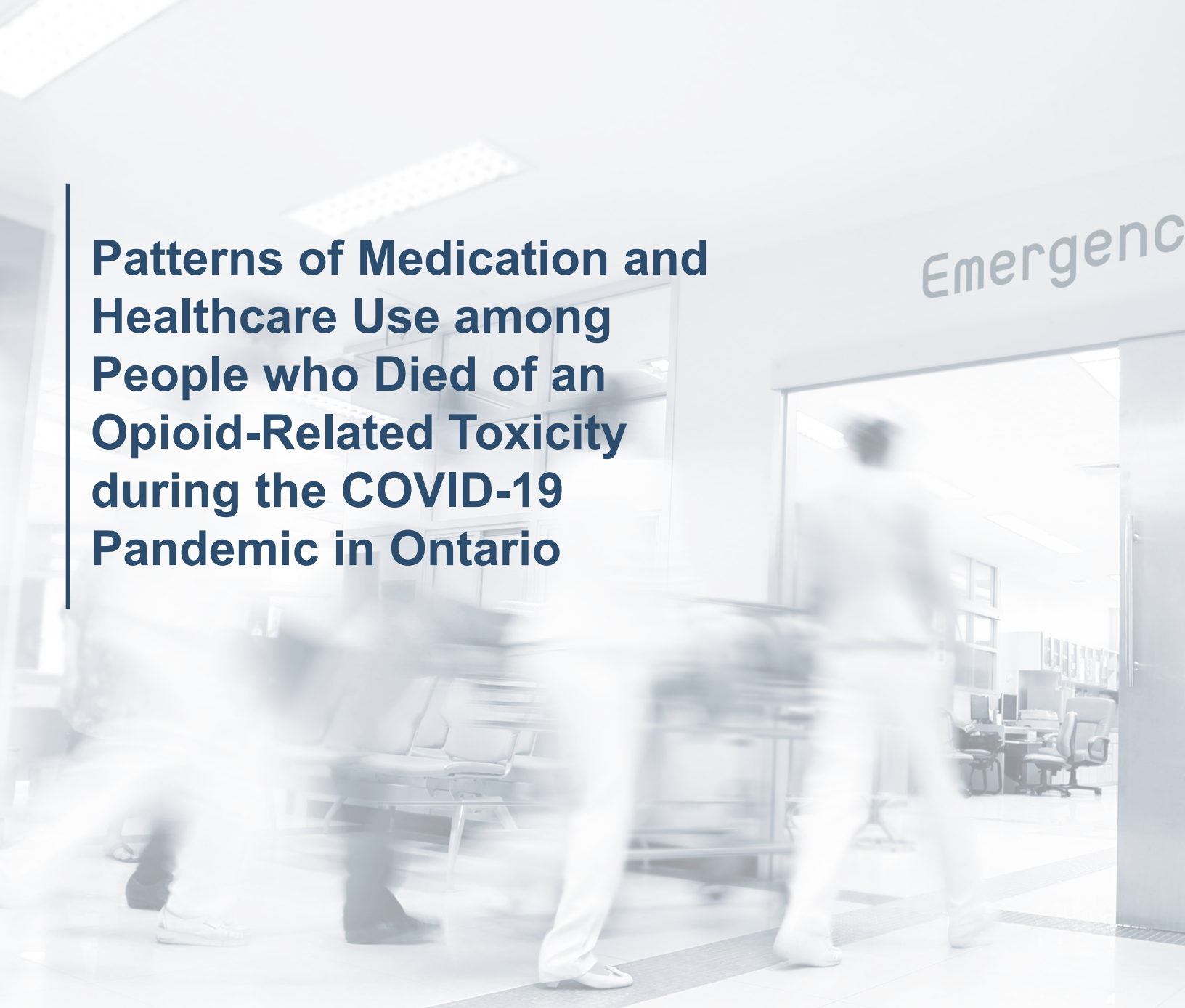

Patterns of Medication and Healthcare Use among People who Died of an Opioid-Related Toxicity during the COVID-19 Pandemic in Ontario

A report prepared by:

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On behalf of:

The Ontario Drug Policy Research Network
The Office of the Chief Coroner for Ontario / Ontario Forensic Pathology Service
Public Health Ontario

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Background

In Ontario, the COVID-19 pandemic has exacerbated the ongoing opioid overdose crisis, leading to a significant rise in unintentional deaths due to opioid-related toxicity. Specifically, between February 2020 – the month before Ontario declared a State of Emergency due to COVID-19 – and December 2020, there was a 79% increase in the number of opioid-related deaths across the province.[1] There are a multitude of reasons for this rapid acceleration in opioid-related deaths, including the increasing unpredictability of the unregulated drug supply, reduced access to healthcare services, limited access to community based-programs that support people who use drugs, and increased social isolation, which led to more people using drugs alone. Furthermore, the pandemic has had a disproportionate impact on opioid-related death among people experiencing homelessness, with 1 in 6 opioid-related deaths occurring within this population during the first eight months of the pandemic.[1]

There is an urgent need to better understand patterns of healthcare use among people who died of an opioid-related toxicity during the pandemic, particularly amid the pandemic-mandated disruptions to healthcare services and increasing rates of opioid-related death since the onset of the COVID-19 pandemic. This information will help identify policy- and program-related interventions to improve access to healthcare and other supportive services for people who use drugs, with the ultimate goal of reducing the loss of life due to overdoses in Ontario and beyond. To help address this need, this report describes the characteristics of people who died of an accidental opioid-related toxicity in Ontario prior to the pandemic (March to December 2019) and during the first two waves of the pandemic (March to December 2020). We also report patterns of healthcare use prior to death and compare these characteristics and patterns to people who died of an opioid-related toxicity prior to the pandemic. In addition, this report will focus on describing these same characteristics and patterns of healthcare use among people who were experiencing homelessness in order to inform supportive approaches that can be tailored specifically for this population.

Methods

We conducted a cross-sectional study to compare characteristics and patterns of healthcare use among people who died of an opioid-related toxicity in Ontario, Canada prior to the COVID-19 pandemic (March 17, 2019 to December 31, 2019) to those who died of an opioid-related toxicity during the first two waves of the COVID-19 pandemic (March 17, 2020 to December 31, 2020). An opioid-related death was defined as an acute intoxication/toxicity death resulting from the direct contribution of consumed substance(s), where one or more of the substances was an opioid, regardless of how the opioid was obtained. We restricted our analysis to confirmed opioid-related deaths that were deemed to be accidental/unintentional (i.e., an injury where death was not intended, foreseen or expected. Inflicted injury did not cause or substantially contribute to the death).

Data Sources

We obtained the data used in this report from ICES (formerly known as the Institute for Clinical Evaluative Sciences), which holds databases containing information on healthcare encounters in Ontario that are covered by the Ontario Health Insurance Plan (OHIP). We identified people who died due to an opioid-related toxicity, and the circumstances surrounding these deaths, using the **Drug and Drug/Alcohol Related Death Database**, which contains records from investigations of probable and confirmed opioid-related deaths completed by the death investigation service at the Office of the Chief Coroner/Ontario Forensic Pathology Service. To examine history of medications dispensed prior to death, we used the **Narcotics Monitoring System**, a database that captures all claims for controlled medications, such as opioids, benzodiazepines and stimulants, dispensed from community pharmacies in Ontario, regardless of payer. For information on visits for outpatient care, we used the **OHIP Claims Database** and the **Community Health Centre Database**. To capture information on emergency department (ED) visits, acute hospital admissions, and mental health-related hospital admissions, we used the Canadian Institute for Health Information's **National Ambulatory Care Reporting System, Discharge Abstract Database**, and **Ontario Mental Health Reporting System**, respectively. To determine history of a major traumatic injury, we used the **Ontario Trauma Registry Database**, and to capture prior diagnosis of HIV, we used the **Ontario HIV Database**. Lastly, we used the **COVID-19 Integrated Testing Database** to identify diagnosis of COVID-19 prior to death. These datasets were linked using unique encoded identifiers and analyzed at ICES. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board.

Measures

We compared several characteristics between people who died due to a confirmed opioid-related toxicity during the pre-pandemic and pandemic time periods. Specifically, we compared the population-adjusted rate of opioid-related death in each period by age group (0 to 24, 25 to 44, 45 to 64, and 65+), sex (female, male), and location of residence (urban vs. rural, and northern vs. southern, see Appendix A for definition). We also compared the distribution of people who died of an opioid-related toxicity by their neighbourhood income quintile assigned using the address associated with their health card, and their living arrangement at the time of death as determined by the death investigation service.

We compared the circumstances surrounding opioid-related deaths in each time period, including the number and types of opioids directly contributing to death, and the prevalence of other substances that directly contributed to the death or were detected in post-mortem toxicology, including alcohol, stimulants, and benzodiazepines. We classified the opioids, benzodiazepines, and stimulants involved in opioid-related deaths as pharmaceutical or non-pharmaceutical (see Appendix A for definition) based on available toxicology results and information about pharmaceuticals approved for use in Canada.

Next, in each of the pre-pandemic and pandemic periods, we compared the percentage of people who had a prescription opioid dispensed in the 30 days prior to death. Among people who died of an opioid-related toxicity that was directly linked to a pharmaceutical opioid, we also examined the percentage of people who had a prescription dispensed for that specific type of opioid in the 30 days prior to death. For example, among people who died of an opioid-related toxicity where oxycodone was a direct contributor to death, we examined the percentage of people who were dispensed an oxycodone prescription in the 30 days prior.

Lastly, we explored differences in prior healthcare encounters and health conditions among people who died of an opioid-related toxicity prior to and during the pandemic. Specifically, in the 7 and 30 days prior to death, we identified encounters for any outpatient care, outpatient primary care, visits to the emergency department, acute

hospital admissions, mental health-related hospital admissions, and emergency department visits or hospital admissions for opioid-related toxicity. To examine the health history of people who died of an opioid-related toxicity, we calculated the percentage of people who had a history of chronic pain; a healthcare encounter for opioid use disorder in the 5 years prior to their death; a prior diagnosis of COVID-19 (as indicated by a laboratory-confirmed viral RNA polymerase chain reaction SARS-CoV-2 test); an outpatient visit, emergency department visit, or hospital admission for a mental health-related diagnosis in the prior 5 years; a hospital admission for infective endocarditis in the prior 180 days; a hospital admission for any serious infection, including skin or soft tissue infections, non-vertebral infections, or spinal infections in the prior 180 days; and a prior diagnosis of HIV. Our previous work[1] has shown an increase in the proportion of opioid-related deaths occurring among people experiencing homelessness (including individuals who were unsheltered, emergency sheltered, provisionally accommodated, or at immediate risk of homelessness as identified by the death investigation service) at time of death. Therefore, we repeated these analyses specifically among this population to develop an understanding of the circumstances surrounding death among people who were experiencing homelessness. For more information about the diagnosis and billing codes used to define the various healthcare encounters and health conditions, please see Appendix B.

For all analyses, we used chi-square tests and t-tests to test for statistically significant differences between the characteristics and healthcare encounters among people who died in the pre-pandemic and pandemic time periods. All analyses were conducted in SAS Enterprise Guide version 7.1.

Key Findings

This report compares accidental/unintentional opioid-related deaths occurring in Ontario during the following two periods:

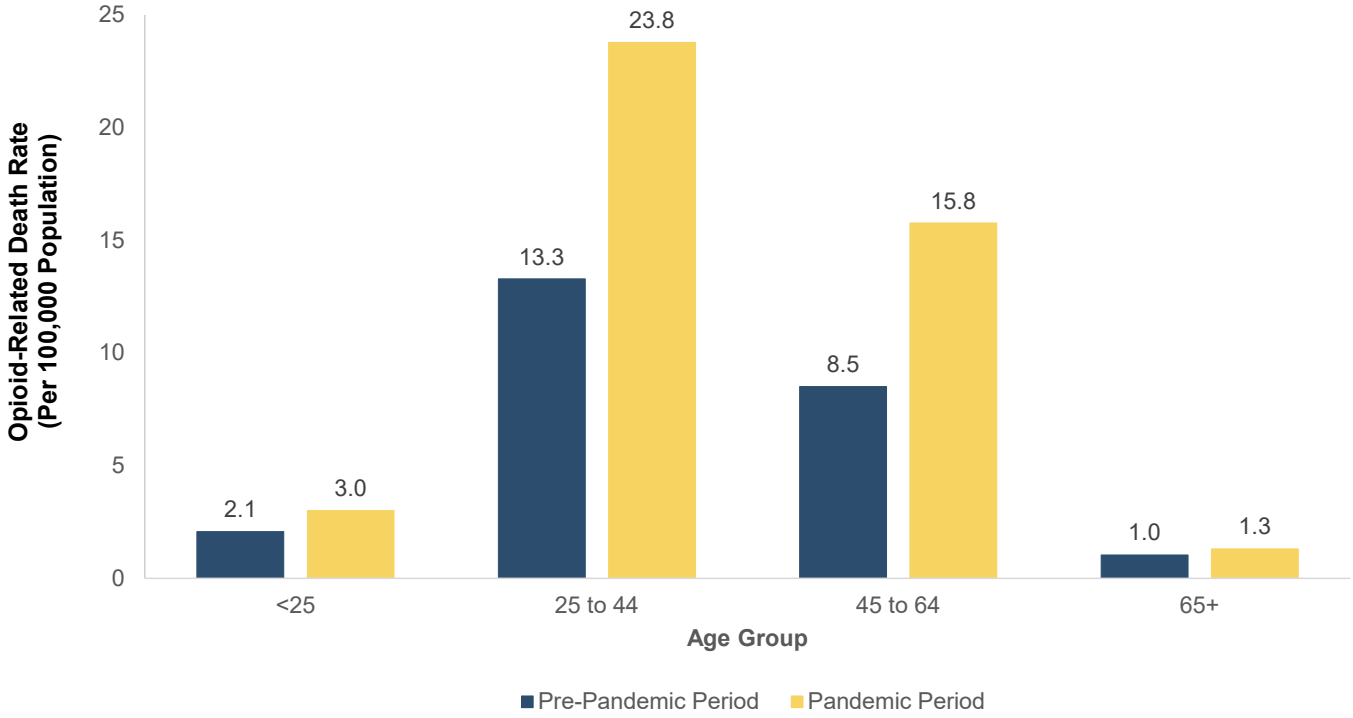
Pre-Pandemic Period
March 17, 2019 - December 31, 2019
(N=1,017)

Pandemic Period
March 17, 2020 - December 31, 2020
(N=1,808)

Overall, there were 3,196 confirmed or probable opioid-related deaths in Ontario during the pre-pandemic [N=1155] and pandemic periods [N=2041]. Of those deaths, 49 (1.5%) in the pre-pandemic period and 95 (4.6%) in the pandemic period were excluded because the individual could not be linked to administrative databases or was not an Ontario resident. Among the remaining 3,052 opioid-related deaths, 54 deaths (1.7%) were still under investigation and not yet confirmed to be due to an opioid-related toxicity by the death investigation service at time of analysis (i.e., probable opioid-related deaths; all in the pandemic period), and 173 (5.5%) were determined to be a non-accidental manner of death (suicide or undetermined; 89 (7.7%) in the pre-pandemic periods and 84 (4.1%) in the pandemic period) and were therefore excluded from this study. This report compares 1,017 opioid-related deaths in the pre-pandemic period to 1,808 opioid-related deaths in the pandemic period.

