

Data Impact Challenge II

What proportion of acute opioid recipients become chronic recipients? What is the rate of opioid-related deaths among chronic opioid recipients?

ICES Central: Opioid Group

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Background

While prescription opioids can be an effective treatment option for acute pain, evidence for their use in chronic pain management is weak. The risks associated with chronic opioid use are numerous and have been the subject of recent research, guidelines and news headlines.¹⁻³ Understanding the relationship between acute and chronic use of opioids for non-cancer related pain and opioid-related deaths among chronic recipients would help to clarify the scope of the issue for policy makers.

Question

First, we aimed to determine the proportion of new, acute opioid recipients that become chronic opioid recipients at 6 and 12 months, excluding cancer-related pain and palliative care patients to restrict our population to those treated with opioids for chronic non-cancer pain (CNCP). Second, we examined the rate of opioid-related deaths among those chronic opioid recipients at 6 and 12 months.

Describing the data and analysis

Data custodian organization(s) and data sources:

- Data Custodian Organization: Institute for Clinical Evaluative Sciences (ICES). All datasets were linked using unique encoded identifiers and analyzed at ICES.

List of datasets used (e.g. names of database and/or data origins):

- Ontario Drug Benefit (ODB) Claims Database: Contains claims for prescription drugs received under the ODB program. In Ontario, individuals aged 65 and older, and individuals younger than 65 years of age who receive social assistance, have high prescription drug costs in relation to their net household income, live in long-term care, are disabled or receive home care, are eligible for prescription coverage through the ODB program.
- Office of the Chief Coroner (OCC) Opioid Death Database: This database was created by conducting a chart abstraction at the Office of the Chief Coroner of Ontario, and contains date of death, toxicology results and basic demographic information for all opioid-related deaths in Ontario. Opioid-related deaths are defined as per the Coroner's assessment after investigation, and is considered the gold standard definition for opioid-related deaths.⁴ Opioid-related deaths are complete up to December 31st 2010.
- Office of the Registrar General Deaths (ORGD) dataset (Vital Statistics): A cumulative dataset containing information on all deaths, including cause of death, registered in Ontario. These data are complete from January 1st 2003 to up to December 31st 2010.
- Registered Persons Database (RPDB): Provides basic demographic information for all individuals who have ever received an Ontario health card number. Data is supplied to ICES by the Ontario Ministry of Health and Long-term Care.
- Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD): Contains detailed diagnosis and procedure information for hospital admissions in Ontario.
- Ontario Health Insurance Plan (OHIP) Claims Database: Contains diagnosis information and fee codes for physicians' services in Ontario.
- Ontario Cancer Registry (OCR): Contains information on all Ontario residents who have been newly diagnosed with cancer or who have died of cancer. All new cases of cancer are registered, except non-melanoma skin cancer. The information is provided to ICES by Cancer Care Ontario.

Nature and size of cohort (e.g. geographic area covered, number of patients included):

- The study was conducted among adults (aged 15 and older) in Ontario, Canada who are beneficiaries of the ODB program. All individuals aged 65 and older are eligible for ODB coverage and were included. To define individuals less than 65 years of age who are ODB beneficiaries, we included individuals who filled at least one prescription for any drug covered by the ODB program in the 181 to 365 days prior to their first opioid prescription. This ensured we had enough look-back time to ascertain new opioid recipients. We included all oral and transdermal opioid products, excluding opioids used to treat dependence (methadone and buprenorphine) (Appendix B).
- **We identified 2,079,741 new opioid recipients over the study period.**
- Exclusions:
 - Individuals with missing age or gender
 - Individuals who died before their opioid initiation date
 - Individuals less than 15 years of age at their opioid initiation date.
 - Individuals with a cancer diagnosis prior to their opioid initiation date, captured in the OCR.
 - Individuals with evidence of palliative care in the 180 days prior to their opioid initiation date (Appendix B).

Data Timeframe

January 1st, 1998 to December 31st, 2015. Specific study period details, as they pertain to each objective, are outlined below.

Brief summary of the analysis methodology

Objective 1: To determine the proportion of new acute opioid recipients that became chronic opioid recipients at 6 and 12 months.

Study Design: Population based repeated cross-sectional study.

Study period: Accrual occurred between January 1st, 1998 and December 31st, 2014. Follow-up ended December 31st, 2015 to allow enough time to define chronic use at 12 months.

