

Codeine in Canada – Don't forget weak opioids...

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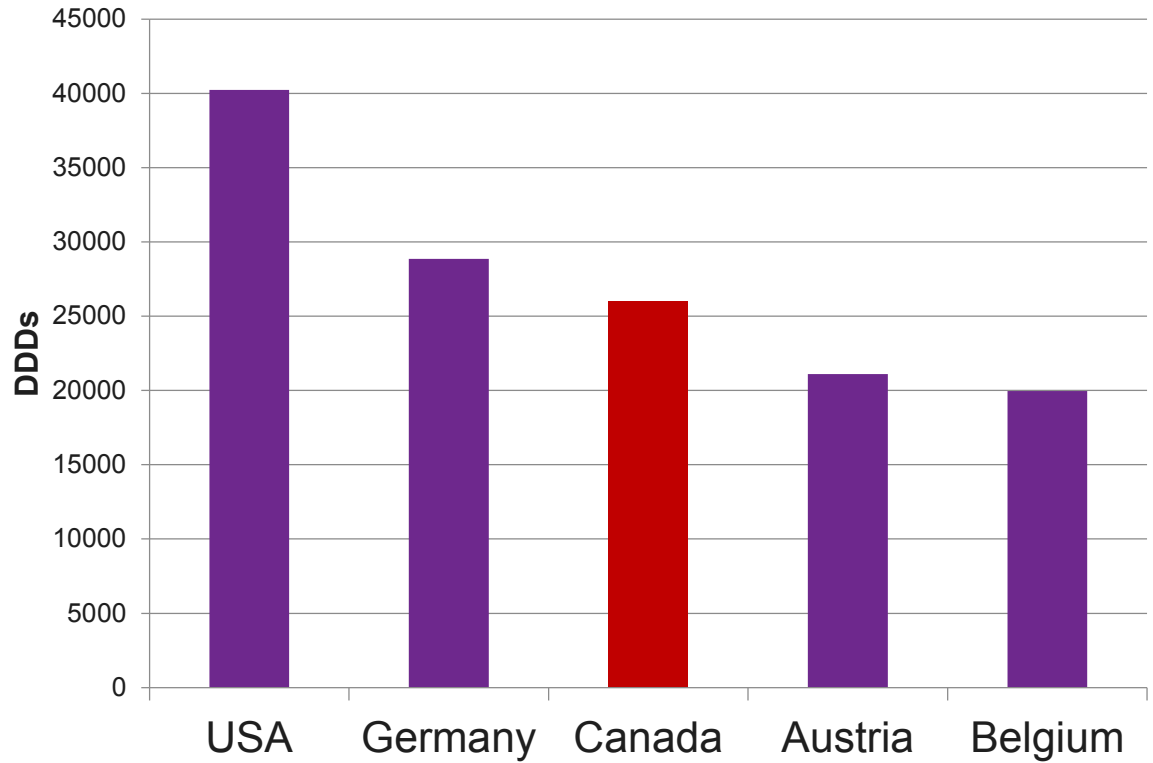
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UNIVERSITY OF TORONTO
LESLIE DAN FACULTY OF PHARMACY



World Rankings: Total DDDs / Million Inhabitants / Day



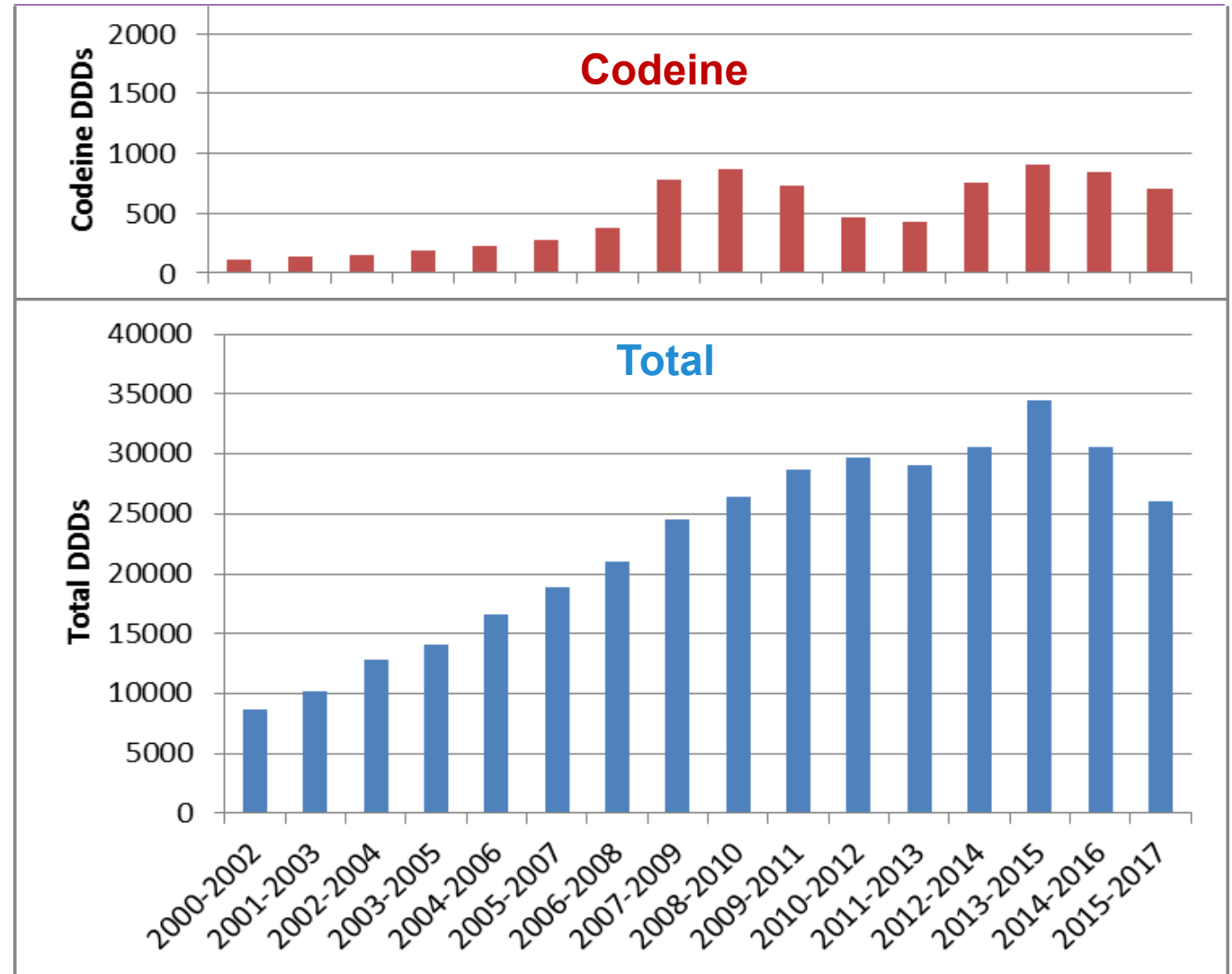
	Codeine DDDs
USA	-
Germany	2
Canada	699
Austria	<<
Belgium	60