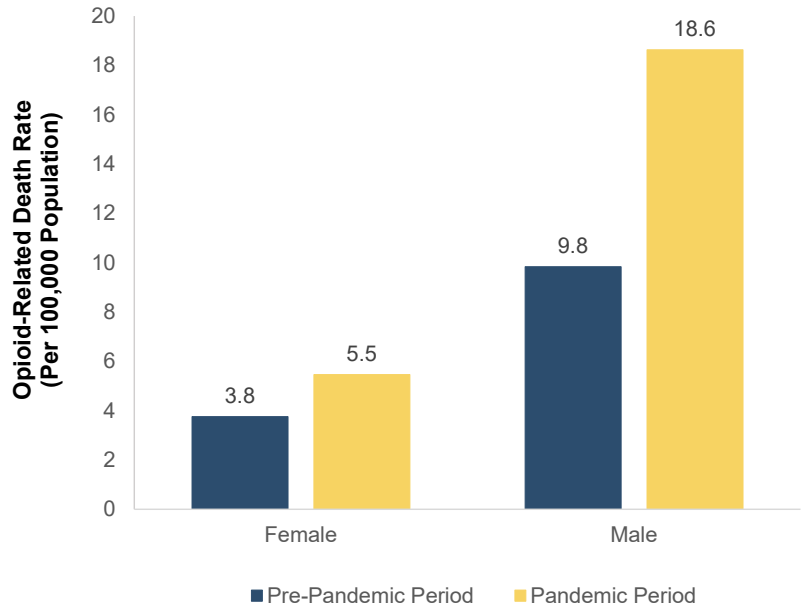
Demographic Characteristics and Circumstances Surrounding Death

Figure 1: Population-adjusted opioid-related death rate **by age** prior to and during the pandemic in Ontario



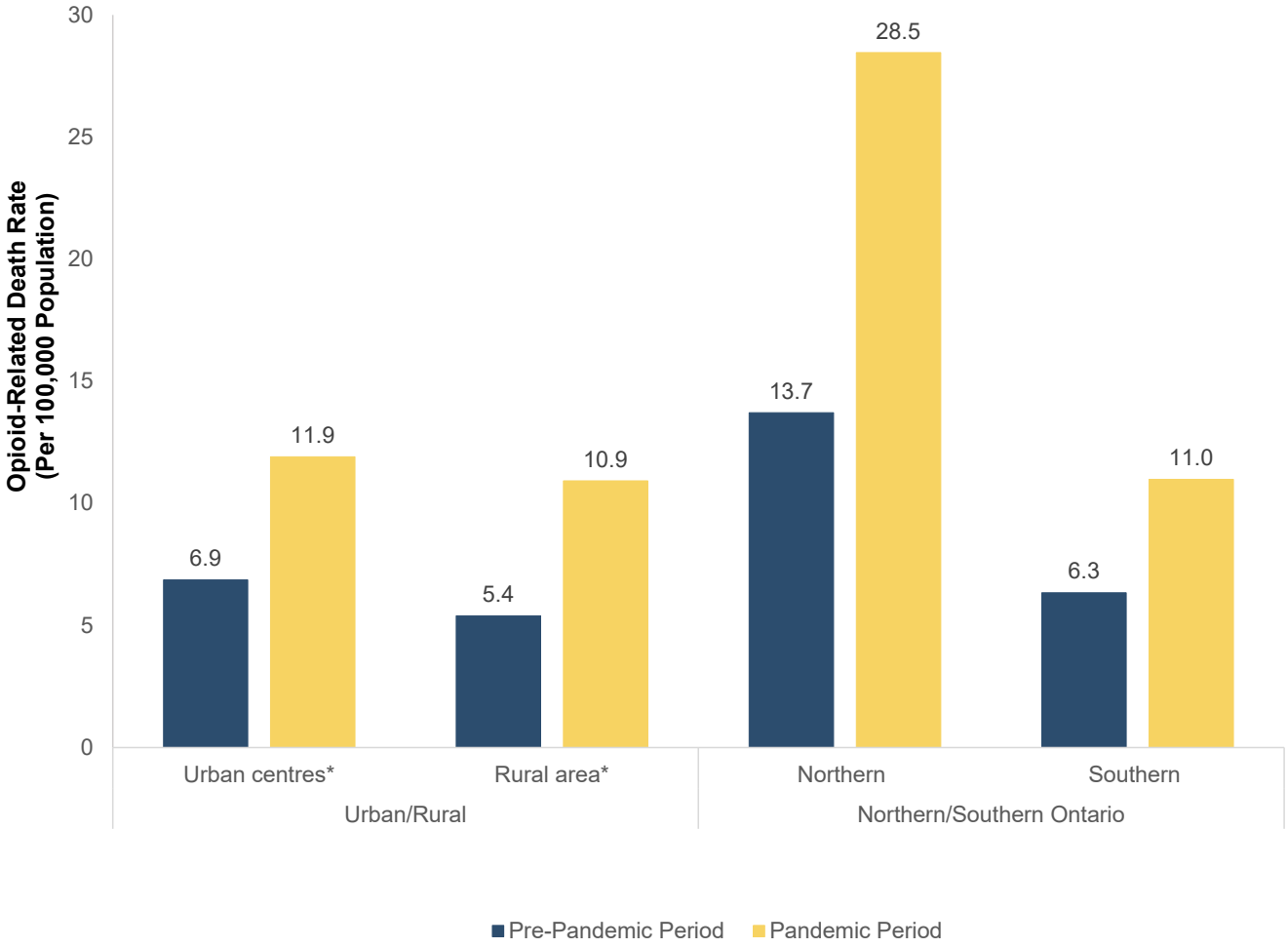
Although there was no statistically significant change in the distribution of opioid-related deaths between age groups during the pandemic[1], there was an increase in the population-adjusted rate of opioid-related deaths in all age groups. The largest absolute increase was among those aged 25 to 44 years, where the rate of opioid-related deaths grew by 79.1% from 13.3 deaths per 100,000 [N=546] to 23.8 deaths per 100,000 population [N=994], whereas the largest relative increase was among those aged 45 to 64 years (85.4% increase to 15.8 deaths per 100,000 population [N=656]).

Figure 2: Population-adjusted opioid-related death rate **by sex** prior to and during the pandemic in Ontario



During the pandemic, there was a statistically significant shift towards more opioid-related deaths occurring among males (76.9% during the pandemic vs. 71.9% in the pre-pandemic period; p=0.003; data not shown). Overall, opioid-related death rates among males nearly doubled during the pandemic, reaching 18.6 deaths per 100,000 population [N=1,390]. The rate of opioid-related deaths among females grew 45.5% to 5.5 deaths per 100,000 population [N=418].

Figure 3: Population-adjusted opioid-related death rate **by geographic location** prior to and during the pandemic in Ontario



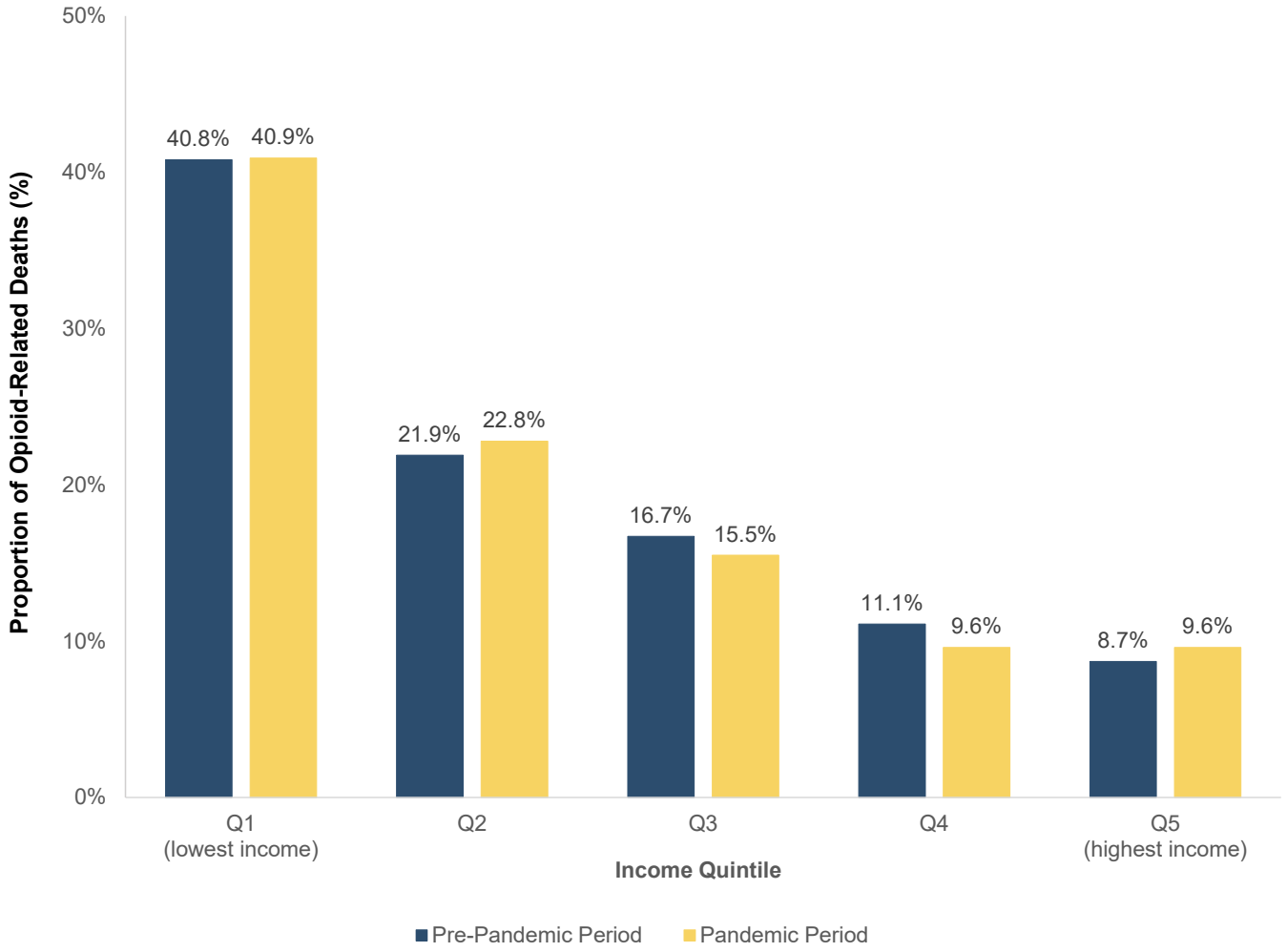
NOTE

* 8 and 28 individuals with missing data on urban/rural location died of an opioid-related death before and during the COVID-19 pandemic, respectively. Rural was defined as residing in a community of ≤10,000 people, community size was assigned by Statistics Canada based on the postal code associated with the individual's health card.

Population-adjusted rates of opioid-related deaths were generally higher in urban parts of Ontario, although they increased more quickly during the pandemic in rural Ontario. Specifically, the rate doubled in rural Ontario (5.4 to 10.9 deaths per 100,000 population), while increasing by 73.3% in urban parts of the province (6.9 to 11.9 deaths per 100,000 population).

Despite the absolute number of opioid-related deaths being much higher in Southern Ontario (1,567 deaths compared to 241 deaths in Northern Ontario during the pandemic), after adjusting for population, the rates of opioid-related deaths were much higher in Northern Ontario. Furthermore, the rate of opioid-related deaths in Northern Ontario more than doubled during the pandemic, reaching 28.5 per 100,000 population, which was nearly three-times the population-adjusted rate in Southern Ontario (11.0 per 100,000 population).

Figure 4: Distribution of opioid-related deaths across **neighbourhood income quintiles** prior to and during the pandemic in Ontario

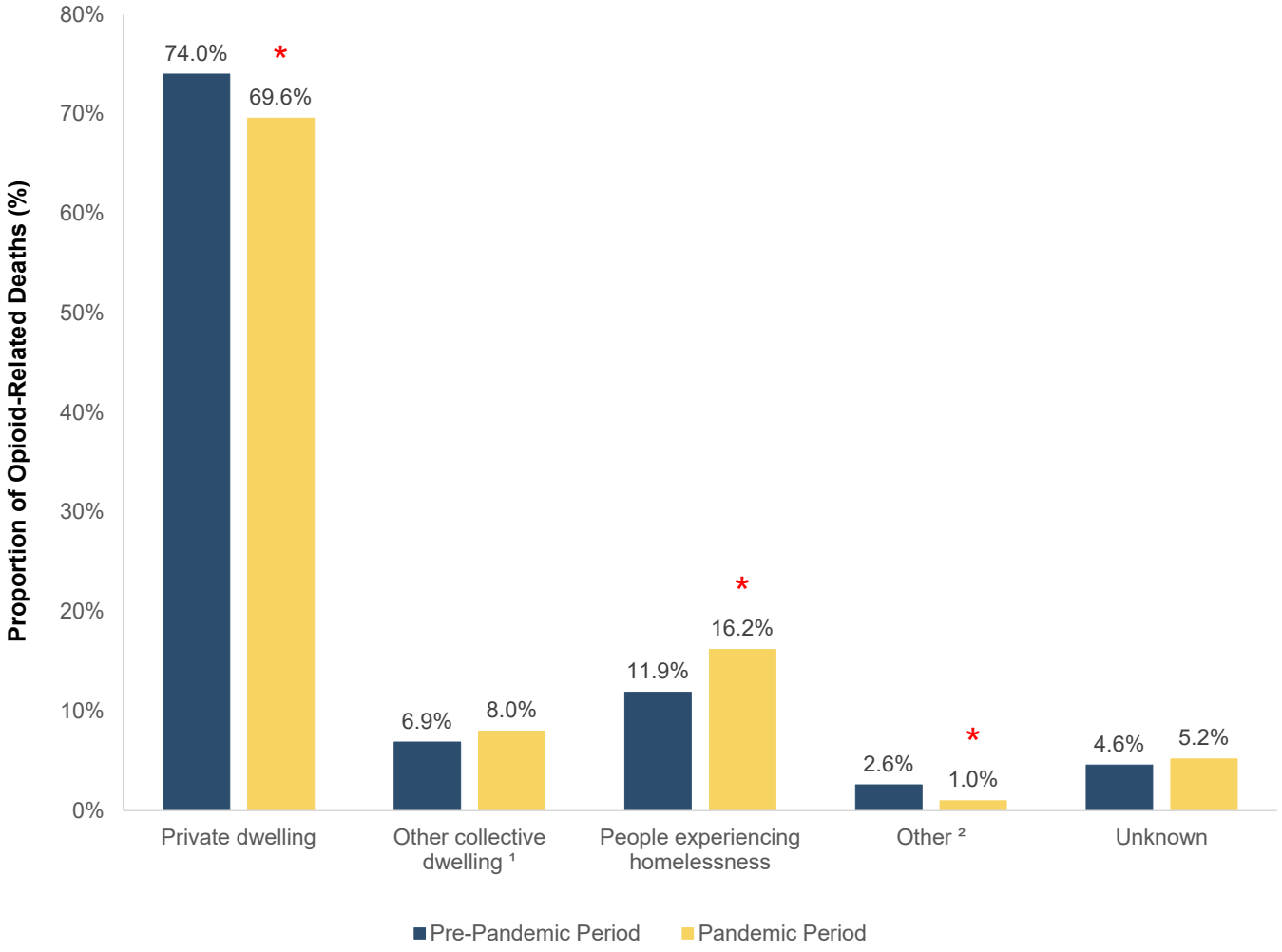


NOTE

There were no significant differences comparing pre-pandemic vs. pandemic periods.