Cohort Definition: New opioid recipients meeting inclusion criteria as defined above.

Index date: Date of first opioid prescription.

Definition of ongoing use: We deemed patients to have continued opioid treatment if they received a subsequent opioid prescription within 120 days; in such cases, observation was continued until the date of last opioid prescription plus the days' supply on final prescription.

Stratifications: Calendar year and age group (15-65 and 66+).

Numerator: Number of individuals with ongoing use of prescription opioids at 6 months (180 days) and at 12 months (365 days).

Denominator: Number of individuals with a new opioid prescription.

Objective 2: To examine the rate of opioid-related deaths among new chronic opioid recipients at 6 and 12 months.

Primary analysis:

Study Design: Population based repeated cross-sectional study.

Study period: Accrual of chronic users occurred between January 1st, 1998 and December 31st, 2008. In cases of multiple periods of chronic use, we used the last date an individual became a chronic user during the accrual period. Follow-up ended in December 31st, 2010,

the last date which cause of death is available in the Ontario coroner's and Vital Statistics database, allowing for at least 2 years of follow-up to identify deaths for all individuals in the cohort.

Cohort Definition: Chronic opioid recipients meeting inclusion criteria as defined above.

Index date: Date of becoming a chronic opioid user.

Definition of opioid-related death: In our primary analysis, we identified opioid-related deaths using the gold standard database, which utilizes the Ontario coroner's data to capture all opioid-related deaths.⁴

Stratifications: Age group (15-65 and 66+).

Numerator: Number of individuals with an opioid-related death during follow-up.

Denominator: Number of individuals with ongoing use of prescription opioids at 6 months (180 days) and at 12 months (365 days).

Secondary analysis:

We used two distinct but complementary methods to identify opioid-related deaths. In a sensitivity analysis we leveraged a previously validated algorithm to identify opioid-related deaths using the Vital Statistics database (sensitivity = 0.75, specificity = 0.99) (Appendix B).⁵ Here, our accrual period started in 2003 instead of 1998 due to data availability. This analysis will be comparable to other provinces leveraging their Vital Statistics database to identify opioid-related deaths and also provide insight on the underestimate of opioid-related deaths.

Key Findings

Objective 1

To determine the proportion of new acute opioid recipients that became chronic opioid recipients who continued therapy at 6 and 12 months in Ontario.

- Between 1998 and 2014, we identified 2,079,741 eligible ODB beneficiaries who newly initiated opioid therapy. Among those, 11.8% (n=245,054) of new opioid recipients became chronic opioid recipients at 6 months, and 6.4% (n=132,926) were chronic recipients at 12 months (Table 1).
- The proportion of new opioid recipients who became chronic opioid recipients was higher among younger beneficiaries (aged 15-65) compared to older beneficiaries (aged 66+) at 6 months (13.6% vs. 11.1%, respectively) and 12 months (8.1% vs. 6.8%, respectively) (Table1).
- Over the study period, there was a slight increase in the number of new opioid recipients who became chronic recipients at 6 months (from 6.0% in 1998 to 6.7% in 2014) and 12 months (from 2.8% in 1998 to 3.7% in 2014) (Figure 1 & 2, Appendix A Table 3). Chronic opioid use was consistently higher among younger beneficiaries.
- In 2000, the proportion of new opioid recipients who became chronic opioid recipients at 6 and 12 months was increasing steadily and peaked in 2003. This increase coincides with the addition of long-acting oxycodone in 2000 to the Ontario provincial drug formulary.
- In 2010, the Narcotics Safety and Awareness Act was enforced to address inappropriate use and prescribing of opioids, which may explain the slight decrease in the percent of new chronic opioid recipients observed in 2011. (Figure 1 & 2, Appendix A Table 4a and 4b).

Table 1: New and chronic opioid recipients in Ontario defined at 6 and 12 months, by age, between 1998-2014

Age	Number of new opioid recipients	Number of chronic opioid recipients at 6 months	% of new opioid recipients that became chronic recipients at 6 months	Number of chronic opioid recipients at 12 months	% of new opioid recipients that became chronic recipients at 12 months
Overall	2,079,741	245,054	11.8	132,926	6.4
<66	552,312	75,280	13.6	44,886	8.1
66+	1,527,429	169,774	11.1	88,040	5.8

Figure 1: Percent of new opioid recipients that became chronic opioid recipients at 6 months after opioid initiation in Ontario, by age, between 1998 and 2014