DDD = Defined Daily Dose (WHO)

INCB Narcotic Drugs 2018 (2015-2017)

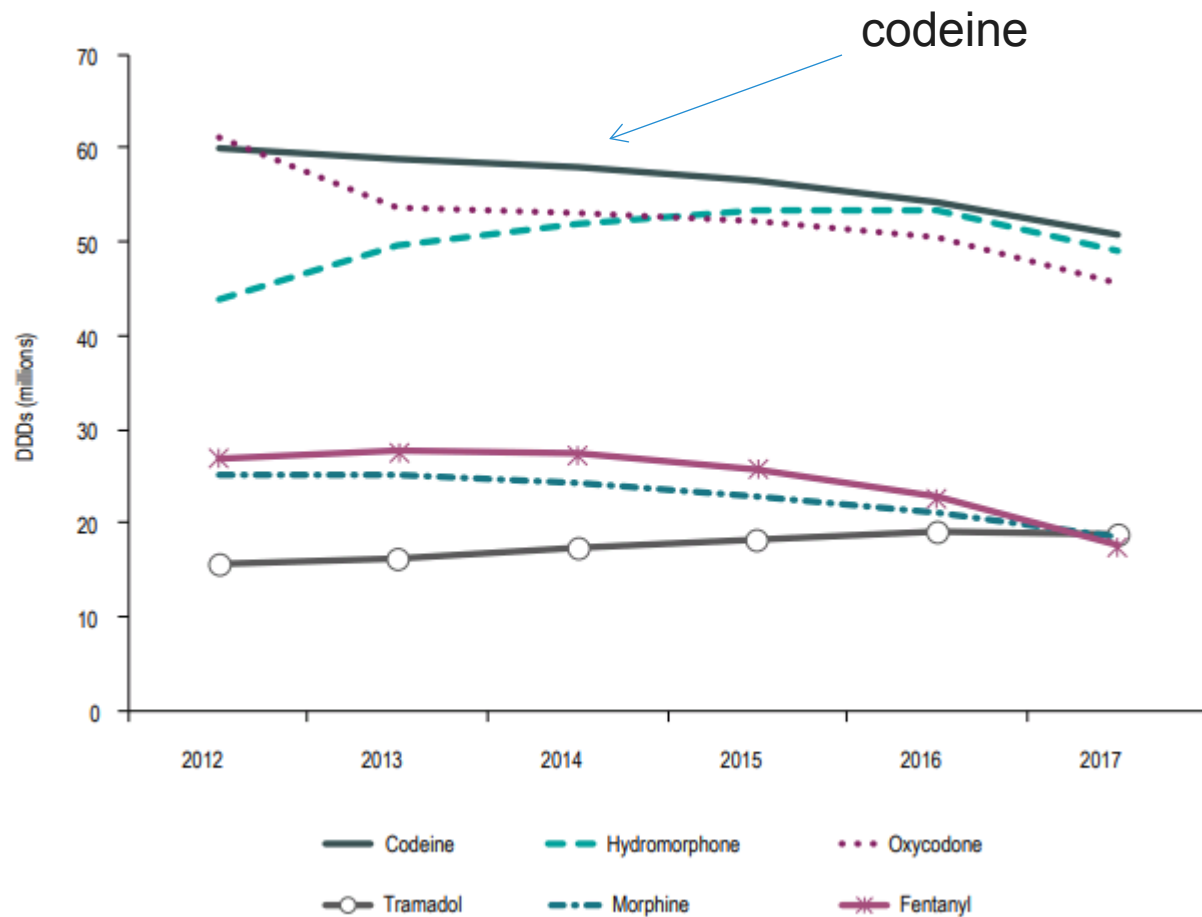
Canadian Consumption Over Time: 2000-2017