There was a strong clustering of opioid-related deaths among people living within neighbourhoods in the lowest income quintile both before (40.8%, N=415 deaths) and during (40.9%, N=739 deaths) the pandemic. In contrast, only 9.6% of opioid-related deaths occurred among people living within the top quintile of neighbourhood income during the pandemic (N=174 of 1,808 deaths). Overall, there were no significant shifts in the distribution of opioid-related deaths by neighbourhood income during the pandemic ($p>0.05$ for all comparisons).

Figure 5: Living arrangement among people experiencing an opioid-related death prior to and during the pandemic in Ontario



NOTE

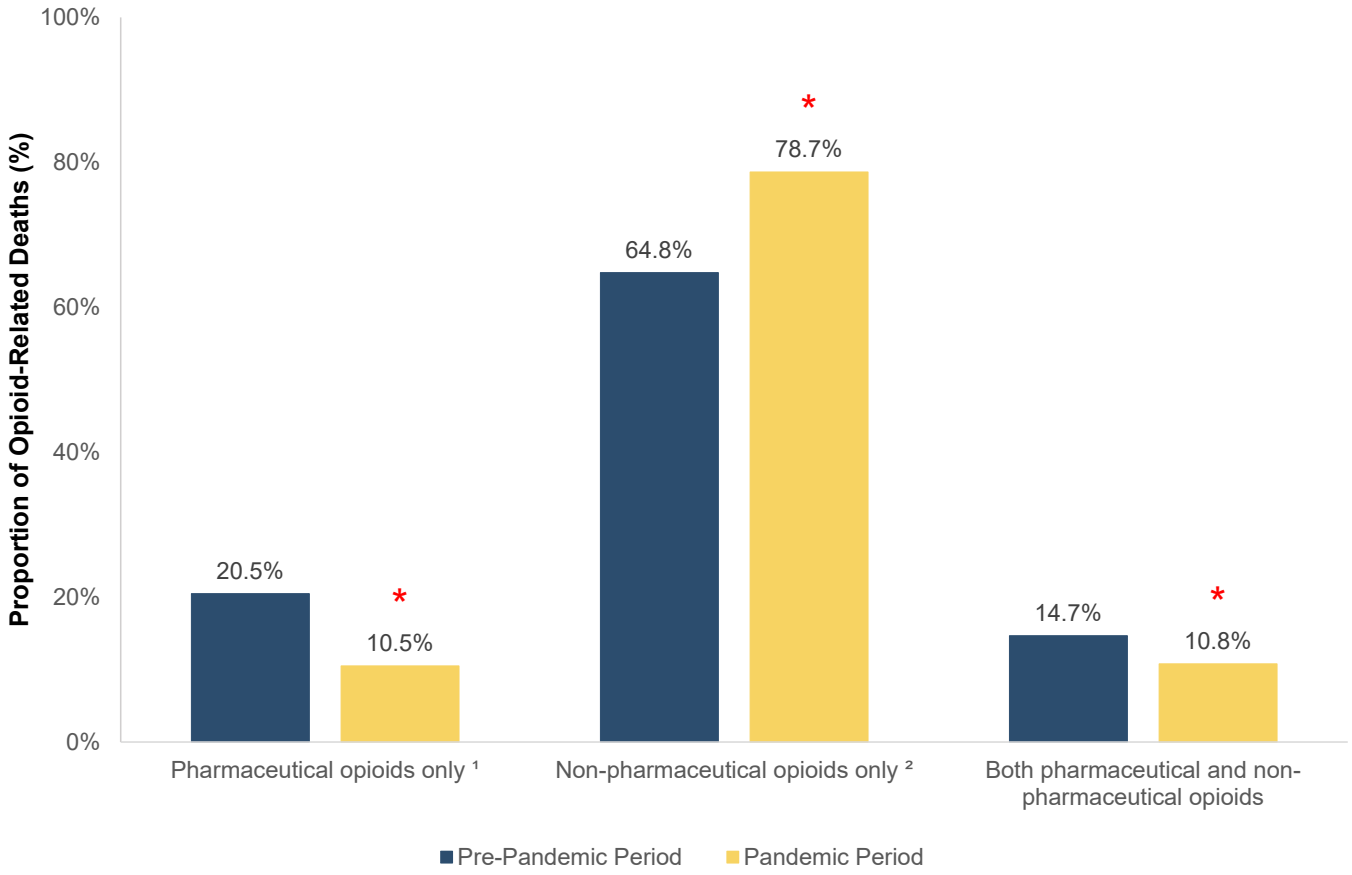
* Red asterisk indicates statistically significant difference between pre-pandemic and pandemic cohorts ($p<0.05$).

1. Includes: Lodging and rooming houses, hotels, military bases, sober living facility
2. Includes: Correctional facility, hospital or long-term care home, mental health facility, motel/hotel, residential care facility, retirement home

The vast majority of opioid-related deaths occurred among people who were living in a private dwelling at time of death; however, this declined significantly during the pandemic (from 74.0% [N=753] to 69.6% [N=1,259], p=0.01). Importantly, the proportion of opioid-related deaths among people experiencing homelessness rose significantly over this time, from 11.9% to 16.2% (p=0.002), and the absolute number of opioid-related deaths in this group more than doubled (N=121 in pre-pandemic period vs. N=293 during the pandemic).

Drug Involvement in Opioid-Related Deaths

Figure 6: Distribution of the **origin of opioids†** directly contributing to opioid-related deaths prior to and during the pandemic in Ontario



NOTE

* Red asterisk indicates statistically significant difference between pre-pandemic and pandemic cohorts ($p<0.05$).
† See Appendix A for origin category definitions. Categories (i.e., pharmaceutical opioids only, non-pharmaceutical opioids only, and both pharmaceutical and non-pharmaceutical opioids only) are mutually exclusive.

Limitations:
1. Some deaths included in the pharmaceutical opioid category could include morphine which was metabolized from heroin.
2. A small number of non-pharmaceutical opioid-related deaths could include prescription opioids (i.e., 1-2% of fentanyl deaths had a fentanyl patch dispensed in the 30 days prior to death).

Both prior to and during the pandemic, the majority of opioid-related deaths involved solely non-pharmaceutical opioids as direct contributors. Furthermore, during the pandemic, the proportion of deaths where non-pharmaceuticals were the only direct contributors rose significantly, from 64.8% [N=659] to 78.7% [N=1,423] ($p<0.001$). Fentanyl and fentanyl analogues accounted for over 99% of deaths where non-pharmaceutical opioids were a direct contributor to death in both time periods. In the pre-pandemic period, approximately 1 in 5 opioid-related deaths (20.5%) had only pharmaceutical opioids as direct contributors, falling to 1 in 10 opioid-related deaths (10.5%) during the pandemic. Importantly, despite a large overall increase in the number of opioid-related deaths during the pandemic, the absolute number of deaths involving only pharmaceutical opioids dropped to 189 deaths (compared to 208 deaths in the pre-pandemic period).

Table 1: Specific types of opioids directly contributing to opioid-related death prior to and during the pandemic in Ontario†

	Pre-Pandemic Period N=1,017	Pandemic Period N=1,808	Stat. Sig.
Non-pharmaceutical opioids			
Fentanyl and fentanyl analogues	802 (78.9%)	1,614 (89.3%)	*
Heroin	52 (5.1%)	27 (1.5%)	*
Opioids indicated for pain			
Hydromorphone	103 (10.1%)	88 (4.9%)	*
Oxycodone	81 (8.0%)	70 (3.9%)	*
Codeine	18 (1.8%)	22 (1.2%)	
Morphine	77 (7.6%)	78 (4.3%)	*
Opioid agonist treatment			
Methadone	132 (13.0%)	179 (9.9%)	*
Buprenorphine	≤5	≤5	

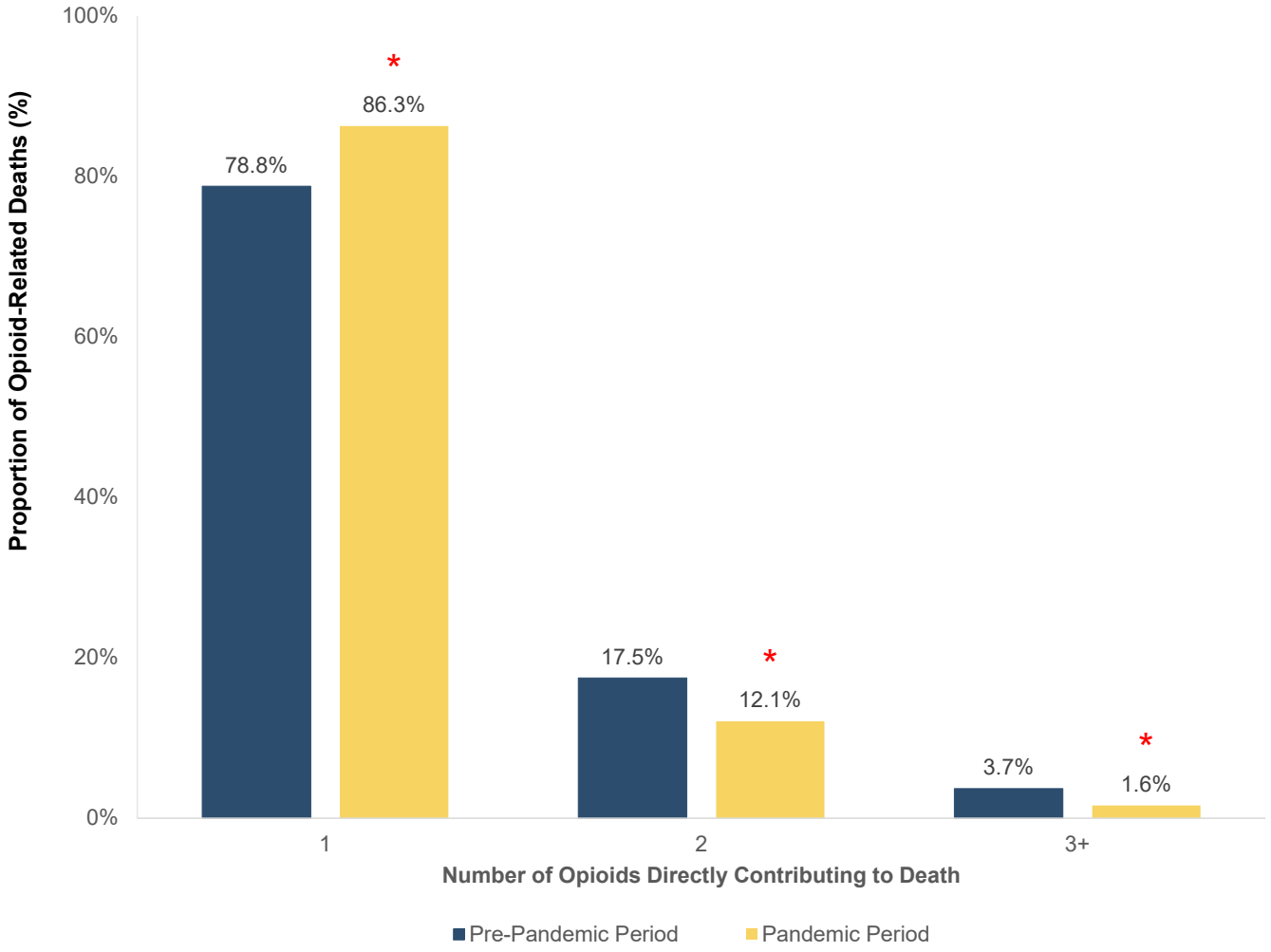
NOTE

* Stat. Sig. = statistical significance, where the presence of a red asterisk indicates $p<0.05$.
† Not mutually exclusive. Some deaths were attributed to multi-drug toxicity where more than one substance can contribute to an individual death.

During the pandemic, the role of fentanyl as a direct contributor to opioid-related deaths continued to increase, rising to 89.3% (N=1,614) from 78.9% (n=802) in the pre-pandemic period ($p<0.001$). The proportional involvement of most other opioids as direct contributors declined significantly during the pandemic, with significant reductions across other non-pharmaceutical opioids, opioids indicated for pain, and those prescribed as opioid agonist treatment (OAT). These patterns are likely due to a changing unregulated drug supply as well as potential interruptions in access to pharmaceutical opioids early in the pandemic, which may have led people to access the unregulated drug supply. Importantly, despite rising access to immediate-release hydromorphone as a safer opioid supply during the pandemic, the percentage and absolute number of opioid-related deaths with hydromorphone as a direct contributor declined over this time (from 10.1% [N=103] to 4.9% [N=88] of opioid-related deaths; $p<0.001$). Similarly, deaths where hydromorphone was detected (regardless of whether it was determined to have contributed to death) also declined from 11.4% of deaths in the pre-pandemic period (N=116) to the 5.9% in the pandemic period (N=107; $p<0.001$) [data not shown].

The findings for methadone also require further consideration. Despite a significant reduction in the proportion of opioid-related deaths with methadone as a direct contributor during the pandemic (from 13.0% to 9.9%, $p=0.012$), there was a small increase in the absolute number of these deaths (N=132 to N=179). Importantly, a high proportion of methadone-related deaths also had fentanyl as a direct contributor both prior to (60 of 132 deaths, 45.5%) and during (98 of 179 deaths, 54.7%) the pandemic. This could reflect gaps in methadone treatment programs meeting the needs of some clients, which could include inadequate methadone doses among people previously using fentanyl, leading to continued use of the unregulated drug supply. However, it is reassuring that the proportion of deaths with methadone as a direct contributor has not risen despite the increased prevalence of take-home OAT doses during the pandemic.[2]

Figure 7: Number of opioids directly contributing to opioid-related deaths prior to and during the pandemic in Ontario



NOTE

* Red asterisk indicates statistically significant difference between pre-pandemic and pandemic cohorts ($p<0.05$).