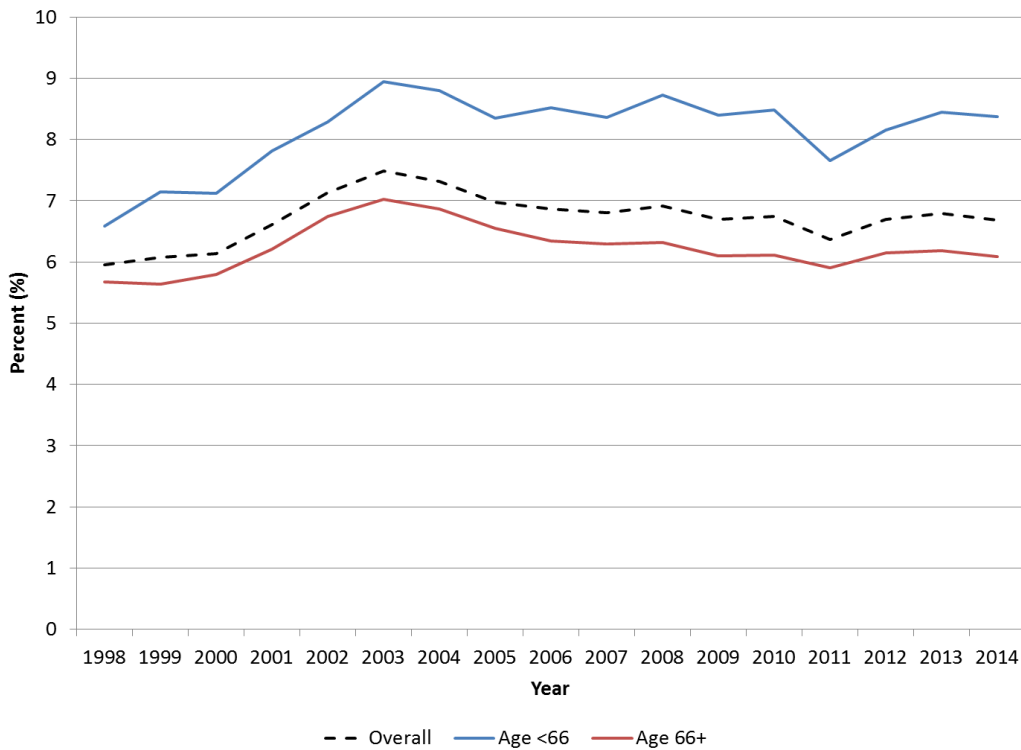
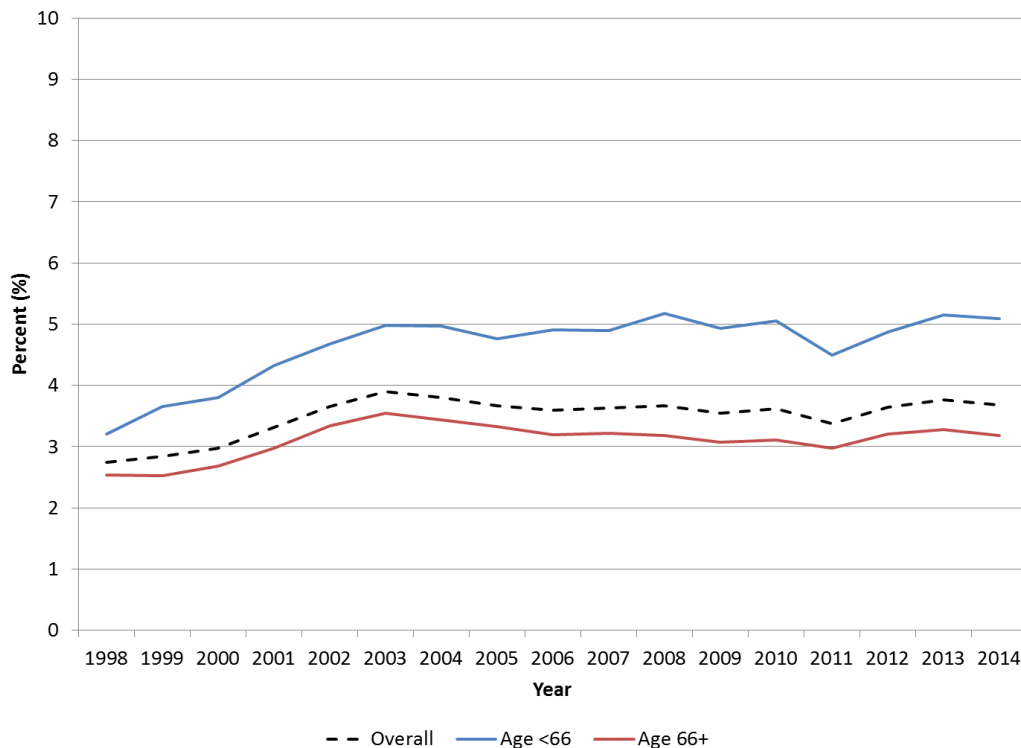