DDD/million inhabitants/day



INCB Narcotic Drugs 2003-2018

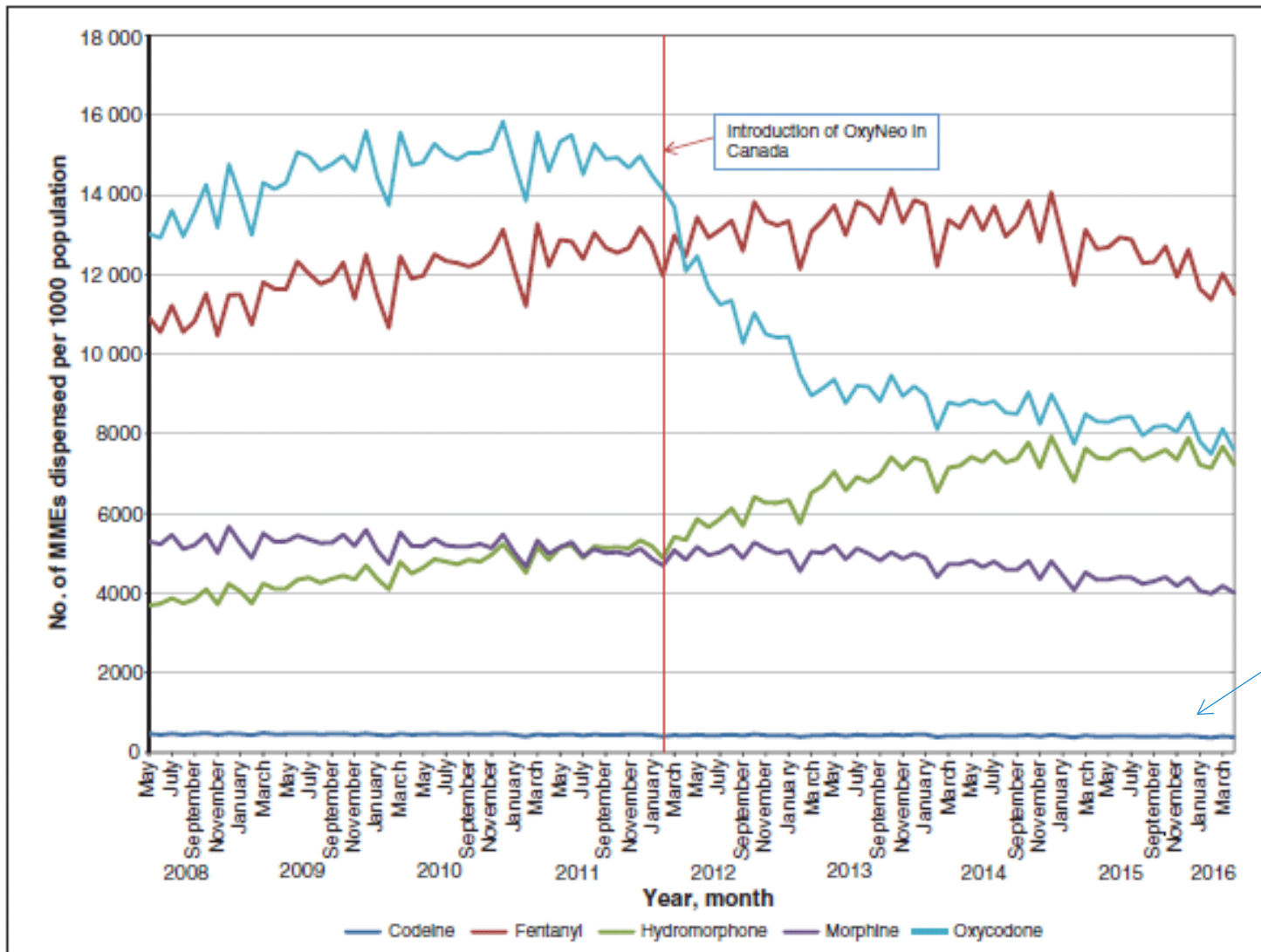
Trends in Canada 2012 – 2017 (DDDs)



Pan-Canadian Trends in the Prescribing of Opioids and Benzodiazepines, 2012 to 2017



<https://www.cihi.ca/sites/default/files/document/opioid-prescribing-june2018-en-web.pdf>

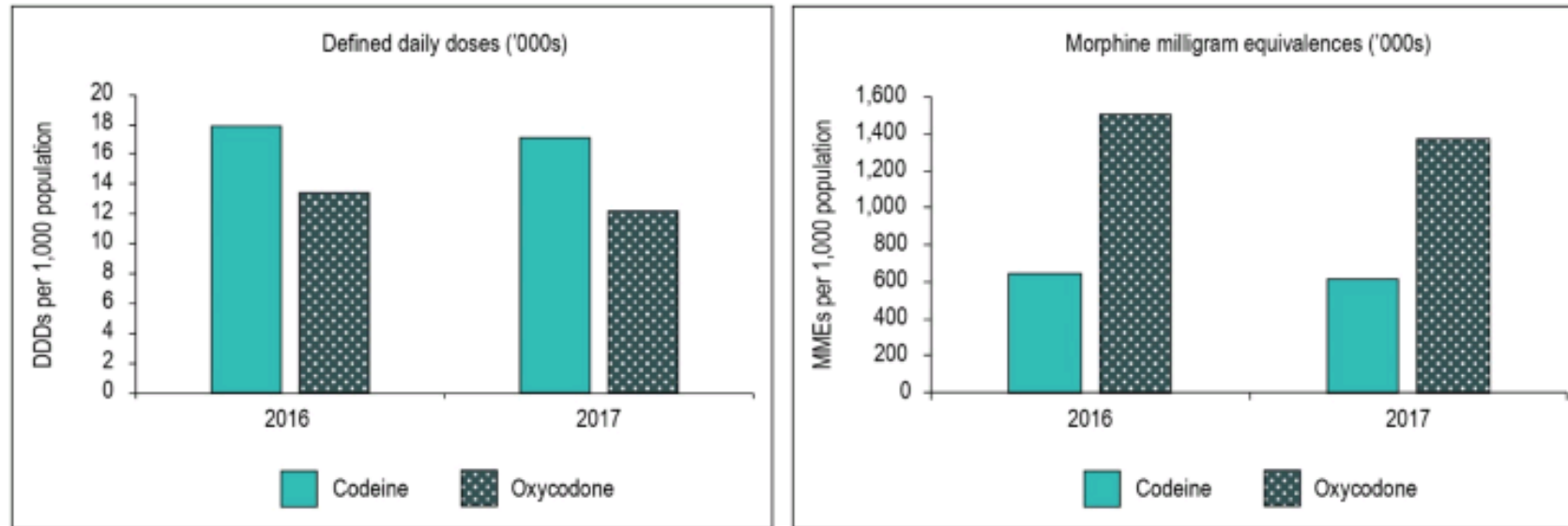


Trends in Canada 2008-2016 (MMEs)

codeine

Figure 3: Rate of dispensing of long-acting opioids (in milligrams of morphine equivalents [MMEs] per 1000 population) in Canada, May 2008–April 2016, by opioid type.

Defined Daily Doses vs Morphine Milligram Equivalence



Source

Canadian Institute for Health Information. [Pan-Canadian Trends in the Prescribing of Opioids and Benzodiazepines, 2012 to 2017 — Data Tables](#). June 2018.