In the pre-pandemic period, the majority (N=801; 78.8%) of opioid-related deaths had only 1 opioid directly contributing to death, and this rose during the pandemic, reaching 86.3% of all deaths (N=1,560; $p<0.001$). This is likely reflective of the increasing contribution of fentanyl to opioid-related deaths during the pandemic. Specifically, fentanyl was responsible for 77.0% of deaths where only 1 opioid directly contributed to death in the pre-pandemic period [N=617 of 801 opioid-related deaths] rising to 89.6% of these deaths [N=1,399 of 1,560 opioid-related deaths] in the pandemic period [data not shown]. Importantly, other non-opioid drugs and substances may have also contributed to these deaths, including alcohol, stimulants, and benzodiazepines.

Table 2: Other non-opioid substances directly contributing and detected in opioid-related deaths prior to and during the pandemic in Ontario

	Pre-Pandemic Period N=1,017	Pandemic Period N=1,808	Stat. Sig.
Other substances that directly contributed to opioid-related death			
Alcohol	131 (12.9%)	242 (13.4%)	
Any stimulant	543 (53.4%)	1,073 (59.3%)	*
Non-pharmaceutical stimulants	540 (53.1%)	1,067 (59.0%)	*
Methamphetamines	231 (22.7%)	482 (26.7%)	*
Cocaine	392 (38.5%)	787 (43.5%)	*
Any benzodiazepine	80 (7.9%)	163 (9.0%)	
Non-pharmaceutical benzodiazepines†	18 (1.8%)	109 (6.0%)	*
Other substances detected in opioid-related death			
Any benzodiazepine	324 (31.9%)	855 (47.3%)	*
Non-pharmaceutical benzodiazepines†	53 (5.2%)	519 (28.7%)	*

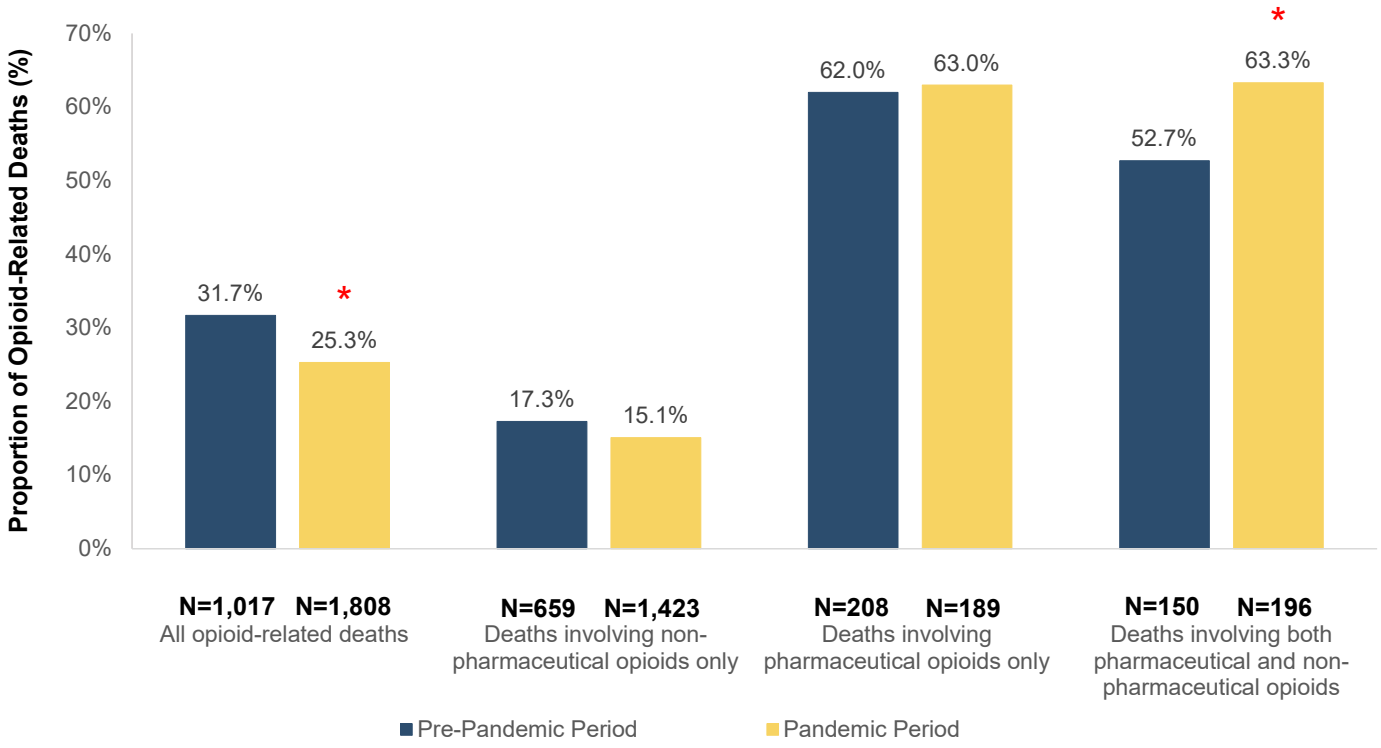
NOTE

* Stat. Sig. = statistical significance, where the presence of a red asterisk indicates $p<0.05$.
† Etizolam makes up over 90% of the non-pharmaceutical benzodiazepines across both time periods.

During the pandemic, there was a significant increase in the proportion of deaths where a combination of opioids and other substances directly contributed to death. In the pandemic period, nearly 60% of opioid-related deaths also had a stimulant directly contributing to death (N=1,067), the vast majority of which involved either cocaine (43.5% of all opioid-related deaths; N=787) or methamphetamines (26.7% of all opioid-related deaths; N=482). Similarly, non-pharmaceutical benzodiazepines (i.e., etizolam, flualprazolam, flubromazolam) were more frequently determined to be a direct contributor to opioid-related deaths during the pandemic, rising from 1.8% of all opioid-related deaths in the pre-pandemic period (N=18) to 6.0% during the pandemic (N=109). Due to evolving methods and best practices around quantifying and defining toxic levels of non-pharmaceutical benzodiazepines, these substances may not be consistently characterized in the cause of death. Therefore, we also explored opioid-related deaths where benzodiazepines were detected in post-mortem toxicology but not determined by the death investigation service to be a direct contributor to death. In this analysis, nearly half of all opioid-related deaths during the pandemic had a benzodiazepine detected (47.3% compared to 31.9% prior to the pandemic; $p<0.001$), and detection of non-pharmaceutical benzodiazepines rose 5-fold from 5.2% prior to the pandemic to 28.7% during the pandemic ($p<0.001$). The vast majority of deaths with non-pharmaceutical benzodiazepines detected during the pandemic involved etizolam (92.7%; 481 of 519 opioid-related deaths).

Role of Prescription and Non-Prescription Opioids

Figure 8: Recent receipt of a **prescription opioid** (within 30 days prior to death) among individuals who died of an opioid-related toxicity prior to and during the pandemic in Ontario†



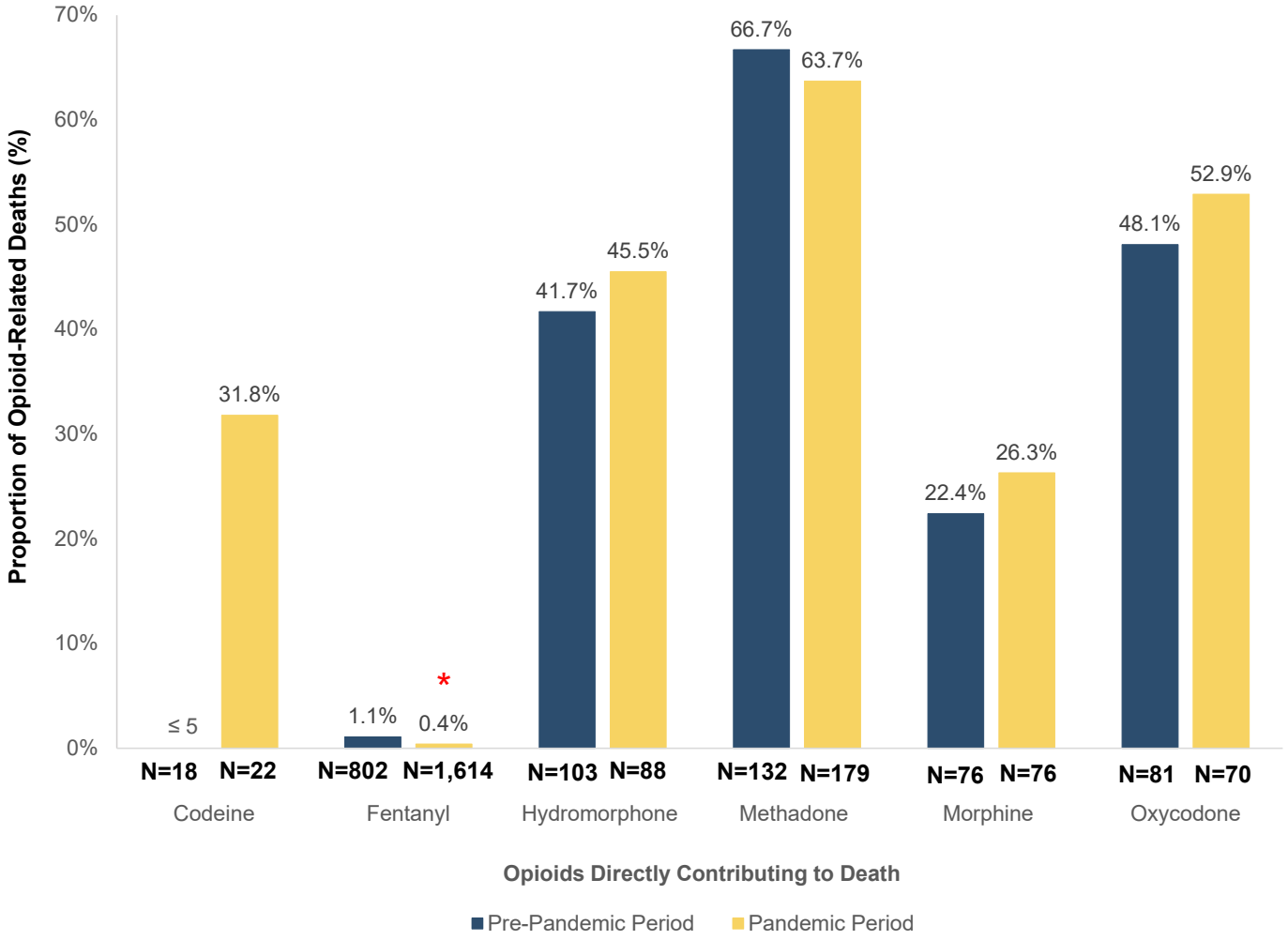
NOTE

* Red asterisk indicates statistically significant difference between pre-pandemic and pandemic cohorts ($p<0.05$).
† Numerator = number of individuals who received any opioid **prescription** 30 days prior to opioid-related death; Denominator = number of individuals where each respective opioid group directly contributed to death. For example, among the 1,423 deaths where non-prescription opioids only were direct contributors to death in the pandemic period, only 15.1% (n=215) of individuals received any opioid from a pharmacy in the 30 days prior to death. Groups are mutually exclusive. Deaths didn't necessarily involve the opioid recently dispensed.

Approximately one-third of opioid-related deaths prior to the pandemic occurred among people who had recently (prior 30 days) been dispensed a prescription opioid (31.7%; N=322); however, during the pandemic, this declined to 25.3% of all opioid-related deaths (N=458; $p<0.001$). Importantly, approximately half of people who were recently prescribed an opioid prior to death were prescribed methadone (44.4% [143 of 322 deaths] in the pre-pandemic period; 46.2% [216 of 458 deaths] in the pandemic period) which suggests that they were engaged in opioid agonist treatment for an opioid use disorder within 30 days prior to death (data not shown).

Both prior to and during the pandemic, the largest number of opioid-related deaths involved non-pharmaceutical opioids only. Overall, the prevalence of receiving a recent opioid prescription within this group was relatively rare, with 15.1% of people having been recently prescribed an opioid during the pandemic. In contrast, the total number of deaths that involved only pharmaceutical opioids was small. However, within this group, nearly two-thirds of people had been dispensed a prescription opioid in the 30 days prior to death, and these rates remained similar prior to (62.0%) and during (63.0%) the pandemic ($p=0.85$). In the small group of opioid-related deaths involving both prescription and non-prescription opioids, the proportion of people who had been recently dispensed a prescription opioid rose significantly during the pandemic (from 52.7% to 63.3% during the pandemic period; $p=0.047$).

Figure 9: Percent of deaths attributable to **specific opioids where the individual was dispensed the same opioid** in the prior 30 days in Ontario†



NOTE

* Red asterisk indicates statistically significant difference between pre-pandemic and pandemic cohorts ($p<0.05$).
† Numerator = number of individuals who received each respective **prescription** 30 days prior to opioid-related death; Denominator = number of individuals where each respective opioid directly contributed to death, **regardless of source** (prescription or non-prescription). For example, among the 1,614 deaths where fentanyl was a direct contributor to death in the pandemic period, only 0.4% (N=6) were **dispensed** fentanyl from a pharmacy in the 30 days prior to death. Not mutually exclusive groups. We were unable to account for the role of metabolites, therefore some deaths where morphine was identified as a direct contributor could be reflective of metabolism of heroin or codeine into morphine.

The prevalence of having recently received a prescription for the same opioid that directly contributed to death among all deaths attributed to that opioid varied by the type of opioid contributing to death. For example, among deaths where fentanyl was a direct contributor, which accounted for the highest number of opioid-related deaths both prior to and during the pandemic, a very small proportion of people (1.1% prior to the pandemic, 0.4% during the pandemic) were dispensed fentanyl in the 30 days prior to death. This is expected, as the unregulated drug supply in Ontario predominantly contains non-pharmaceutical fentanyl, which has been shown to be a driver of rising overdoses across Canada.