Figure 2: Percent of new opioid recipients who became chronic opioid recipients at 12 months after opioid initiation in Ontario, by age, between 1998 and 2014



Objective 2

To examine the rate of opioid-related mortality among new chronic opioid recipients who continued therapy at 6 and 12 months in Ontario.

Primary Analysis: Opioid-related deaths in recipients accrued between 1998 and 2008 using Coroner's Data

- We followed new opioid recipients who had ongoing opioid use at 6 and 12 months for a median of 8 years after becoming a chronic user (Table 2a)
- Between 1998 and 2008, we identified 147,470 new opioid recipients who became chronic opioid recipients at 6 months and 79,317 new opioid recipients who became chronic opioid recipients at 12 months after opioid initiation (Table 2a & Figure 3).
- We found a higher rate of opioid-related mortality among new opioid recipients who became chronic opioid recipients at 12 month (299 opioid-related deaths per 100,000 chronic recipients at 12 months) compared to those who became chronic opioid recipients at 6 months (222 opioid-related deaths per 100,000 chronic recipients at 6 months) (Table 2a & Figure 3).
- Among individuals with chronic opioid use at 6 months, the rate of opioid-related mortality was largely driven by deaths among younger chronic recipients (aged 15-65) compared to older chronic recipients (aged 66+) (716 deaths vs. 15 deaths per 100,000 chronic recipients, respectively). However, older chronic recipients had a shorter median time to opioid-related death compared to younger chronic recipients (1 year [IQR 1-4 years] compared to 3 years [IQR 2-5 years], respectively).
- Similarly, among individuals with chronic opioid use at 12 months the rate of opioid-

related mortality was largely driven by deaths among younger chronic recipients compared to older chronic recipients (895 deaths vs. 15 deaths per 100,000 chronic recipients). Again, older chronic recipients had a shorter median time to opioid-related death compared to younger chronic recipients (less than 1 year [IQR 0-3 years] compared to 3 years [IQR 2-5 years]).

- 1 in 451 new chronic opioid users at 6 months and 1 in 335 chronic opioid users at 12 months died from an opioid-related cause within a median of 3 years after becoming a chronic user.
- This was particularly high among younger chronic opioid users (age 15-65). In this population, approximately 1 in 140 chronic opioid users at 6 months and 1 in 112 chronic opioid users at 12 months died within a median of 3 years of becoming a chronic user.

Secondary Analysis: Opioid-related deaths in recipients accrued between 2003 and 2008 using Coroner's Data and Vital Statistics Data

- We observed higher rates of opioid-related mortality using the data abstracted from the Coroner's data compared to when using a previously validated algorithm using Vital Statistics data. The lower rates identified using the Vital Statistics are expected based on a previous validation study which found this dataset underestimates deaths (Table 2b).⁵

Figure 3: Opioid-related deaths in chronic opioid recipients identified between 1998 to 2008 (no maximum follow-up)