<https://www.cihi.ca/sites/default/files/document/measuring-prescription-opioid-use-dec2018-en.pdf>

Behind the Prescriptions

A snapshot of opioid use across all Ontarians

ODPRN ONTARIO
DRUG POLICY
RESEARCH NETWORK

A Report by the Ontario Drug Policy Research Network
August 22, 2017

PAIN

OPEN

Clinical indications associated with opioid initiation for pain management in Ontario, Canada: a population-based cohort study

Sachin V. Pasricha^a, Mina Tadrous^{b,c,d}, Wayne Khoo^b, David N. Juurlink^{b,e,f,g,h}, Muhammad M. Mamdani^{b,c,d,f,h,i}, J. Michael Paterson^{b,h,j}, Tara Gomes^{a,b,c,d,h}

2016 – all prescriptions

- N=1,663,181 individuals dispensed opioid Rx for pain
- 98% of individuals received immediate-release opioids (&11% long-acting)
- Of those receiving IR opioids, 52% received codeine combination products

April 2015 – March 2016 – new starts

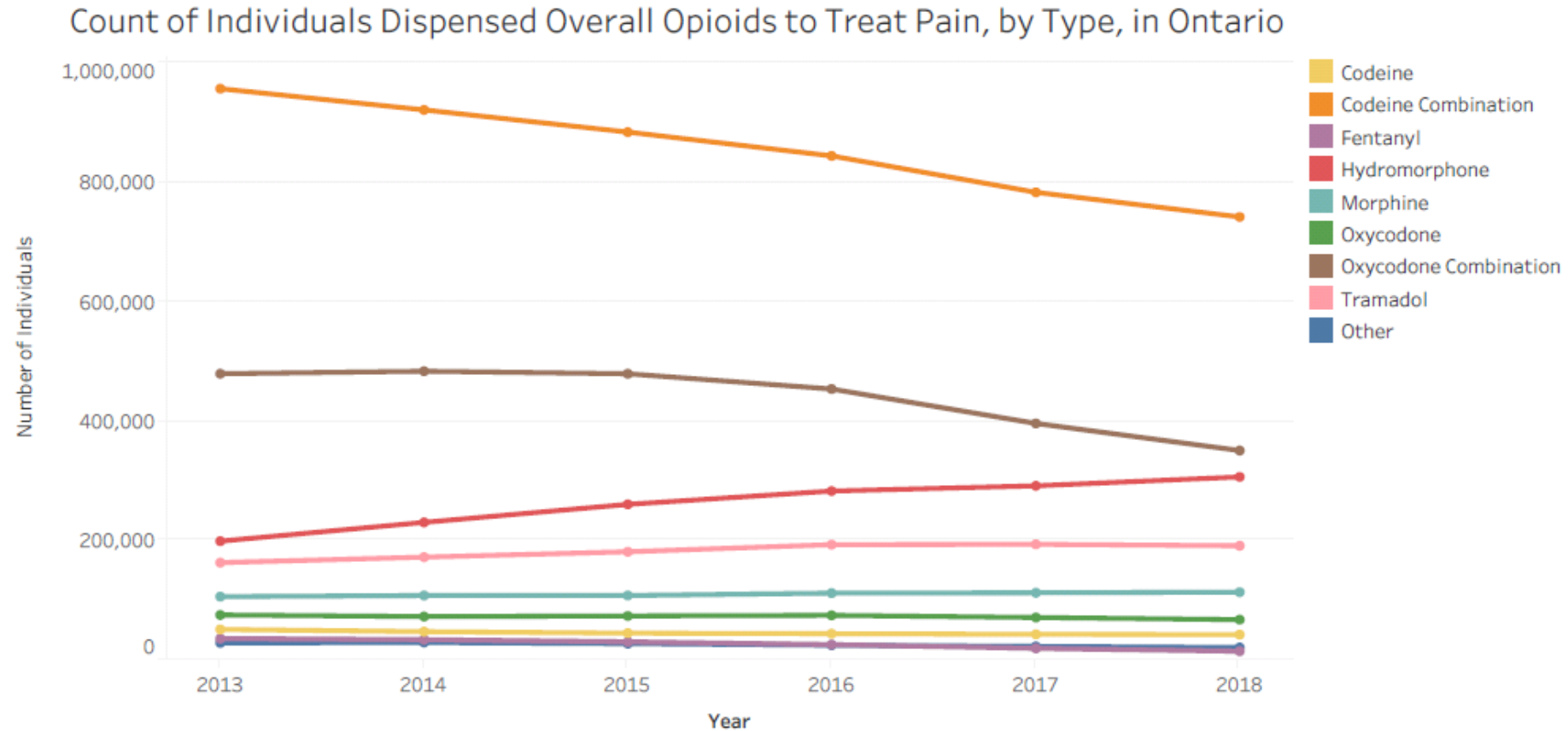
- N=653,993 individuals newly initiated opioid Rx
- 99% were immediate-release opioids
- 24% had daily dose >50 mg MME
- 17% had > 7 days' supply
- Of the immediate-release products, 53% were codeine combination products

Gomes T, Pasricha S, Martins D, Greaves S, et al. *Behind the Prescriptions: A snapshot of opioid use across all Ontarians*. Toronto: Ontario Drug Policy Research Network; August 2017.

Pasricha - Pain 2018;159:1562-8.

www.odprn.ca

Ontario Prescription Opioid Tool



Early Days...

THE ADDICTION LIABILITY OF CODEINE

C. K. HIMMELSBACH, M.D.
Assistant Surgeon, U. S. Public Health Service
FORT LEAVENWORTH, KAN.

JAMA 1934

CONCLUSION

Codeine possesses definite addiction liability.

COMMENT

It is felt that the material presented should be interpreted with due regard to the practical aspects that prevent codeine addiction from becoming prevalent. Codeine is relatively much more expensive than morphine, for narcotic doses are larger. It is inconvenient to administer, because its low solubility and high dosage require large volumes. Codeine is not readily available to the purveyors of illegitimate narcotics.