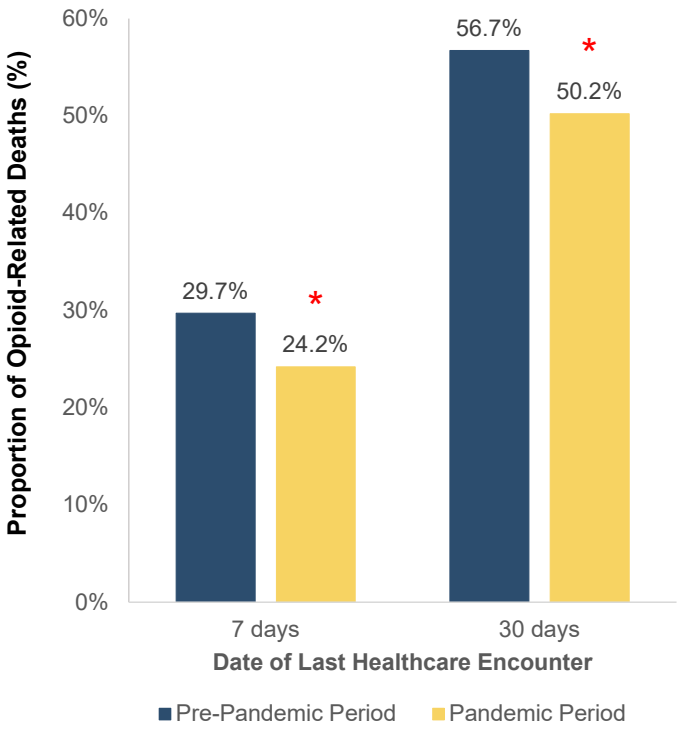
In contrast, among opioid-related deaths where methadone directly contributed to death, approximately two-thirds of people had been dispensed methadone in the 30 days prior to death in both periods. In the pandemic period, the median methadone dose dispensed was 70mg. Recent OAT recommendations

suggest that a methadone dose above 100mg is often required among people who use fentanyl regularly.[3] Therefore, while we cannot determine the specific circumstances around these deaths, it is possible that our findings reflect inadequate methadone doses among some OAT recipients, leading them to continue accessing the unregulated drug supply, and thus being put at increased risk of an overdose (e.g., high potency, unknown concentration); about half of deaths also involved fentanyl across both time periods. Further, the fact that approximately one-third of people with methadone as a direct contributor to death had no recent methadone dispensed implies that methadone diversion is also contributing to fatal overdoses, reinforcing the known overdose risk from methadone when it is rapidly titrated or taken by a person with low or no opioid tolerance.

Among all other opioid-related deaths where pharmaceutical opioids indicated for pain directly contributed to death, the prevalence of receiving a prescription for the same drug in the 30 days prior to death varied between 20% and 50% and did not change considerably during the pandemic. Generally, deaths involving pharmaceutical opioids indicated for pain occurred much less frequently compared to those involving fentanyl and methadone. Further, a large proportion of people dying of a pharmaceutical opioid toxicity had not been recently prescribed the medication. They may, therefore, have been accessing diverted prescription opioid supplies or prescriptions that had been dispensed more than 30 days prior to death, at which point they may have reduced tolerance to the prescribed opioid dose.

Recent Interactions with the Healthcare System

Figure 10: Recent healthcare encounters prior to opioid-related death in Ontario



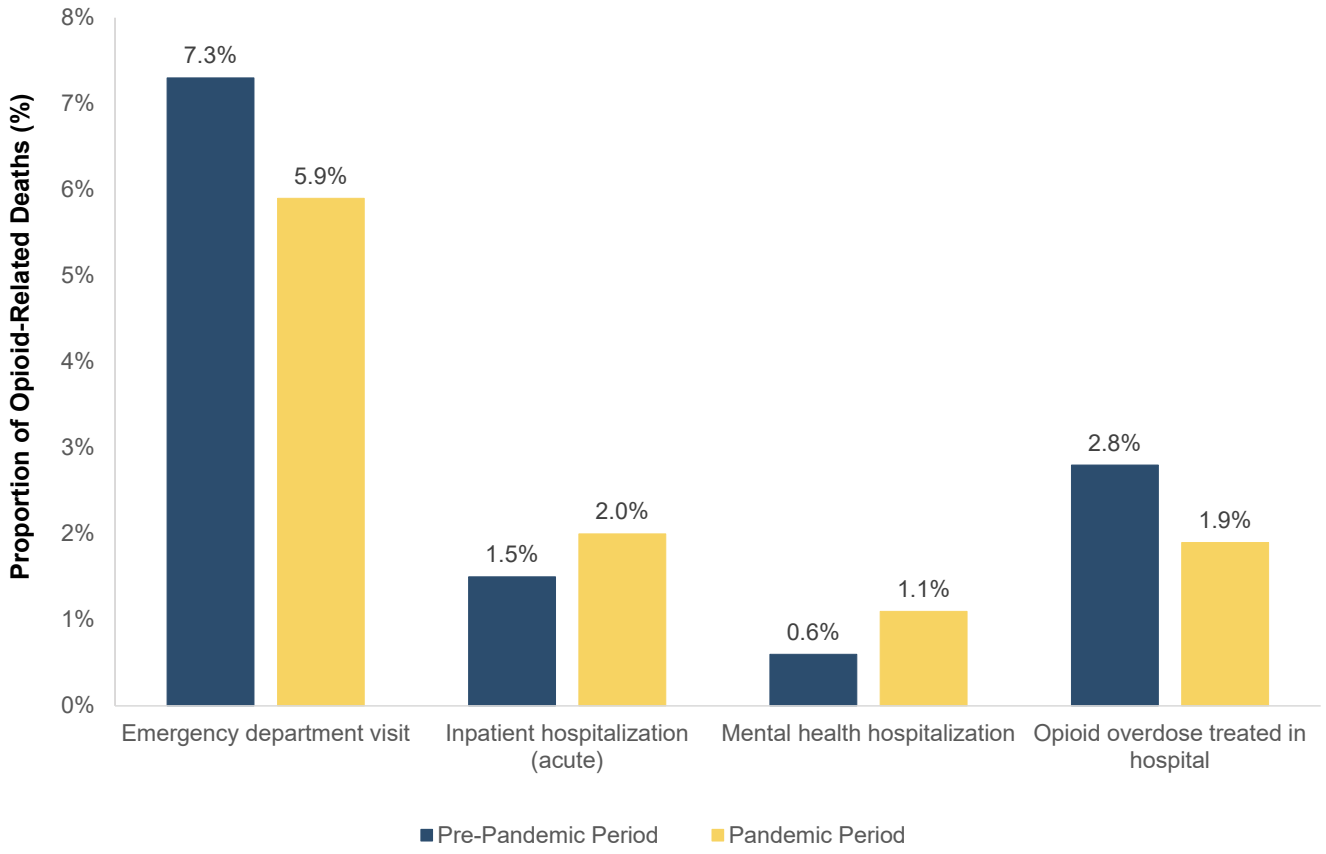
NOTE

* Red asterisk indicates statistically significant difference between pre-pandemic and pandemic cohorts ($p<0.05$).

Any inpatient hospitalization or ED visit that resulted in an opioid-related death was excluded as a healthcare encounter.

Prior to the pandemic, nearly 30% of people who died of an opioid-related toxicity had interacted with the healthcare system (outpatient visits (including primary care), emergency department visits, or hospital admissions) in the week before death, and 56.7% of people had healthcare contact in the month prior to death. Although the prevalence of healthcare interactions declined significantly during the pandemic, this is likely reflective of changing patterns of healthcare access among the general population that have been noted elsewhere.[4] Despite these trends, patterns of high contact with the healthcare system in the period prior to death highlights the many potential opportunities for providers to engage people at risk of an overdose and connect them with low-barrier access to treatment or harm reduction services. This also supports calls for broader integration of OAT and harm reduction approaches directly into hospital and primary care settings.

Figure 11: Recent hospital encounters in the seven days prior to opioid-related death in Ontario

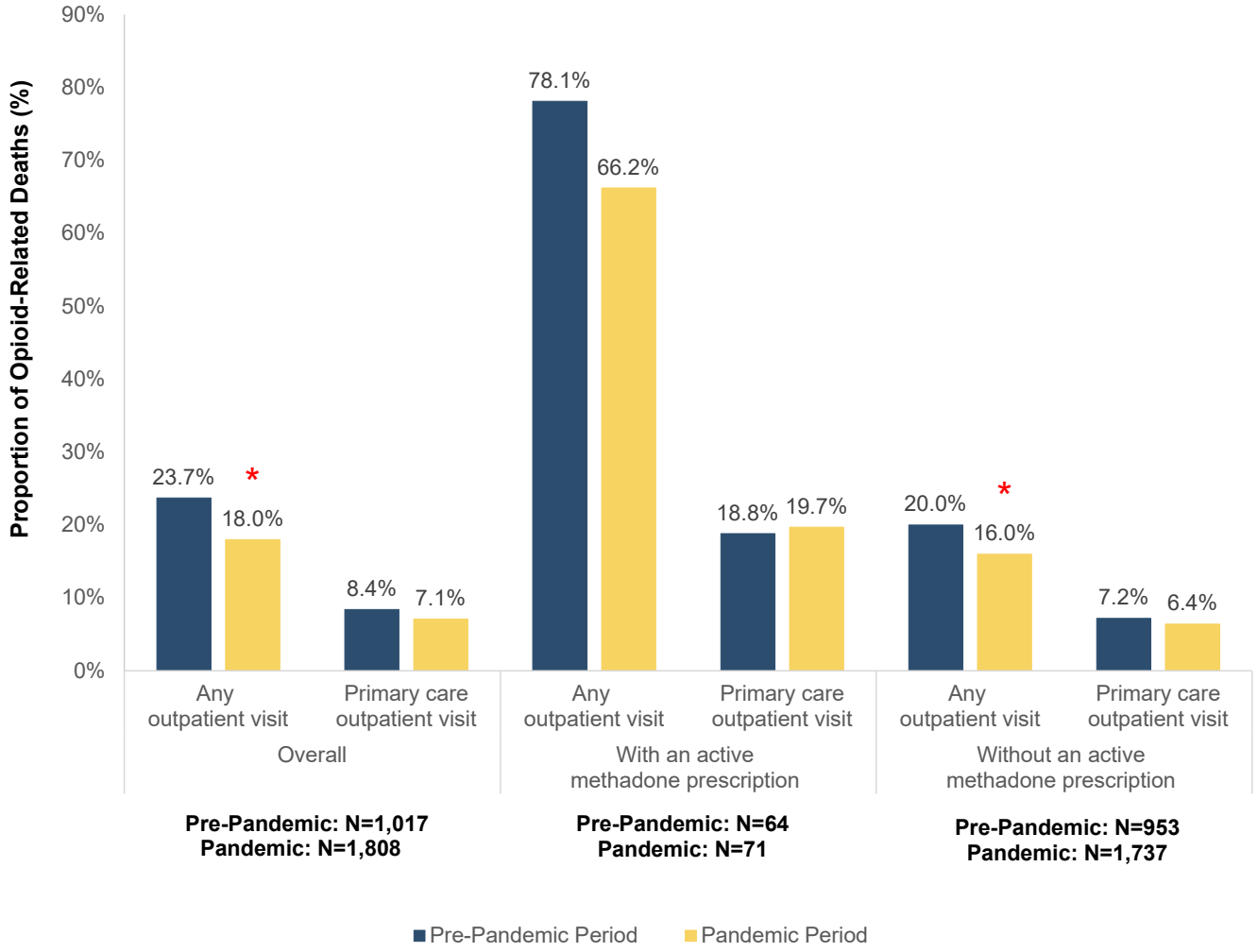


NOTE

1. There were no significant differences comparing pre-pandemic vs. pandemic periods.
2. Any inpatient hospitalization or ED visit that resulted in an opioid-related death was excluded as a healthcare encounter.

Overall, there were no statistically significant changes in the prevalence of hospital encounters in the 7 days prior to death between the pre-pandemic and pandemic periods. However, the prevalence of emergency department visits declined slightly, as did the prevalence of overdoses treated in hospital. In contrast, the prevalence of having been discharged from an inpatient hospitalization (either acute or mental health) in the 7 days prior to death increased slightly during the pandemic. Importantly, nearly 6% of opioid-related deaths during the pandemic occurred among people who had visited an ED in the previous week (5.9%; 107/1,808), rising to 17.5% of people who had visited an ED in the prior 30 days (317/1,808; data not shown).

Figure 12: Recent outpatient visit in the seven days prior to opioid-related death, overall and stratified by whether people were actively treated with methadone at the time of death in Ontario*



NOTE

* Red asterisk indicates statistically significant difference between pre-pandemic and pandemic cohorts ($p<0.05$).

Overall, nearly 1 in 5 opioid-related deaths during the pandemic occurred among individuals who had received outpatient care in the prior week (18.0%; N=325) with 7.1% of people (N=128) having had a visit with a primary care provider. This varied considerably according to whether people were active recipients of methadone to treat opioid use disorder (OUD), which is expected due to high requirements for physician interaction among OAT recipients. Specifically, among people actively treated with methadone during the pandemic who died of an opioid-related toxicity (N=71), approximately two-thirds had received outpatient care and nearly 20% had seen a primary care provider in the week prior to death. In general, there were declines in the prevalence of recent outpatient visits prior to opioid-related death during the pandemic, which may be attributed to disruptions in access to care or change in OAT care guidance, particularly early in the pandemic.[2]

Clinical Characteristics

Table 3: Distribution of pain diagnoses and opioid use disorder among those who died of an opioid-related toxicity in Ontario

	Pre-Pandemic Period N=1,017	Pandemic Period N=1,808	Stat. Sig.
History of chronic pain† (N,%)	340 (33.4%)	505 (27.9%)	*
Indication of opioid use disorder in prior 5 years (opioid agonist treatment or other opioid–related diagnosis)† (N,%)	668 (65.7%)	1,186 (65.6%)	
History of chronic pain and indication of opioid use disorder in prior 5 years* (N,%)	244 (24.0%)	338 (18.7%)	*