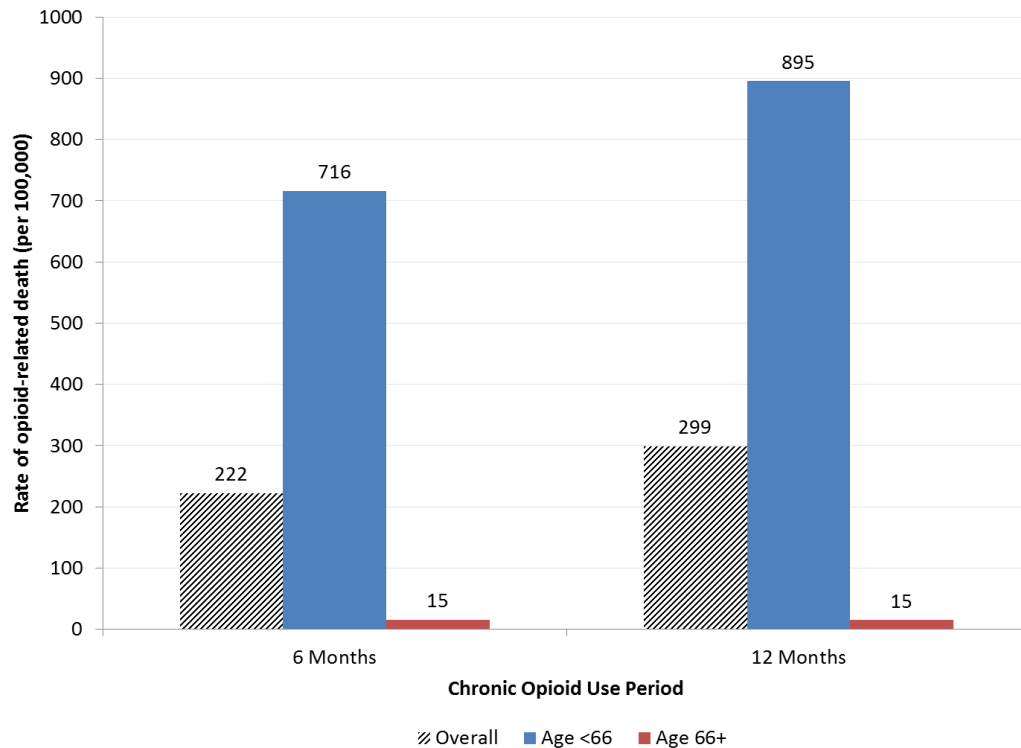


Table 2a: Opioid-related deaths in chronic opioid recipients identified between 1998 to 2008 (no maximum follow-up)

Chronic opioid use period	Age	Number of chronic opioid recipients	Coroner's Data†			
			Number of opioid-related deaths	Rate of opioid-related death (per 100,000)	Median (IQR) years of follow-up available	Median (IQR) years to opioid-related death
6 Months	Overall	147,490	327	222	8 (6-10)	3 (2-5)
	Age <66	43,443	311	716	8 (6-10)	3 (2-5)
	Age 66+	104,047	16	15	9 (7-10)	1 (1-4)
12 Months	Overall	79,317	237	299	8 (5-10)	3 (1-5)
	Age <66	25,583	229	895	8 (5-10)	3 (2-5)
	Age 66+	53,734	8	15	8 (6-9)	0 (0-3)

†Death data available up to 31 December 2010

Table 2b: Opioid-related deaths in chronic opioid recipients identified between 2003 to 2008 (no maximum follow-up)

Chronic opioid use period	Age	Number of chronic opioid recipients	Coroner's Data†				Vital Statistics Data†			
			Number of opioid-related deaths	Rate of opioid-related death (per 100,000)	Median (IQR) years of follow-up available	Median (IQR) years to opioid-related death	Number of opioid-related deaths	Rate of opioid-related death (per 100,000)	Median (IQR) years of follow-up available	Median (IQR) years to opioid-related death
6 Months	Overall	88,128	135	153	5 (4-7)	3 (1-4)	101	115	5 (4-7)	3 (1-4)
	Age <66	25,501	128	502	5 (4-7)	3 (2-4)	95	373	5 (4-7)	3 (2-4)
	Age 66+	62,627	7	11	7 (3-7)	1 (1-4)	6	10	4 (3-7)	0 (0-1)
12 Months	Overall	48,477	103	212	5 (3-6)	2 (1-4)	76	157	5 (3-6)	3 (1-4)
	Age <66	15,382	97-102*	*	5 (3-6)	2 (1-4)	70-75*	**	5 (4-6)	3 (1-4)
	Age 66+	33,095	≤5*	*	5 (3-6)	0 (0-1)	≤5*	*	3 (3-3)	0 (0-0)

†Death data available up to 31 December 2010

*In accordance with ICES privacy policies, in cases where the number of total recipients is ≤5, this number has been suppressed to ensure confidentiality. In cases where there is only one record being suppressed, the other record has been reported as a range in order to avoid residual disclosure issues