Severe dependence on oral opioids

Usoa E Busto PharmD, Beth A Sproule PharmD, Kathryn Knight PT,
Myroslava K Romach MSc MD, Edward M Sellers MD PhD

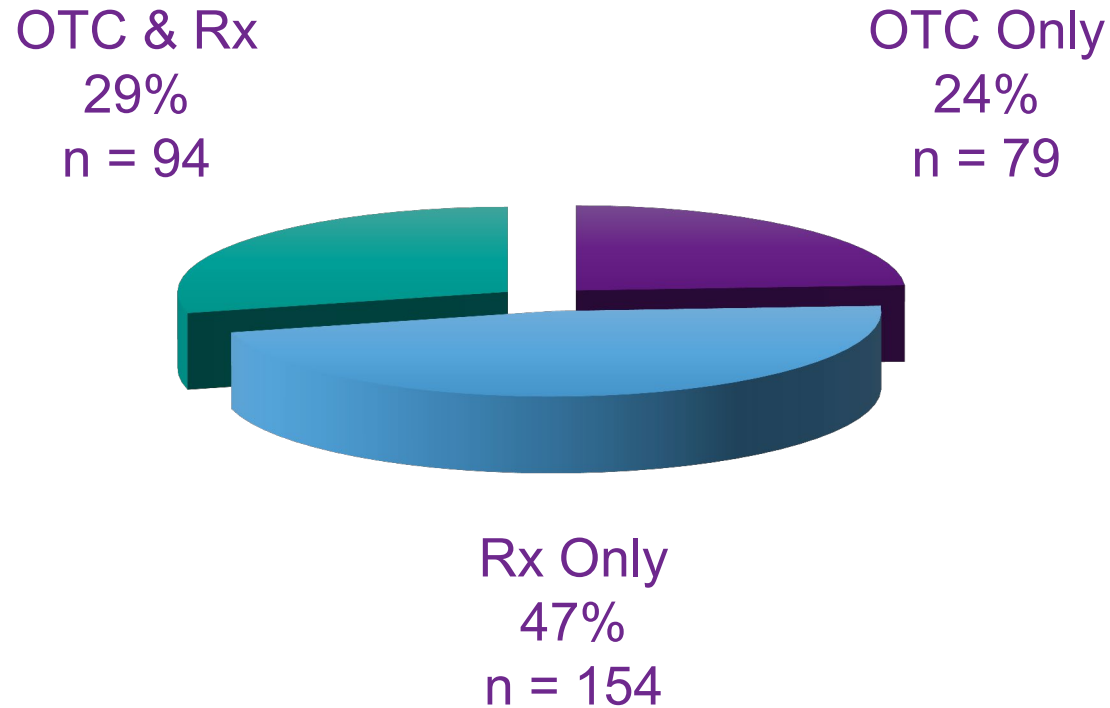
1990-1991

- n=58 inpatients on medical unit of Addiction Research Foundation (June 1990-April 1991)
- 40% female, mean age 35 ± 10 years
- 52% used codeine as primary opioid (Rx or OTC)
- 12% with OTC codeine as primary opioid
- codeine mean daily dose = 554 ± 343 mg, (range 120-1500 mg)

Can J Clin Pharmacol 1998

Survey of Regular Codeine Users

1994



- n=339
- mean age 43 ± 12 ys
- % addicted
 - 33% Rx only users
 - 34% OTC only users
 - 44% OTC/RX users
- most using for pain, but not as effective in addicted
- more psychiatric and other substance use problems in addicted

1997-1999

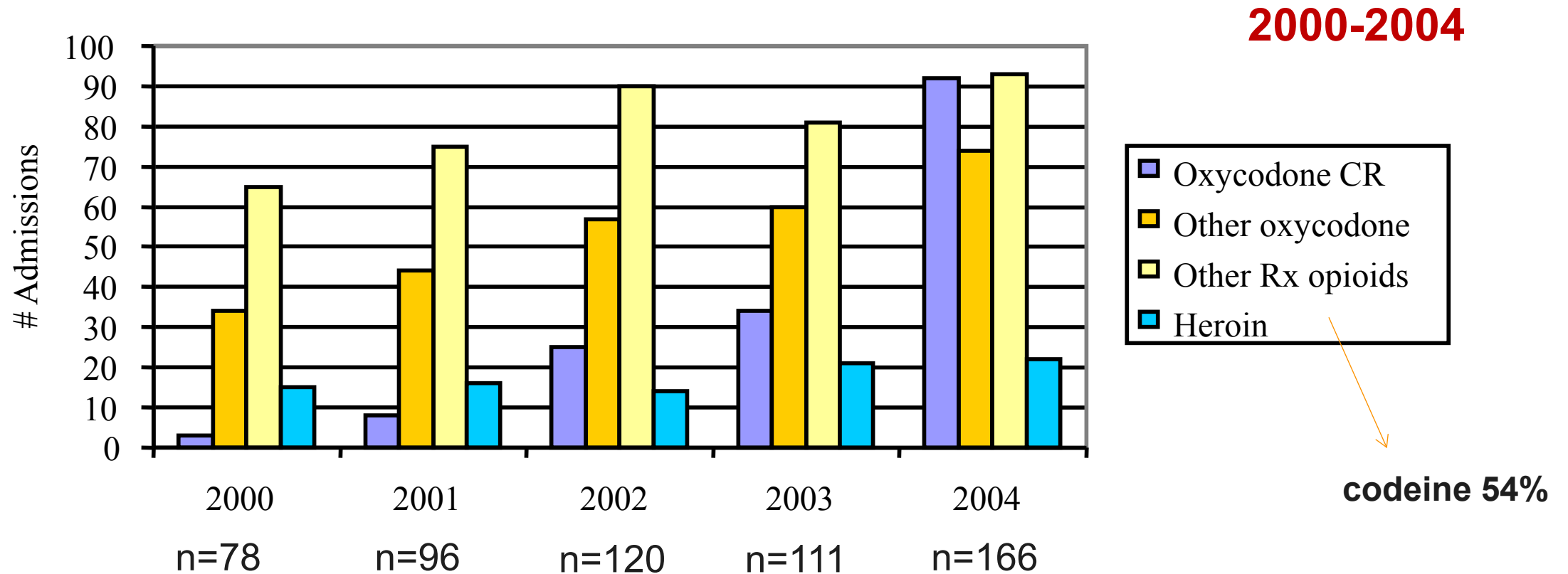
Prescription opioid abuse in patients presenting for methadone maintenance treatment

Bruna Brands^{a,b,*}, Joan Blake^a, Beth Sproule^{a,c,d}, Douglas Gourlay^a, Usoa Busto^{a,b,d}

Prescription opioid use in the 30 days prior to admission^a (1997–1999, $n = 178$, mean age = 34.5 ± 0.7 years, 65% male)