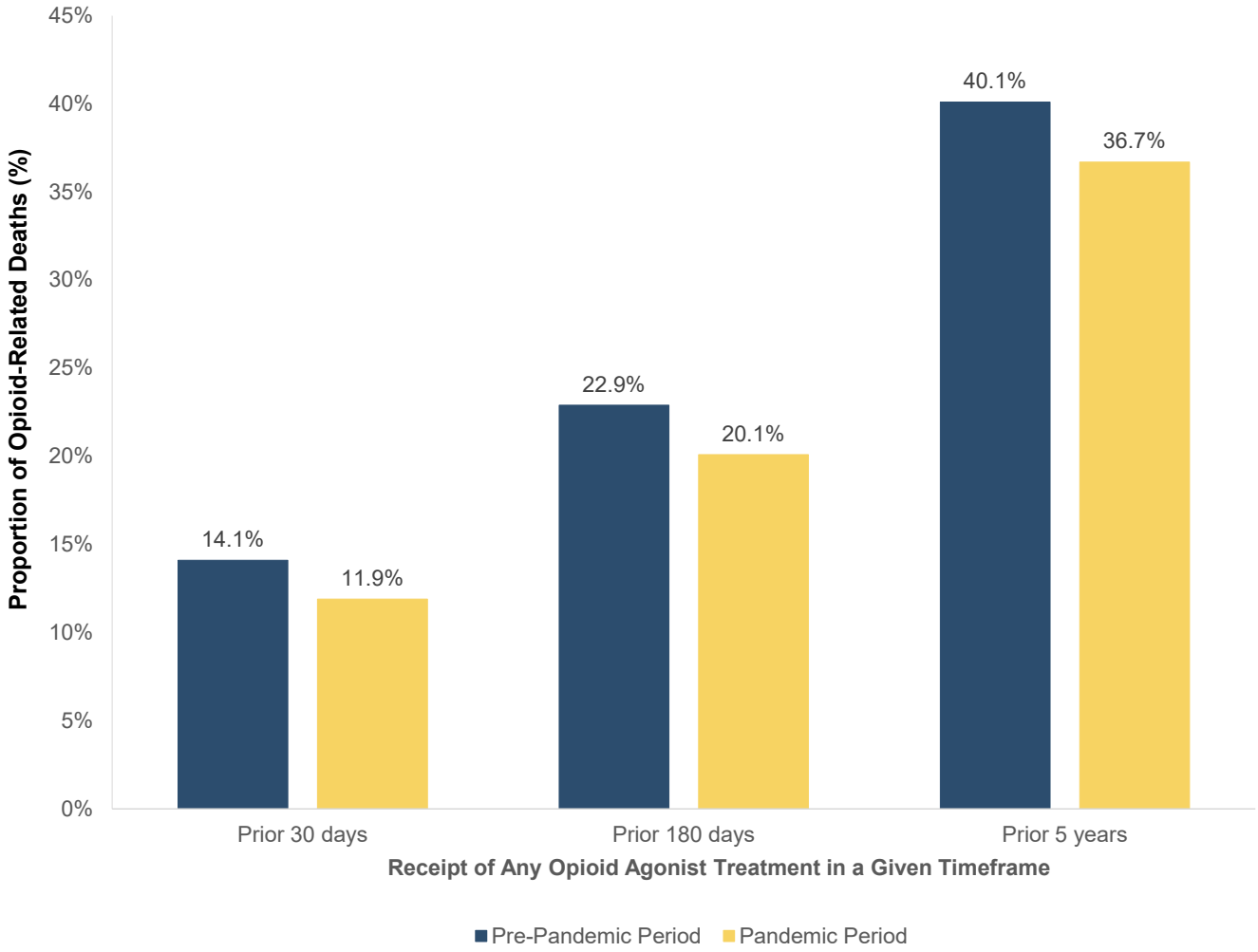
NOTE

* Stat. Sig. = statistical significance, where the presence of an asterisk indicates p<0.05.
† See Appendix A for definition

Approximately two-thirds of opioid-related deaths occurred among people who engaged with the healthcare system for reasons related to opioid agonist treatment or other indications of OUD in the 5 years prior to death, and this did not change considerably during the pandemic. While it is expected that many fatal overdoses would occur among people with OUD, this finding also indicates the potential risks of overdose faced by people without OUD who occasionally use drugs. Another possible explanation for this finding is fentanyl contamination of the stimulant supply which has been described sporadically in the literature.[5,6] However, this phenomenon is not consistently identified, and there is little indication that this occurs frequently in the Ontario context; therefore the degree to which this contributes to these findings is unclear.

In contrast, there was a slight decrease in the prevalence of chronic pain diagnoses among people who died of an opioid-related toxicity during the pandemic, declining from 33.4% in the pre-pandemic period to 27.9% during the pandemic (p=0.002). Overall, there was a relatively high rate of concurrent diagnoses among people having a fatal overdose, with nearly 1 in 5 opioid-related deaths during the pandemic occurring among individuals with both a history of chronic pain and OUD. Among those with a history of chronic pain, 66.9% had a concurrent OUD diagnosis.

Figure 13: Recent receipt of opioid agonist treatment among people who died of an opioid-related toxicity in Ontario



NOTE

There were no significant differences comparing pre-pandemic vs. pandemic periods.

Although nearly two-thirds of opioid-related deaths occurred among people with a prior diagnosis related to OUD during the pandemic (1,186 of 1,808), only 11.9% (216 of 1,808) were prescribed OAT in the 30 days prior to death (8.0% received methadone; 4.5% received buprenorphine). This proportion increased when looking for evidence of more remote treatment, with approximately one-third of people dying from an opioid overdose having been engaged in treatment in the previous 5 years. Given the strong evidence of benefit of OAT in preventing overdose,[7] more efforts are needed to expand access to treatment for OUD across Ontario and engage people who use drugs to ensure that these services are patient-centred, and are provided in safe, inclusive, and supportive spaces.

Table 4: Healthcare encounters for mental health-related diagnosis among people who died of an opioid-related toxicity in Ontario

	Pre-Pandemic Period N=1,017	Pandemic Period N=1,808	Stat. Sig.
Healthcare encounter for mental health-related diagnosis (prior 5 years†)	881 (86.6%)	1,607 (88.9%)	
Emergency department visit or hospitalization	554 (54.5%)	1,010 (55.9%)	
Community Health Centre visit	94 (9.2%)	184 (10.2%)	
Other outpatient visit	845 (83.1%)	1,532 (84.7%)	
Psychotic disorders	129 (12.7%)	293 (16.2%)	*
Mood and anxiety disorders	676 (66.5%)	1,243 (68.8%)	
Substance use disorders	622 (61.2%)	1,118 (61.8%)	
Non-psychotic disorders	185 (18.2%)	344 (19.0%)	
Other	102 (10.0%)	237 (13.1%)	*

NOTE

* Stat. Sig. = statistical significance, where the presence of an asterisk indicates p<0.05.
† Outpatient visit, emergency department visit, or hospital admission for mental health-related diagnosis, see Appendix B for definitions

The prevalence of a mental health-related healthcare encounter in the 5 years prior to opioid-related death was high, reaching almost 90% among people who died during the pandemic (88.9%, 1,607 of 1,808 deaths). Mental health-related encounters most commonly occurred in an outpatient setting; however, over half of opioid-related deaths occurred among people who had visited a hospital for a mental health-related reason in the 5 years prior to death. In general, there were no large changes in the prevalence of mental health-related encounters among individuals that died during the pandemic. Exceptions included an increase in opioid-related deaths occurring among people with outpatient visits related to psychotic disorders (from 12.7% to 16.2%; p=0.012), and those with hospital visits related to schizophrenia or related disorders (7.8% to 11.6%; p=0.001), or trauma/stressor-related disorders (9.5% to 14.0%; p<0.001; data not shown).

Table 5: Health conditions among people who died of an opioid-related toxicity in Ontario

	Pre-Pandemic Period N=1,017	Pandemic Period N=1,808	Stat. Sig.
Infective endocarditis in the prior 180 days	10 (1.0%)	7 (0.4%)	*
Any other serious infection in the prior 180 days	22 (2.2%)	49 (2.7%)	
Diagnosed with HIV† prior to death	20 (2.0%)	42 (2.3%)	
Diagnosis of COVID-19 prior to death	N/A	≤5	

NOTE

* Stat. Sig. = statistical significance, where the presence of an asterisk indicates p<0.05.

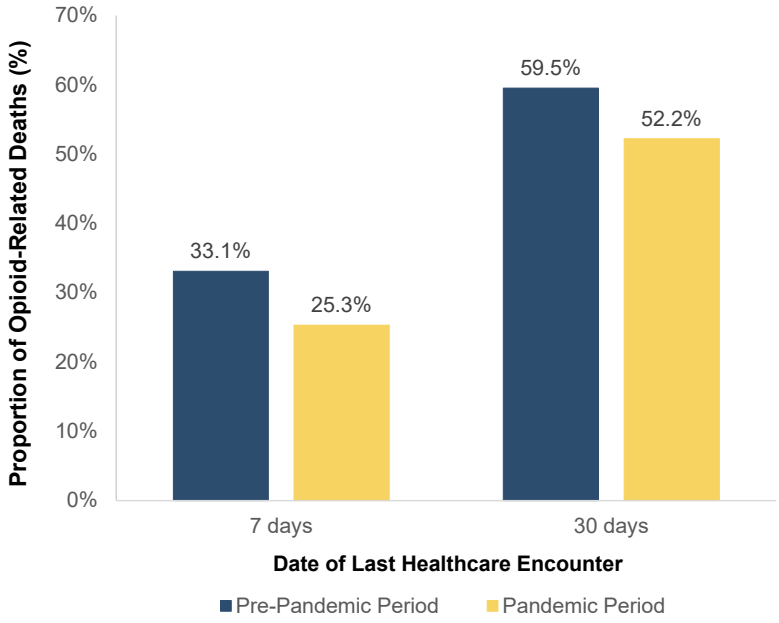
† HIV = Human Immunodeficiency Virus

Having received a diagnosis of COVID-19 during the first 10 months of the pandemic was relatively rare in this cohort, occurring in less than 6 individuals who had a fatal opioid overdose. There was a significant but modest decrease in the number of individuals who died of acute opioid toxicity and were diagnosed with infective endocarditis prior to death during the pandemic, this may be because individuals were less likely to engage with the health care system during the pandemic and fewer cases were diagnosed.

Pre-Pandemic Period
March 17, 2019 - December 31, 2019
(N=121)

Pandemic Period
March 17, 2020 - December 31, 2020
(N=293)

Figure 14: Recent healthcare encounters prior to opioid-related death among people who experienced homelessness in Ontario



Patterns of prior healthcare encounters among people experiencing homelessness during the pandemic were similar to those observed among all people who died of an opioid-related toxicity, with approximately one-quarter having a healthcare encounter in the week prior to death, and just over half having an encounter in the 30 days prior to death.

NOTE (for both figures)

1. There were no significant differences comparing pre-pandemic vs. pandemic periods.
2. Any inpatient hospitalization or ED visit that resulted in an opioid-related death was excluded as a healthcare encounter.

Figure 15: Recent hospital encounters in the seven days prior to opioid-related death among people who experienced homelessness in Ontario

Recent emergency department visits prior to opioid-related death during the pandemic declined, but remained more common among people experiencing homelessness (10.2% having visited an ED in the 7 days prior to death and 27.6% with ED visit in 30 days prior to death) compared to the prevalence among all people who died of an opioid-related toxicity (5.9% and 17.5%, respectively). In general, having recently had an inpatient hospitalization (acute or mental health-related) became more common during the pandemic, a finding which aligned with the overall population studied.

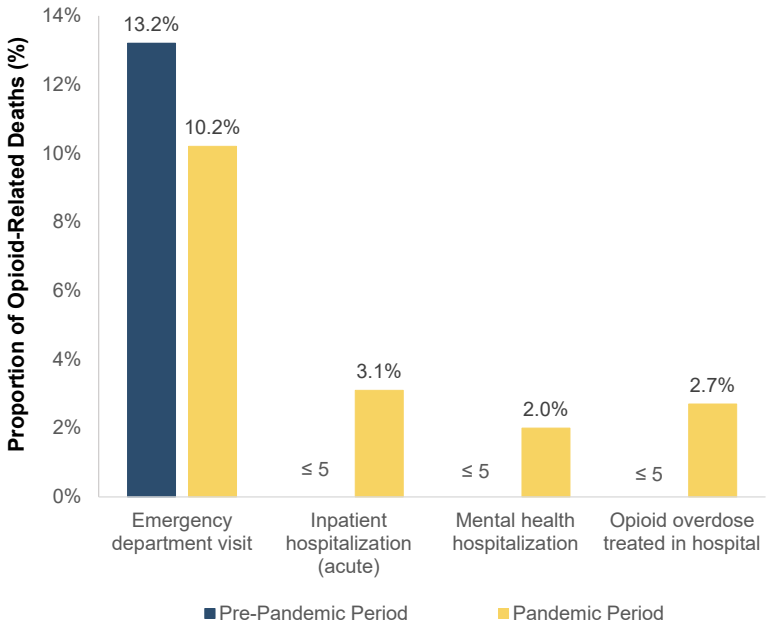
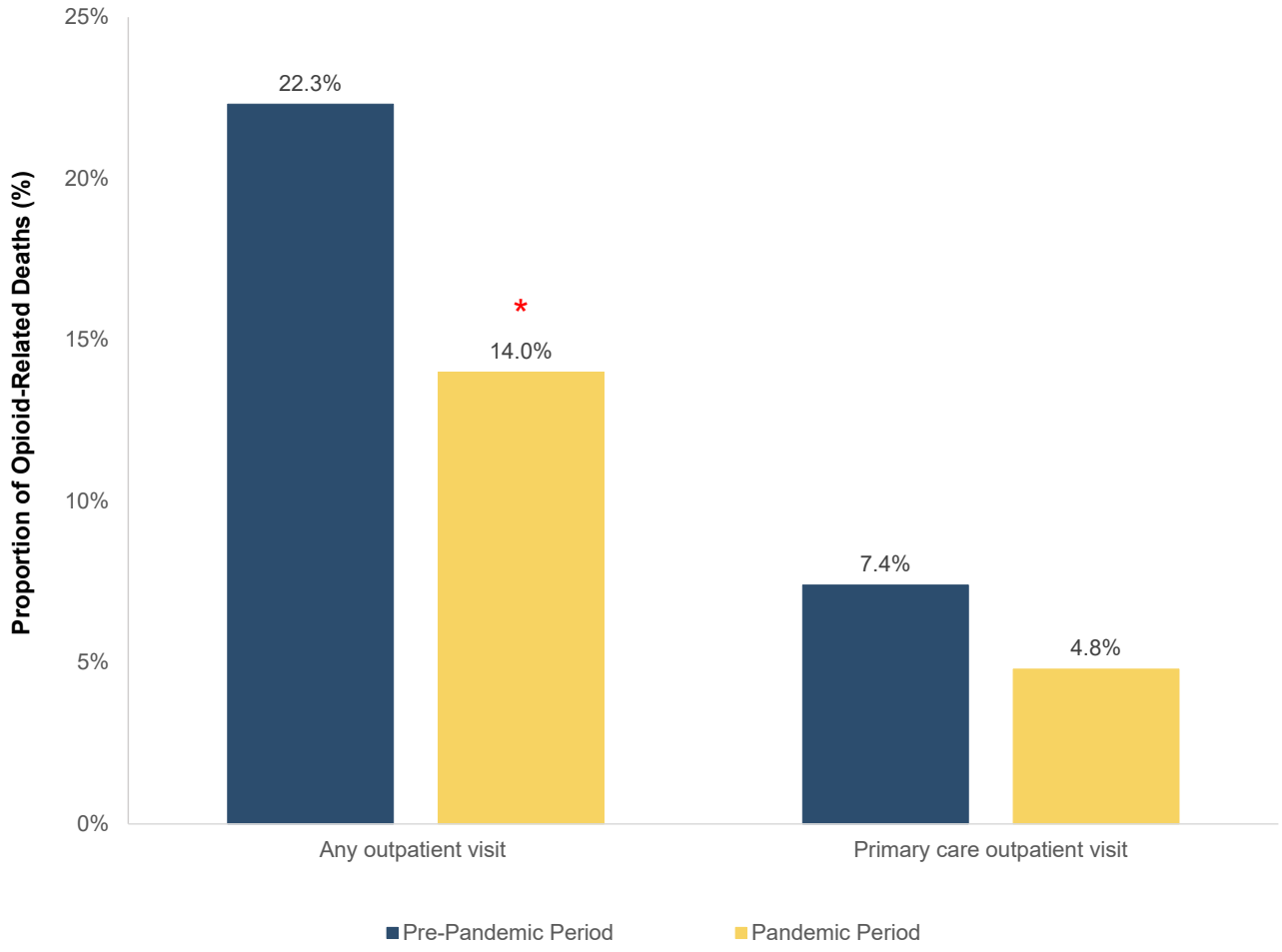


Figure 16: Recent outpatient visit in the seven days prior to opioid-related death among people who experienced homelessness in Ontario



NOTE

* Red asterisk indicates statistically significant difference between pre-pandemic and pandemic cohorts ($p<0.05$).