Conclusions

- The prevalence of chronic opioid recipients at 6 months and 12 months increased among new opioid recipients between 1998 and 2003. This increase was likely driven by the addition of long-acting oxycodone to the Ontario provincial drug formulary in 2000. However, rates have remained relatively stable between 2004 and 2014. There was a slight decrease observed in the prevalence of chronic opioid recipients in 2011 which was likely influenced by the 2011 Ontario Narcotics Safety and Awareness Act that was enforced to address inappropriate use and prescribing of opioids.
- Although there were a higher number of new opioid users recipients aged 66 and older (compared to aged 65 or younger), chronic opioid use at 6 and 12 months was more prevalent in the younger population.
- 1 in 451 new opioid recipients who continue opioid use for more than 6 months die of opioid-related causes, and this increases to 1 in 140 among recipients aged 15-65 at time of opioid initiation.
- 1 in 335 new opioid recipients who continue opioid use for more than a year die of opioid-related causes, and this increases to 1 in 112 among recipients aged 15-65 at time of opioid initiation.
- Despite the underestimate of capturing opioid-related deaths using the Vital Statistics data, relative differences in death rates between age groups and periods of chronic use are similar to that observed when using the Coroner's data. Therefore, the Vital Statistics data may be a useful tool for pan-Canadian comparisons given its national scope.

Limitations:

- The results of this analysis may not be generalizable to everyone aged 65 or younger. In Ontario, people younger than age 65 are eligible for public drug coverage if they receive social assistance, have high prescription drug costs in relation to their net household income, live in long-term care, are disabled or receive home care. In addition, changes to ODB coverage among those aged <65 will impact the number of beneficiaries and opioid-users that are captured
- Opioid-related death data are only available up to 2010, which may lead us to underestimate the rate of opioid-related death in more recent years if the rate of death has continued to increase in Ontario. Our team is currently conducting an abstraction to update this dataset to include the most recent years of available coroner's data (2011-2014), therefore these analyses will be easily replicable with the most recent years of data in the near future.

Policy Implications:

- The high rate of opioid-related death among chronic opioid recipients aged 65 years and younger highlight a patient population where continued policy interventions addressing the safety and appropriateness of opioids should be targeted.
- The rate of opioid-related death was higher among chronic recipients at 12 months compared to chronic recipients at 6 months, which suggests that policies should consider addressing the length of time individuals are continuously prescribed opioids for non-cancer related pain.

Appendix A

Table 3: New and chronic opioid recipients in Ontario defined at 6 and 12 months, by year, between 1998-2014

Year	Number of new opioid recipients	Chronic opioid use defined at 6 months: numerator	Chronic opioid use defined at 6 months: Rate per 100	Chronic opioid use defined at 12 months: numerator	Chronic opioid use defined at 12 months: Rate per 100
1998-2014	2,079,741	245,054	11.78	132,926	6.39
1998	217,083	12,932	5.96	5,959	2.75
1999	213,206	12,949	6.07	6,064	2.84
2000	207,739	12,757	6.14	6,183	2.98
2001	209,828	13,867	6.61	6,946	3.31
2002	211,775	15,089	7.13	7,760	3.66
2003	213,158	15,944	7.48	8,303	3.9
2004	220,262	16,107	7.31	8,373	3.8
2005	229,512	16,008	6.97	8,419	3.67
2006	230,951	15,853	6.86	8,322	3.6
2007	231,866	15,774	6.8	8,427	3.63
2008	239,162	16,556	6.92	8,786	3.67
2009	242,042	16,208	6.7	8,603	3.55
2010	249,517	16,805	6.74	9,030	3.62
2011	249,341	15,885	6.37	8,419	3.38
2012	241,436	16,159	6.69	8,818	3.65
2013	253,932	17,238	6.79	9,584	3.77
2014	260,711	17,423	6.68	9,582	3.68

Table 4a: New and chronic opioid recipients in Ontario defined at 6 and 12 months among individuals aged 65 or younger, by year, between 1998-2014