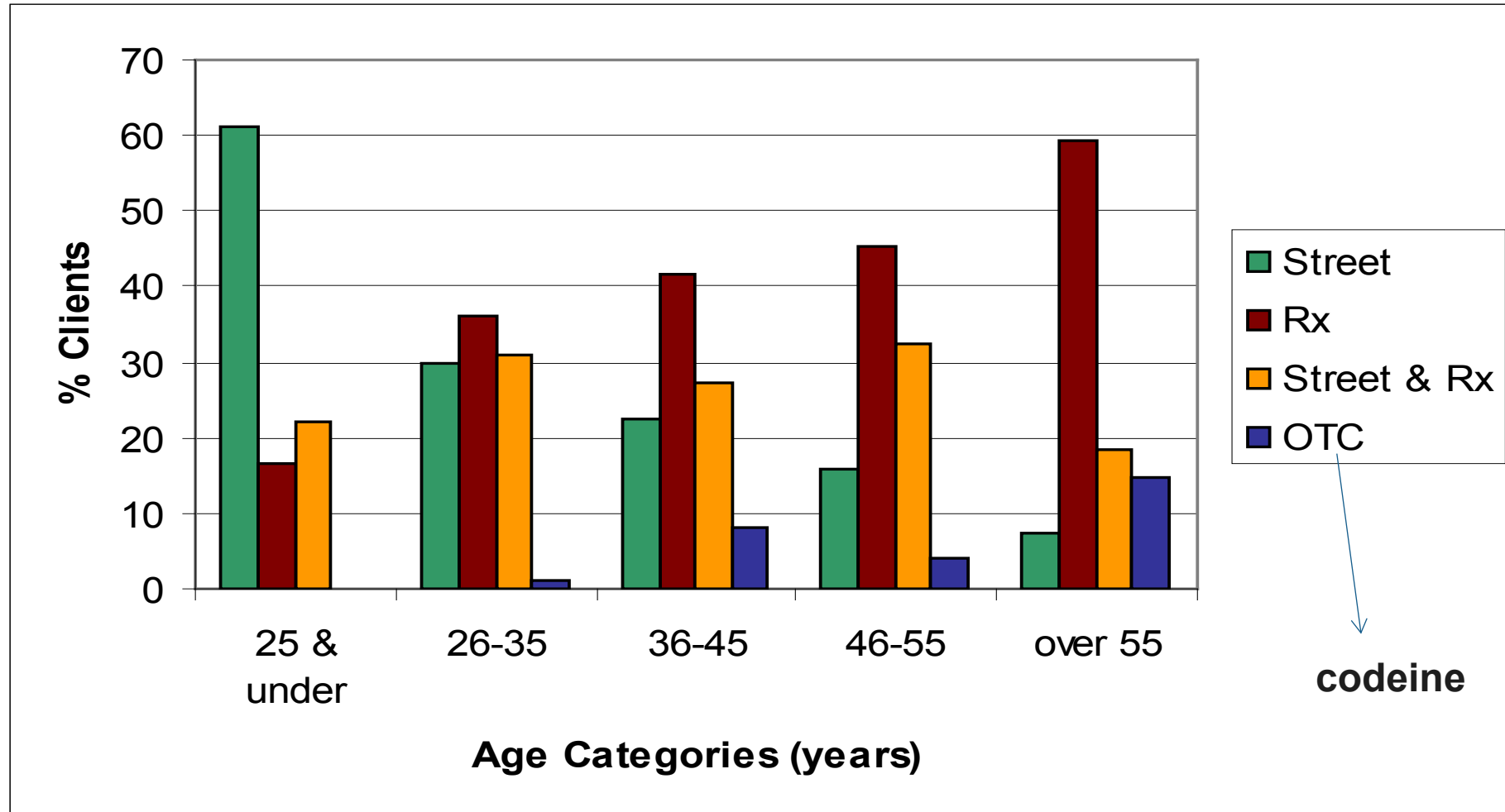
	Rx opioid only	Rx opioid initially + heroin	Heroin initially + Rx opioid
<i>N</i>	43	39	49
Codeine (<i>n</i>)	11	18	12
Daily dose (tablets) ^b	22.7 ± 6.1	17.1 ± 6.1	11.4 ± 3.9
Range	6–60	3–60	1–48
Oxycodone (<i>n</i>)	21	17	17
Daily dose (tablets) ^b	20.8 ± 3.2	20.8 ± 5.6	16.6 ± 4.8
Range	3–65	2–90	2–90
Morphine (<i>n</i>)	6	10	15
Daily dose (mg) ^b	205 ± 47	162 ± 33	279 ± 59
Range	60–400	45–400	10–800
Hydromorphone (<i>n</i>)	3	2	8
Daily dose (mg) ^b	61 ± 31	34	39 ± 9
Range	15–120	20–48	5–90
OTC codeine (<i>n</i>)	14	17	15
Daily dose (tablets) ^b	23.2 ± 6.1	18.2 ± 3.0	21.9 ± 5.5
Range	2–80	4–50	1–60

CAMH Opioid Withdrawal Management Admissions



Sproule BA, et.al., *Changing patterns in opioid addiction: Characterizing users of oxycodone and other opioids. Canadian Family Physician, 2009;55:68-9.e1-5.*