Prior to the pandemic, among people who were experiencing homelessness, the prevalence of having an outpatient visit in the 7 days prior to death was similar to that among all people who died of an opioid-related toxicity, with approximately 1 in 5 people having received outpatient care in the previous week. However, this fell more dramatically during the pandemic among people experiencing homelessness, reaching 14.0% (compared to 18% for overall deaths). Before the pandemic, the prevalence of people experiencing homelessness who had contact with a primary care provider in the week prior to death was also comparable to the prevalence among all people who died of an opioid-related toxicity, but fell to 4.8% among people experiencing homelessness during the pandemic (compared to 7% for overall deaths). While these rates still suggest a potential missed opportunity for intervention and connection with services among people at risk of overdose, it also suggests that access to outpatient care during the pandemic may have had a more pronounced decline among people experiencing homelessness. Alternatively, while we included visits to community health centers there may have been other sources of care introduced during the pandemic (including care provided in shelter settings).[8]

Focused Analysis among People Experiencing Homelessness

Table 6: Distribution of pain diagnoses and opioid use disorder among people who experienced homelessness and died of an opioid-related toxicity in Ontario

	Pre-Pandemic Period N=121	Pandemic Period N=293	Stat. Sig.
History of chronic pain* (N,%)	22 (18.2%)	60 (20.5%)	
Indication of opioid use disorder in prior 5 years (opioid agonist treatment or other opioid–related diagnosis)* (N,%)	90 (74.4%)	222 (75.8%)	
History of chronic pain and indication of opioid use disorder in prior 5 years* (N,%)	19 (15.7%)	51 (17.4%)	

NOTE

* Stat. Sig. = statistical significance, where the presence of an asterisk indicates p<0.05.
* See Appendix A for definition/inclusion criteria

Among people who were experiencing homelessness, over three-quarters of opioid-related deaths occurred among those who had a healthcare encounter related to OAT or other diagnoses indicating OUD in the 5 years prior to death, which is much higher than what was observed in the broader population of people who died of an opioid-related toxicity (66%). Despite this, prior access to OAT was similar to the broader population of people who died of an opioid-related toxicity, with only 36.2% of people experiencing homelessness who died of an opioid-related toxicity having been prescribed OAT in the previous 5 years (data not shown).

Although the prevalence of diagnosed chronic pain appears to be lower among people experiencing homelessness who died of an opioid related cause (20.5% vs. 27.9% in overall population), it is possible that this is reflective of under-treatment of chronic pain in this population as diagnosis in our data is largely reliant on access to pain medication, pain specialists, and specialty care (e.g., nerve block injections).

Focused Analysis among People Experiencing Homelessness

Table 7: Healthcare encounters for mental health-related diagnosis among people who experienced homelessness who died of an opioid-related toxicity in Ontario

	Pre-Pandemic Period N=121	Pandemic Period N=293	Stat. Sig.
Healthcare encounter for mental health-related diagnosis (prior 5 years†)	107 (88.4%)	271 (92.5%)	
Emergency department visit or hospitalization	87 (71.9%)	217 (74.1%)	
Community Health Centre visit	19 (15.7%)	33 (11.3%)	
Other outpatient visit	107 (88.4%)	260 (88.7%)	
Psychotic disorders	27 (22.3%)	79 (27.0%)	
Mood and anxiety disorders	84 (69.4%)	203 (69.3%)	
Substance use disorders	84 (69.4%)	209 (71.3%)	
Non-psychotic disorders	31 (25.6%)	72 (24.6%)	
Other	13 (10.7%)	48 (16.4%)	

During the pandemic, more than 90% of people experiencing homelessness who died of an opioid-related toxicity had a healthcare encounter for a mental health-related reason in the 5 years prior to death, with increases in individuals with outpatient healthcare encounters related to psychotic disorders during the pandemic (from 22.3% to 27.0%). Furthermore, the 5-year prevalence of hospital visits related to mental health diagnoses was much higher among people experiencing homelessness, reaching 74.1% among those who died of an opioid-related toxicity during the pandemic. Specifically, the 5-year prevalence of previous hospital visits for schizophrenia or related disorders (20.8%) and trauma/stressor-related disorders (21.5%) was much higher among people experiencing homelessness who died of an opioid-related toxicity during the pandemic compared to the overall population (11.6% and 14.0%, respectively) reinforcing the high burden of mental health diagnoses in this population.

Table 8: Health conditions among people who experienced homelessness who died of an opioid-related toxicity in Ontario

	Pre-Pandemic Period N=121	Pandemic Period N=293	Stat. Sig.
Infective endocarditis in the prior 180 days	0 (0.0%)	≤5	
Any other serious infection in the prior 180 days	≤5	13 (4.4%)	
Diagnosed with HIV* prior to death	7 (5.8%)	11 (3.8%)	
Diagnosis of COVID-19 prior to death	N/A	≤5	

Similar to the overall population, having received a diagnosis of COVID-19 during the first 10 months of the pandemic was rare in this cohort, occurring in less than 6 individuals who had a fatal opioid overdose. There were no significant differences in health conditions in the pre-pandemic compared to pandemic periods.

NOTE (for both tables)

* Stat. Sig. = statistical significance, where the presence of an asterisk indicates $p<0.05$.
† Outpatient visit, emergency department visit, or hospital admission for mental health-related diagnosis
* HIV – Human Immunodeficiency Virus

Limitations

1. The Office of the Chief Coroner/Ontario Forensic Pathology Service OCC/OFPS has not concluded all investigations for opioid-related deaths that occurred during the pandemic period. Therefore, we restricted our analysis to confirmed opioid-related deaths to ensure complete information; however, this means that some deaths that may ultimately be determined to be opioid-related are not included in this analysis.

2. We also excluded deaths that could not be linked to the administrative health databases at ICES. This may have disproportionately excluded individuals experiencing homelessness who did not have a valid Ontario health card, however since the proportions were similar in both time periods, we do not believe that this would have biased our results. Additionally, it is possible that the address associated with an individual's health card was not representative of their current living arrangement, and therefore we could have misassigned some individuals' neighbourhood income quintile or geographic location (e.g. urban/rural). Again, this limitation may have disproportionately impacted individuals experiencing homelessness who did not have a permanent address and therefore may have used the address of a temporary or previous residence.

3. The number of individuals experiencing homelessness reported by the death investigation service may be under-reported. It may not always be clear to an death investigation service whether an individual was provisionally accommodated or at immediate risk of homelessness. It is also likely that a proportion of the 7% of individuals with an unknown living arrangement were experiencing homelessness.

4. The circumstances surrounding opioid-related deaths have shifted in Ontario over the past decade, even in the absence of the COVID-19 pandemic. Therefore, the observed differences between people who died in the pre-pandemic period and the pandemic period could be attributed to the COVID-19 pandemic or may be due to pre-existing temporal changes.

5. Data related to opioid prescribing is based on pharmacy dispensing data. Therefore, we do not know if people who were dispensed opioids took the medication as prescribed.

6. Opioid use disorder is not well defined in administrative health data, and therefore we relied on prior receipt of opioid agonist treatment or healthcare encounters related to opioid use disorders in the previous 5 years to define a population with high likelihood of having a diagnosed opioid use disorder. However, it is likely that we are not capturing all people with opioid use disorder with this definition and therefore may be underestimating its prevalence in this analysis.

7. Some misclassifications of the origin of the opioid may have occurred for some cases. For example, some deaths with morphine as a direct contributor could be caused by heroin, which is metabolized to morphine. 6-Monoacetylmorphine (6-MAM), a metabolite of heroin, is rapidly cleared from the body such that its absence does not allow complete determination of whether morphine was the substance consumed or if the morphine detected was a metabolite of heroin. Heroin-related deaths may therefore be underreported. Morphine can also be a metabolite of codeine, more typically occurring at higher concentrations of codeine. Although we have attempted to address this in our methods (i.e., by removing morphine as a direct contributor if other metabolites of heroin (i.e. 6-MAM) are found in post-mortem toxicology), there remains the possibility of some misclassification. Similarly, we classified all deaths with fentanyl as a direct contributor as non-pharmaceutical opioid-related deaths. Although it is possible that prescription fentanyl could be involved in these deaths, this is anticipated to be very rare, with only ~1% of fentanyl-related deaths having evidence of a fentanyl patch or fentanyl prescription at the scene of the overdose.

Discussion

Our prior report[1] demonstrated a 79% increase in the monthly number of opioid-related deaths in Ontario following the provincial declaration of a State of Emergency in March 2020 and described changing circumstances surrounding these deaths, including the volatility of the unregulated drug supply and changing access to health care services and community-based programs for people who use drugs. In this report, we further explored the changing contribution of prescription opioids to opioid-related deaths, and potential missed opportunities for engagement of people who use drugs in the healthcare system in the days and weeks prior to fatal overdoses. Importantly, we found that - although absolute numbers were lower - rates of opioid-related deaths in rural and Northern parts of Ontario were much higher than urban and Southern regions in the province. We also found very high rates of mental health diagnoses among people dying of an opioid-related toxicity, with increased prevalence of individuals with previous known diagnoses of psychotic disorders and trauma/stressor-related disorders among people dying during the pandemic. Further, during the pandemic an even higher proportion of opioid-related deaths involved only non-pharmaceutical opioids, with 86% of all opioid-related deaths having only one opioid as a direct contributor, and fentanyl directly contributing to 9 out of every 10 opioid-related deaths. Additionally, when prescription opioids were direct contributors to opioid-related deaths, methadone was most commonly involved, and the presence of hydromorphone (both detected and as a direct contributor) declined, despite its increasing use during the pandemic within 'safer opioid supply' prescribing, where it is prescribed as an alternative to the unregulated drug supply.

Our findings related to methadone warrant further discussion because of the strong evidence that opioid agonist treatment plays an important role in preventing overdose.[7] However, during the pandemic, we have increasingly observed methadone-related deaths where fentanyl was also found to be directly contributing to death, with only moderate methadone doses typically being prescribed prior to overdose (median 70mg methadone). This aligned with concerns that have been raised elsewhere[3] that when fentanyl is the predominant drug in the unregulated drug supply, inadequate methadone doses that do not properly account for high opioid tolerance from exposure to fentanyl may lead people to continue relying on this supply, putting them at continued risk of overdose. However, one-third of deaths where methadone was a direct contributor occurred among people who had not been dispensed methadone in the last month. Although it is reassuring that there was no significant change in this pattern during the pandemic – a period of time when more flexible take-home doses are being dispensed[2] – this finding demonstrates the potential risks of diverted methadone and reinforces the need to ensure low barrier access to OAT so that people are not relying on diverted sources. This is particularly important because we found that two-thirds of opioid-related deaths occurred among people with a recent healthcare encounter related to OUD, but that only one-third had accessed OAT in the prior 5 years. As fatal overdoses continue to climb across the country[9], there is a clear need for focused efforts and investments into developing accessible, patient-centred OAT programs that are designed to meet the needs of at-risk communities and focus on measures to improve retention in treatment, and that provide a variety of choices, including injectable OAT (iOAT), methadone, buprenorphine/naloxone, slow release oral morphine, and newer longer-acting buprenorphine formulations. Furthermore, it is important to recognize that not all people with OUD will choose OAT or find it to be effective,[10-13] and it is therefore necessary to continue investing more broadly in comprehensive harm reduction programs, including supervised consumption services designed to support both injection and inhalation of drugs, and in safer opioid supply and risk mitigation prescribing. Given the increasing rates of overdose among people experiencing homelessness during the pandemic[1], the scale-up of supervised consumption services in shelter settings and easily accessible treatment options is warranted.

Although the majority of opioid-related deaths during the pandemic occurred among people with diagnoses indicating OUD in the previous 5 years, we found that approximately one-third of these deaths occurred among people without a healthcare encounter related to OUD. While this may in part reflect our inability to identify all OUD diagnoses in our databases, particularly among those with more remote diagnoses who no longer interact frequently with the healthcare system, this also implies that a considerable number of opioid-related deaths are occurring among people without an OUD. These deaths may be occurring among people who use opioids intermittently who have not developed a high tolerance to opioids and are therefore at a high risk of overdose when using an increasingly toxic, unpredictable drug supply or among people unintentionally overdosing on opioids prescribed to manage pain. The role of fentanyl adulteration of the stimulant drug supply has also been suggested in some parts of North America[5,6,14], although this is not a phenomenon that has been widely observed in drug checking services in Canada, including in Ontario.[15] Therefore, the degree to which accidental fentanyl exposure through the unregulated stimulant supply is contributing to overdose deaths is unknown, though it is likely infrequent. Despite this, there is clear evidence that poly-substance use with opioids and stimulants is common, and there are relatively fewer options for support or treatment for people who primarily use stimulants. This reinforces the need for also optimizing health and social care for people who use stimulants and expanding harm reduction approaches in this population, including the expansion of supervised consumption services that include supervised inhalation and smoking spaces, and safer stimulant prescribing.

Healthcare encounters within hospitals and outpatient offices present an important opportunity for connection of people who use drugs with programs and services, including access to OAT, comprehensive care including mental health services, harm reduction services, and housing support. However, we found that half of opioid-related deaths occurred among people who had interacted with the healthcare system in the last month, and one-quarter had a healthcare encounter in the 7 days prior to death. Although we were unable to determine whether services were offered during these interactions,[16-18] this suggests that there is a large missed opportunity for supporting people at risk of overdose when they seek medical care. With 90% of decedents having a mental-health related healthcare encounter, and 1 in 5 having concurrent diagnoses of OUD and chronic pain, this represents a group of people frequently engaging with both outpatient providers and hospital settings. There is, therefore, an urgent need to better integrate comprehensive substance use care, including OAT and harm reduction approaches, into hospital settings and improve transitions of care for community-based follow-up.[19] Furthermore, with widespread evidence of experiences of stigma within the healthcare system towards people who use drugs[20-22], it is imperative that services integrated within healthcare settings are provided in non-stigmatizing, respectful environments where providers are trained to provide care that is free from judgment and discrimination.

With 1 in 6 opioid-related deaths during the pandemic occurring among people experiencing homelessness, particular attention must also be paid to this population where we observed high rates of mental health diagnoses, infectious complications from drug use, and emergency department visits in the week prior to opioid-related death. The COVID-19 pandemic has had a disproportionate impact on people experiencing homelessness, who are also grappling with a worsening overdose crisis.[1,23] With evidence of lowering engagement with the healthcare system prior to opioid-related death during the pandemic, there is an urgent need to expand access to affordable housing, to harm reduction services such as supervised consumption sites (that include spaces for supervised inhalation and smoking) within shelter settings, and to ensure ongoing, equitable access to healthcare among people experiencing homelessness.