Year	Number of new opioid recipients	Chronic opioid use defined at 6 months: numerator	Chronic opioid use defined at 6 months: Rate per 100	Chronic opioid use defined at 12 months: numerator	Chronic opioid use defined at 12 months: Rate per 100
1998-2014	552,312	75,280	13.63	44,886	8.13
1998	66,242	4,366	6.59	2,129	3.21
1999	60,974	4,356	7.14	2,232	3.66
2000	55,240	3,932	7.12	2,100	3.80
2001	51,967	4,063	7.82	2,245	4.32
2002	51,180	4,245	8.29	2,396	4.68
2003	51,045	4,566	8.95	2,542	4.98
2004	51,915	4,566	8.80	2,582	4.97
2005	54,397	4,543	8.35	2,589	4.76
2006	55,203	4,703	8.52	2,712	4.91
2007	56,746	4,746	8.36	2,781	4.9
2008	59,754	5,214	8.73	3,087	5.17
2009	63,014	5,294	8.40	3,106	4.93
2010	65,822	5,581	8.48	3,326	5.05
2011	66,884	5,120	7.66	3,006	4.49
2012	64,780	5,289	8.16	3,156	4.87
2013	66,945	5,659	8.45	3,445	5.15
2014	67,536	5,656	8.37	3,439	5.09

Table 4b: New and chronic opioid recipients in Ontario defined at 6 and 12 months among individuals aged 66 or older, by year, between 1998-2014

Year	Number of new opioid recipients	Chronic opioid use defined at 6 months: numerator	Chronic opioid use defined at 6 months: Rate per 100	Chronic opioid use defined at 12 months: numerator	Chronic opioid use defined at 12 months: Rate per 100
1998-2014	1,527,429	169,774	11.12	88,040	5.76
1998	150,841	8,566	5.68	3,830	2.54
1999	152,232	8,593	5.64	3,832	2.52
2000	152,499	8,825	5.79	4,083	2.68
2001	157,861	9,804	6.21	4,701	2.98
2002	160,595	10,844	6.75	5,364	3.34
2003	162,113	11,378	7.02	5,761	3.55
2004	168,347	11,541	6.86	5,791	3.44
2005	175,115	11,465	6.55	5,830	3.33
2006	175,748	11,150	6.34	5,610	3.19
2007	175,120	11,028	6.3	5,646	3.22
2008	179,408	11,342	6.32	5,699	3.18
2009	179,028	10,914	6.1	5,497	3.07
2010	183,695	11,224	6.11	5,704	3.11
2011	182,457	10,765	5.9	5,413	2.97
2012	176,656	10,870	6.15	5,662	3.21
2013	186,987	11,579	6.19	6,139	3.28
2014	193,175	11,767	6.09	6,143	3.18

Appendix B

Table 5: Data Sources and Codes

Medical Diagnoses:		
Cancer	OCR	At least 1 incident cancer diagnosis except non-melanoma skin cancer at any time prior to opioid initiation.
Palliative Care	OHIP or DAD	1 code during 180 look back of the following: CIHI-DAD: Main patient service= Palliative Care OR OHIP: Feecode A945, B998, C945, C882, C982, K023, W872, W882, W972 or W982
Opioid-related death (secondary)	ORGD	Primary cause of death equal to any poisoning code: unintentional poisoning (X40-X49), or intentional poisoning (X60-69), or homicide poisoning (X85-X90), or poisonings of undetermined intent (Y10-Y19). AND Other cause of death is equal to opioid poisoning—defined as: T40.2 (poisoning by other opioids), and/or T40.3 (poisoning by methadone), and/or T40.4 (poisoning by other synthetic narcotics), and/or T40.6 (other and unspecified narcotics)
Drugs of Interest:		
Opioids for pain management	ODB	<ul style="list-style-type: none"> • Acetaminophen and codeine phosphate • Acetaminophen, caffeine and codeine phosphate • Acetaminophen and oxycodone • Acetylsalicylic acid and caffeine • Acetylsalicylic acid and codeine • Acetylsalicylic acid and oxycodone • Acetylsalicylic acid, butalbital, caffeine and codeine phosphate • Acetylsalicylic acid, caffeine, codeine phosphate and meprobamate • Acetylsalicylic acid, caffeine, and codeine phosphate • Anileridine • Belladonna and opium • Codeine • Dextropropoxyphene • Fentanyl • Hydrocodone and phenyltoloxamine • Hydrocodone bitartrate • Hydrocodone bitartrate and phenyltoloxamine • Hydrocodone bitartrate, pheniramine maleate, phenylpropanolamine HCL and pyrilamine maleate • Hydromorphone • Kaolin, opium and pectin • Levorphanol tartrate • Meperidine • Morphine • Opium • Oxycodone • Oxymorphone • Propoxyphene • Sufentanil
Opioids for opioid dependence treatment	ODB	<ul style="list-style-type: none"> • Buprenorphine and naloxone • Methadone

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