Prescription Opioid Source by Age Group



2000-2004

Survey of Non-Medical Use of Prescription Drugs Program Canada 3rd Quarter 2017

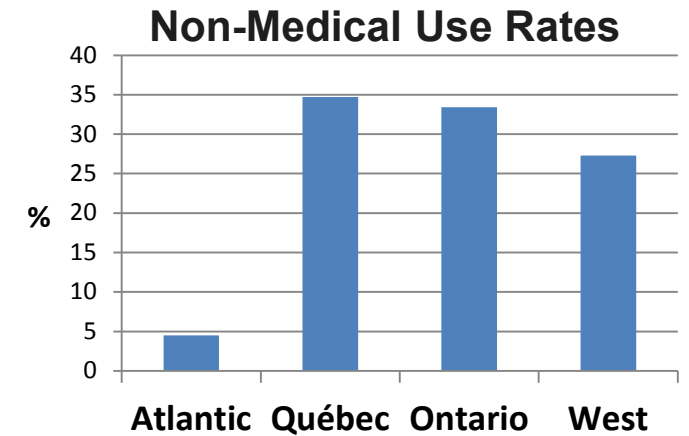
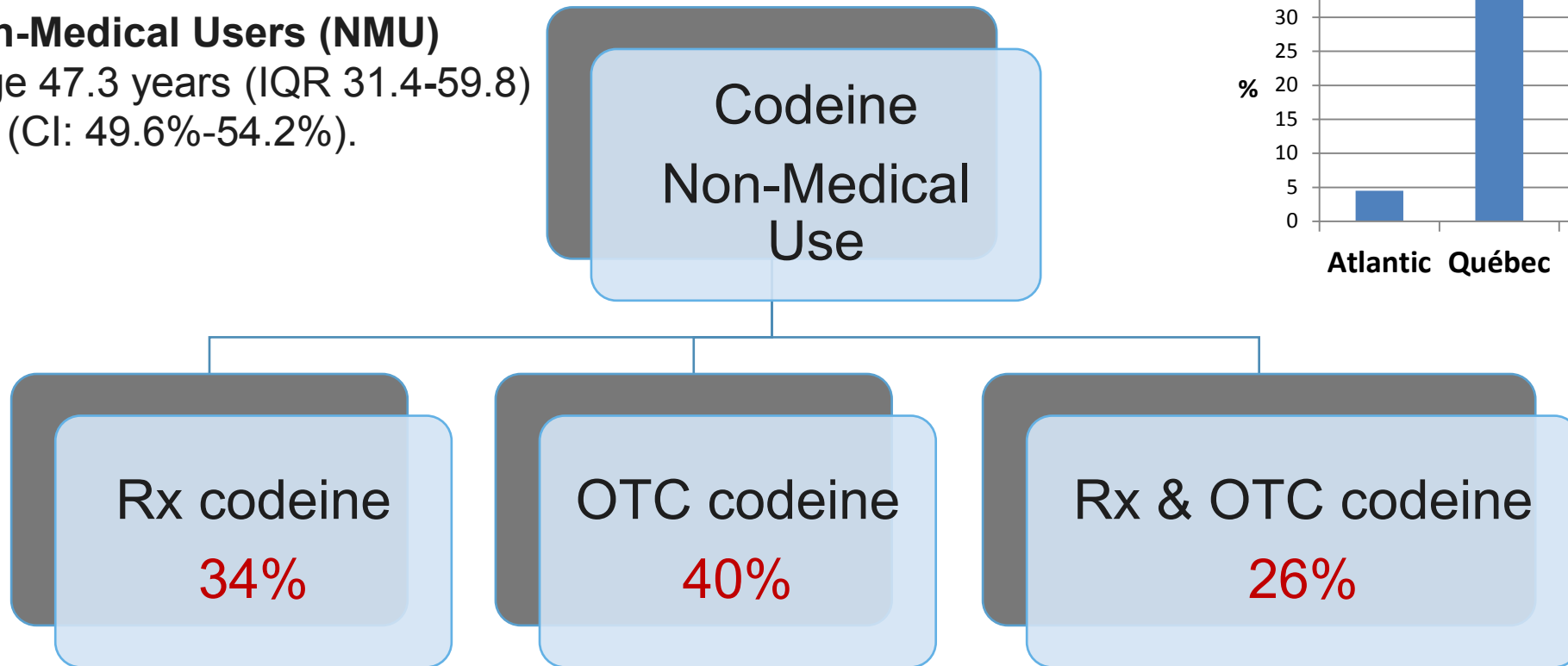
Non-medical use (NMU) = *“use of codeine for any reason other than what was recommended by their doctor/ dentist/ pharmacist/ packet insert or without a doctor's prescription for prescription products”*

	Lifetime Use		Non-Medical Use Among Users
Codeine	69%	→	22%
Morphine	20%	→	7%
Oxycodone	18%	→	14%
Hydromorphone	10%	→	13%
Fentanyl	4%	→	15%

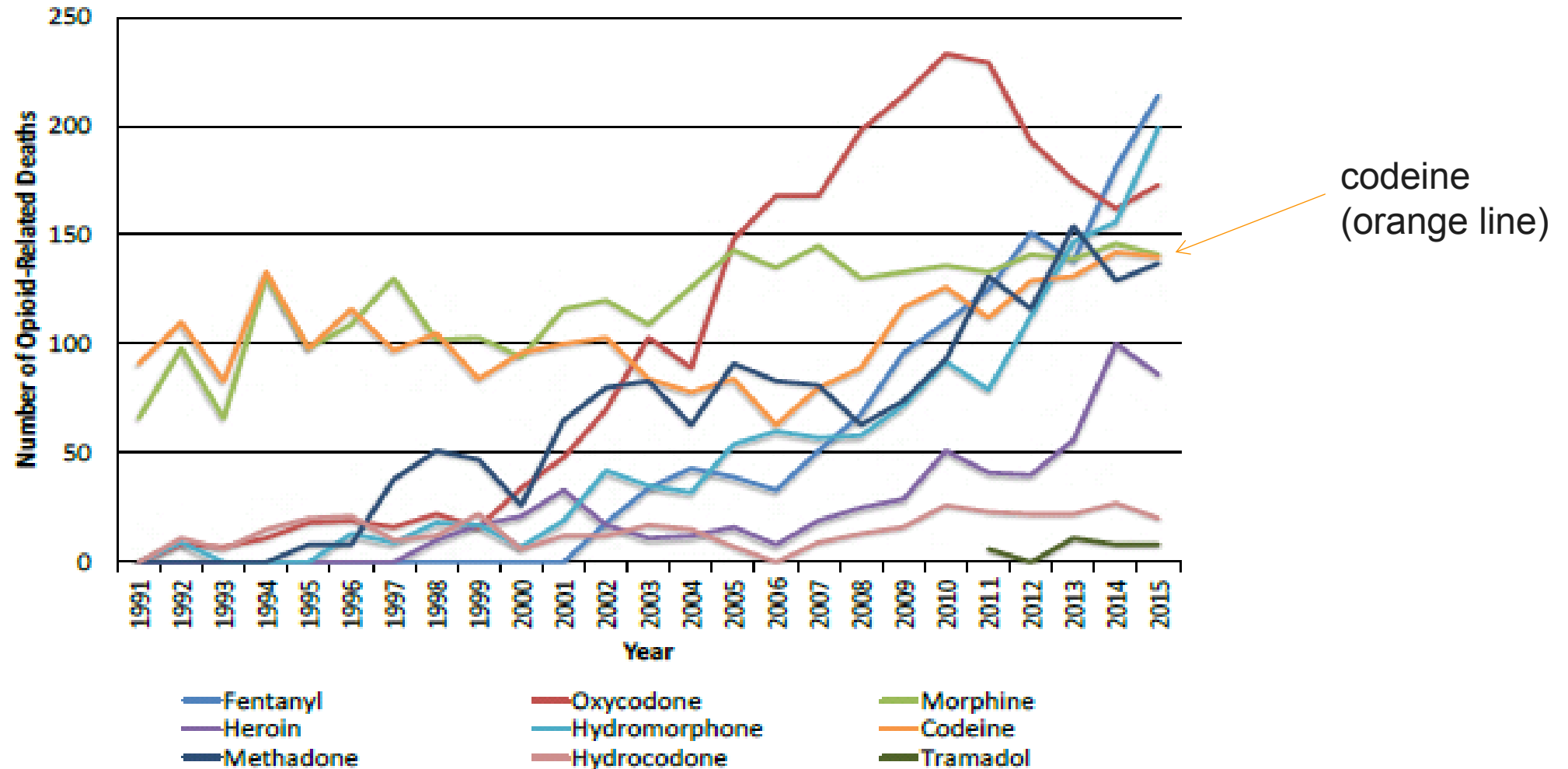
Survey of Non-Medical Use of Prescription Drugs Program Canada 3rd Quarter 2017