Conclusion

The findings of this work continue to build on those reported previously in Ontario and elsewhere across Canada[1,24-26], demonstrating the changing landscape of opioid-related harm across Ontario and the need for a multi-pronged response. The high number of single-opioid deaths which are being driven by the fentanyl-dominated unregulated drug supply, the high healthcare needs and health service utilization of people at risk of overdose, and the increasing prevalence of deaths involving both methadone and fentanyl reinforce the need for expanded access to a broad suite of programs designed to support people who use drugs. This should include low barrier access to OAT in multiple healthcare settings, including emergency department visits where many people frequent in the weeks prior to a fatal overdose. However, although a vital element of the overdose response, OAT is also clearly not sufficient to prevent the rising tide of opioid-related deaths across Ontario. With many fatal overdoses also occurring among people without OUD diagnoses, who may only intermittently use opioids or other unregulated substances, it is imperative that investments are also focused on comprehensive health and social care for all people who use substances, and expanded harm reduction with access to safer opioid supply programs and supervised consumption services that include spaces for supervised inhalation and smoking in all communities across the province.

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**.

Office of the Chief Coroner/Ontario Forensic Pathology Service

Together the Office of the Chief Coroner/Ontario Forensic Pathology Service (OCC/OFPS) provide death investigation services in Ontario serving the living through high quality investigations and inquests to ensure that no death will be overlooked, concealed or ignored. The findings are used to generate recommendations to help improve public safety and prevent further deaths. In Ontario, coroners are medical doctors with specialized training in the principles of death investigation. Coroners investigate approximately 17,000 deaths per year in accordance with section 10 of the Coroners Act. The OFPS provides forensic pathology services in accordance with the Coroners Act. It provides medicolegal autopsy services for public death investigations under the legal authority of a coroner. The OFPS performs approximately 7,500 autopsies per year. For more information, visit **mcscs.jus.gov.on.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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Office of the Chief Coroner – Privacy Statement

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Appendix A: Definitions

Opioids:
A family of substances that include pharmaceutical opioids available through prescription for the treatment of pain and opioid use disorder (e.g., oxycodone) and non-pharmaceutical opioids (e.g., heroin).

Opioid-Related Death:
An acute intoxication/toxicity death resulting from the direct contribution of consumed substance(s), where one or more of the substances was an opioid, regardless of how the opioid was obtained.

Opioid Use Disorder:
Opioid use disorder (OUD) is a medical condition associated with cravings for opioids that may lead to chronic use of opioids and behaviours that may interfere with the activities of daily life.[27] Opioid agonist treatment is often used first-line for the management of OUD.

Opioid Agonist Treatment:
Opioid agonist treatment (OAT) is recommended in the care of people with OUD.[28] Two of the most common types of OAT, and the types that are examined in this report, are methadone and the combination product buprenorphine/naloxone (commonly known by its brand name Suboxone®). We also included a newer longer-acting buprenorphine formulations (Sublocade® and Probuphine®). Both medications are opioids that aid in the prevention of opioid withdrawal and cravings, and can block the euphoric effect of other opioids.

Origin of Opioids:
- Opioids with **non-pharmaceutical origin** include:
  - Heroin, heroin metabolites (morphine where monoacetylmorphine (6-MAM) was also detected), U-47700
  - Fentanyl, fentanyl analogues (including carfentanil)
- Opioids with **pharmaceutical origin** 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.

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 not approved for medical use in Canada, such as cocaine and methamphetamine.

Substance involvement in opioid-related 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.

Living arrangement:
- **Collective dwelling**: May include lodging and rooming houses, hotels, motels, tourist establishments, campgrounds and parks, sober living facilities, school residences and training centre residences, work camps, religious establishments, military bases and commercial vessels.
- **Experiencing homelessness**: Without stable, permanent, appropriate housing or the immediate prospect, means and ability of acquiring it; includes no fixed address. This includes people who are unsheltered, emergency sheltered, provisionally accommodated or at immediate risk of homelessness.
- **Private dwelling**: A separate set of living quarters designed for or converted for human habitation. Must include a source of heat or power and must be an enclosed space that provides shelter/protection from the elements. May include apartments/condominiums, row houses/townhouses, trailers/mobile homes, single-detached houses, semi-detached houses and community housing.
- **Other**: Includes locations not applicable to other categories such as hospital, long-term care home, retirement home (including senior residences), correctional facilities and residential care facilities (including group homes).

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: Diagnosis Codes Used to Identify Healthcare Encounters and Health Conditions

Healthcare Encounters

Type of Encounter	Criteria	Data Source	Codes
Any outpatient care	Any visit with a physician or nurse practitioner in an office, home care, virtual, long-term care, or community health centre setting	OHIP Claims Database, Community Health Centre Database	N/A
Outpatient primary care	Outpatient primary care visits were defined as either of the following: • Any visit to a community health centre with a physician (i.e. General Practitioner) or nurse practitioner • A visit outside of a community health centre with a physician practicing in family medicine, pediatrics, or community medicine, or to a nurse practitioner, in which billing codes related to primary care were submitted. Visits must have occurred in an office, home care, virtual, or long-term care setting	OHIP Claims Database, Community Health Centre Database	OHIP billing codes: A001, A002, A003, A007, A903, E075, G212, G271, G372, G373, G365, G538, G539, G590, G591, K005, K013, K017, P004, K130, K131, K132, K030, K080, K081, K082, A261, A268, K267, K269
Emergency department visit	Any visit to an emergency department	National Ambulatory Care Reporting System	N/A
Acute hospital admission	Any acute-care related hospital admission. Excludes admissions to adult-designated mental health beds. Includes admissions related to mental health care for children and adolescents (i.e., people less than 18 years of age)	Discharge Abstract Database	N/A
Mental health-related hospital admission	Any admission to an adult-designated (i.e., people 18 years of age or older) mental health bed in a hospital	Ontario Mental Health Reporting System	N/A
Opioid toxicity- related emergency department visits and hospitalizations	Emergency department visit or hospital admission for opioid-related toxicity	National Ambulatory Care Reporting System, Discharge Abstract Database	ICD-10 diagnosis codes: T40.0, T40.1, T40.2, T40.3, T40.4, T40.6

Health Conditions: History of Chronic Pain

History of chronic pain was defined as meeting any one of the criteria below:

Criteria	Data Source	Codes
• Any outpatient visit with a physician practicing in the area of pain or anesthesiology in the year prior to death • Or any outpatient visit with a physician practicing in family medicine who billed 40 or more claims related to pain management in the year prior to death	OHIP Claims Database	OHIP billing code: A937
Experienced any traumatic injury in the 10 years prior to death	Ontario Trauma Registry	See Appendix B in the following document: https://www.cihi.ca/sites/default/files/services_otr_cds_dict_en_0.pdf
Received 10 or more nerve block injections in outpatient settings in the year prior to death	OHIP Claims Database	OHIP billing codes: G228, G123, G238, G246, G370, G371, G214, G226, G230, G231, G223, G240, G227, G235, G250
Received 90 days or more of opioids used for the treatment of pain in the 100 days prior to death	Narcotics Monitoring System	N/A
Coroner investigation determined that the individual had a medical history of a pain disorder or a traumatic injury	Drug and Drug/Alcohol Related Death Database	N/A

Health Conditions: History of Opioid Use Disorder

History of opioid use disorder was defined as meeting any one of the criteria below:

Criteria	Data Source	Codes
Any outpatient visit with a diagnosis code for drug use in the 5 years prior to death	OHIP Claims Database	OHIP diagnosis code: 304
Any emergency department visit or acute hospital admission with a diagnosis code for opioid-related disorder in the 5 years prior to death	National Ambulatory Care Reporting System, Discharge Abstract Database	ICD-10 diagnosis code: F11
Any mental health-related hospital admission with a diagnosis code for opioid use disorder in the 5 years prior to death	Ontario Mental Health Reporting System	DSM diagnosis codes: 304.0, 305.5 ICD-10 diagnosis code: F11
Received a prescription for opioid agonist treatment (methadone, the combination product buprenorphine/naloxone, Probuphine, or Sublocade) in the 5 years prior to death	Narcotics Monitoring System	N/A

Health Conditions: History of a Mental Health-Related Healthcare Encounter

History of a mental health-related healthcare encounter was defined as meeting any one of the criteria below:

Criteria	Data Source	Codes
Outpatient visits (in settings other than community health centres) for mental health-related reasons		
Any visit with a diagnosis code for **anxiety or mood disorders** in the 5 years prior to death	OHIP Claims Database	OHIP diagnosis codes: 296, 300, 311
Any visit with a diagnosis code for **substance-related disorders** in the 5 years prior to death	OHIP Claims Database	OHIP diagnosis codes: 303, 304
Any visit with a diagnosis code for **psychotic disorders** in the 5 years prior to death	OHIP Claims Database	OHIP diagnosis codes: 295, 297, 298
Any visit with a diagnosis code for **other non-psychotic disorders** in the 5 years prior to death	OHIP Claims Database	OHIP diagnosis codes: 301, 302, 306, 309
Any visit with a diagnosis code for **other mental health-related disorders** in the 5 years prior to death	OHIP Claims Database	OHIP diagnosis codes: 291, 292, 299, 307, 313, 314, 315, or other OHIP diagnosis codes accompanied by billing codes indicating mental health-related services
Outpatient visits in community health centres for mental health-related reasons		
Any visit with a diagnosis code for any mental health condition or disorder in the 5 years prior to death	Community Health Centre Database	Any ICD-10 diagnosis code between F06 and F99 in the primary diagnostic position, excluding dementia and delirium-related diagnoses, or ICD-10 codes X60-X84, Y10-Y19, Y28 in the secondary diagnostic positions when the primary diagnosis is not between F06 and F99
Emergency department visit or acute hospital admission for mental health-related reasons, or admission in adult-designated mental health bed		
Any emergency department visit, acute hospital admission, or admission to an adult-designated mental health bed with a diagnosis code for the following in the 5 years prior to death:		
Any mental health and addictions	National Ambulatory Care Reporting System, Discharge Abstract Database, Ontario Mental Health Reporting System	ICD-10 diagnosis codes: DX10CODE1= F06-F99 or DX10CODE2-DX10CODE25 = X60-X84, Y10-Y19, Y28 when DX10CODE1 not equal to F06-F99 Any OMHRS record

Criteria	Data Source	Codes
Anxiety disorders	National Ambulatory Care Reporting System, Discharge Abstract Database, Ontario Mental Health Reporting System	ICD-10 diagnosis codes: F06.4, F40, F41, F93.0, F93.1, F93.2, F94.0 DSM diagnosis codes: 293.84, 300.0, 300.2, 309.21, 313.23 Ontario Mental Health Reporting System Provisional Diagnosis: 5
Substance-related disorders	National Ambulatory Care Reporting System, Discharge Abstract Database, Ontario Mental Health Reporting System	ICD-10 diagnosis codes: F10, F11, F12, F13, F14, F15, F16, F17, F18, F19, F55, F63.0 DSM diagnosis codes: 291, 292, 303, 304, 305, 312.31 Ontario Mental Health Reporting System Provisional Diagnosis: 16
Schizophrenia spectrum and other related disorders	National Ambulatory Care Reporting System, Discharge Abstract Database, Ontario Mental Health Reporting System	ICD-10 diagnosis codes: F06.0, F06.1, F06.2, F20, F22, F23, F24, F25, F26, F27, F28, F29, F53.1 DSM diagnosis codes: 293.81, 293.82, 295, 297, 298 Ontario Mental Health Reporting System Provisional Diagnosis: 2
Mood disorders	National Ambulatory Care Reporting System, Discharge Abstract Database, Ontario Mental Health Reporting System	ICD-10 diagnosis codes: F06.3, F30, F31, F32, F33, F34, F38, F39, F53.0 DSM diagnosis codes: 293.83, 296, 300.4, 301.13, 311, 625.4 Ontario Mental Health Reporting System Provisional Diagnosis: 3, 4
Trauma/stressor-related disorders	National Ambulatory Care Reporting System, Discharge Abstract Database, Ontario Mental Health Reporting System	ICD-10 diagnosis codes: F43, F94.1, F94.2 DSM diagnosis codes: 308.3, 309.0, 309.24, 309.28, 309.3, 309.4, 309.81, 309.89, 309.9, 313.89 Ontario Mental Health Reporting System Provisional Diagnosis: 7
Obsessive compulsive disorder and related disorders	National Ambulatory Care Reporting System, Discharge Abstract Database, Ontario Mental Health Reporting System	ICD-10 diagnosis codes: F42, F45.2, F63.3 DSM diagnosis codes: 300.3, 300.7, 312.39, 698.4. Ontario Mental Health Reporting System Provisional Diagnosis: 6
Personality disorders	National Ambulatory Care Reporting System, Discharge Abstract Database, Ontario Mental Health Reporting System	ICD-10 diagnosis codes: F07.0, F21, F60, F61, F62, F68, F69 DSM diagnosis codes: 301, 310.1 Ontario Mental Health Reporting System Provisional Diagnosis: 18
Deliberate self-harm	National Ambulatory Care Reporting System, Discharge Abstract Database	ICD-10 diagnosis codes: X60-X84, Y10-Y19, Y28 where main problem or most responsible diagnosis is not one of the ICD-10 diagnosis codes between F06 and F99
Other mental health disorders	National Ambulatory Care Reporting System, Discharge Abstract Database, Ontario Mental Health Reporting System	ICD-10 diagnosis codes: Any other diagnosis code between F06 and F99 not included in the categories above, excluding dementia and delirium-related diagnoses. DSM diagnosis codes: Any DSM code not included in the categories above, excluding dementia and delirium-related diagnoses.

Recent Healthcare Encounter for Infective Endocarditis

Criteria	Data Source	Codes
Any acute hospital admission with a diagnosis code for infective endocarditis in the 180 days prior to death	Discharge Abstract Database	ICD-10 diagnosis codes: I33.0, I33.9, I38, I39, B37.6

Recent Healthcare Encounter for a Serious Infection

A recent healthcare encounter for a serious infection was defined as meeting any one of the criteria below:

Criteria	Data Source	Codes
Any acute hospital admission with a diagnosis code for a skin or soft tissue infection in the 180 days prior to death	Discharge Abstract Database	ICD-10 diagnosis codes: L03, L02, M76.2
Any acute hospital admission with a diagnosis code for a non-vertebral bone infection in the 180 days prior to death	Discharge Abstract Database	ICD-10 diagnosis codes: M86, M00
Any acute hospital admission with a diagnosis code for a spinal infection in the 180 days prior to death	Discharge Abstract Database	ICD-10 diagnosis codes: G06.1, M46.2, M46.3, M46.4, M46.5