Codeine Non-Medical Users (NMU)

- median age 47.3 years (IQR 31.4-59.8)
- 52% male (CI: 49.6%-54.2%).



Opioid-Related Deaths in Ontario (1991-2015)



Overdose Risk in Young Children of Women Prescribed Opioids

Yaron Finkelstein, MD,^{a,b,c,d} Erin M. Macdonald, MSc,^d Alejandro Gonzalez, MSc,^d Marco L.A. Sivilotti, MD, MSc,^{e,f} Muhammad M. Mamdani, PharmD,^{d,g,h} David N. Juurlink, MD,^{d,i,j} Canadian Drug Safety And Effectiveness Research Network (CDSERN)

- Mothers with opioid prescription → substantially increased risk of child opioid overdose
 - odds ratio = 2.41
- Most commonly implicated opioids
 - **codeine (53%)**
 - oxycodone (32%),
 - methadone (15%).

Codeine Safety Initiatives

- Health Canada
 - Consultation on the availability of non-prescription low-dose codeine products (2017)
 - Safety Alert: Recommendation that children and youth not use cough and cold products that contain opioids (2019)
- Canadian Pharmacogenomics Network for Drug Safety (CPNDS) Clinical Recommendations Group
 - Clinical practice guideline: CYP2D6 genotyping for safe and efficacious codeine therapy. (Madadi - J Popul Ther Clin Pharamcol 2013;20(3):e369-e396)
- College of Pharmacists of Manitoba
 - Requires prescription for OTC codeine products – pharmacists can prescribe (2016)
- Saskatchewan College of Pharmacy Professionals
 - Many years ago instituted OTC codeine restrictions (e.g., max 50 tabs, documentation)
 - Proposing banning OTC codeine sales (Dec 2018)



COLLEGE OF PHARMACISTS OF MANITOBA NEWSLETTER

WINTER 2017

Low-dose Codeine in Manitoba: The Case for Pharmacy Care and Patient Safety

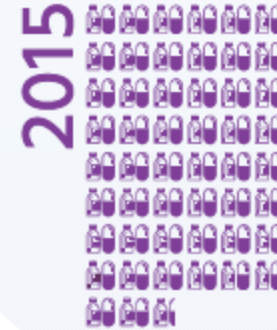
In February 2016, Manitoba became one of only a few provinces in Canada to apply further restrictions on the provision of exempted codeine products (or low-dose codeine products). With implementation of the practice direction on "Exempted Codeine Preparations", pharmacists may only dispense low-dose codeine products that have been prescribed by a practitioner, as defined in the federal *Controlled Drugs and Substances Act (CDSA)* or a pharmacist. This practice direction was developed with the specific goal of supporting pharmacists to reduce the use, misuse and abuse of low-dose codeine products. The success of this initiative has been great and is demonstrated in the adjacent graphic.

The practice direction provides pharmacists with the authority to prescribe low-dose codeine products only for patients they have seen and assessed in person, and have conducted a careful review of the risks and benefits relevant to the patient's care and safety. Pharmacists are also required to advise patients of therapeutic alternatives and provide additional information to help patients make informed decisions. Should a patient's symptoms be more serious in nature, or if treatment with a low-dose codeine product is inadequate, pharmacists must refer the patient to the appropriate health provider.

Pharmacists must enter all low-dose codeine prescriptions into the Drug Program Information Network (DPIN), review the patient's profile for previous low-dose codeine products and other narcotic or controlled drug use, and identify potential drug interactions. When low-dose codeine prescriptions are entered into DPIN, Manitoba patients receive added health benefits by improving medication safety and preventing the misuse of these drugs.

With the introduction of the practice direction on Exempted Codeine Preparations, Manitoba's pharmacists have proven themselves to be valuable contributors to the healthcare system's efforts to reduce the harms of opioids. Health Canada has since recognized the potential for a national strategy to mitigate the harms of low-dose codeine (cont'd on page five).

Manitoba has seen a 90 per cent decrease in the number of units of low-dose codeine products purchased by Manitoba pharmacies since the introduction of the *Exempted Codeine Preparations* practice direction in 2015 (Quintiles IMS Canadian Drug Store and Hospital Purchases Audit (CDH)).



**Choosing
Wisely
Canada**



CANADIAN
PHARMACISTS
ASSOCIATION

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DU CANADA



Pharmacist | Canadian Pharmacists Association

Don't recommend the use of over-the-counter medications containing codeine for the management of acute or chronic pain. Counsel patients against their use and recommend safe alternatives.

<https://choosingwiselycanada.org/campaign/opioid-wisely/>

Conclusions

Codeine:

- is widely available in Canada
- is associated with non-medical use (by a large proportion of users)
- users are seeking treatment for opioid use disorder (for both OTC and Rx products)
- use is implicated in overdose deaths

Just because it is a ‘weak’ opioid, does not make it safer.

Thank You

camh