Pharmaceutical Misuse and its Challenges: Opioid Use in Ontario

Ontario Harm Reduction Conference

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ODPRN

ONTARIO DRUG POLICY RESEARCH NETWORK

Objectives

- **To review the prescription opioid crisis**
- To understand the extent of opioid-related harm in Ontario
- To review some potential strategies to reduce opioid-related harm

Opioid Prescribing and Safety

- Recent guidelines have suggested that the risks of long-term, high-dose opioid use for chronic non-cancer pain often exceed their benefits.
- **Marketing:**
  - No intrinsic upper dose threshold
  - OxyContin was initially marketed as being less likely to be abused due to its long-acting formulation.
- **However:**
  - OxyContin can be crushed, and inhaled or injected
  - Increasing trends in opioid-related mortality suggest that opioid use at high doses or in combination with other drugs is dangerous
- Many clinical guidelines now suggest **200 mg morphine (or equivalent)** as a ‘watchful’ dose.

Opioids : A Public Health Crisis

- Safety issues associated with opioids include:
  - Abuse
  - Addiction
  - Diversion
  - Opioid-related side effects including death

- There were over 20,000 prescription drug overdose deaths in the USA in 2008.
  - Opioids were involved in 73.8% (14,800) of these deaths
  - This has more than tripled since 1999

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How are Opioids being Prescribed in Ontario?

- How has opioid prescribing changed in Ontario over the past 20 years?
- Has opioid-related mortality increased over this time?
- How has dosing of opioids changed over time?
- Are higher doses associated with risk of mortality?

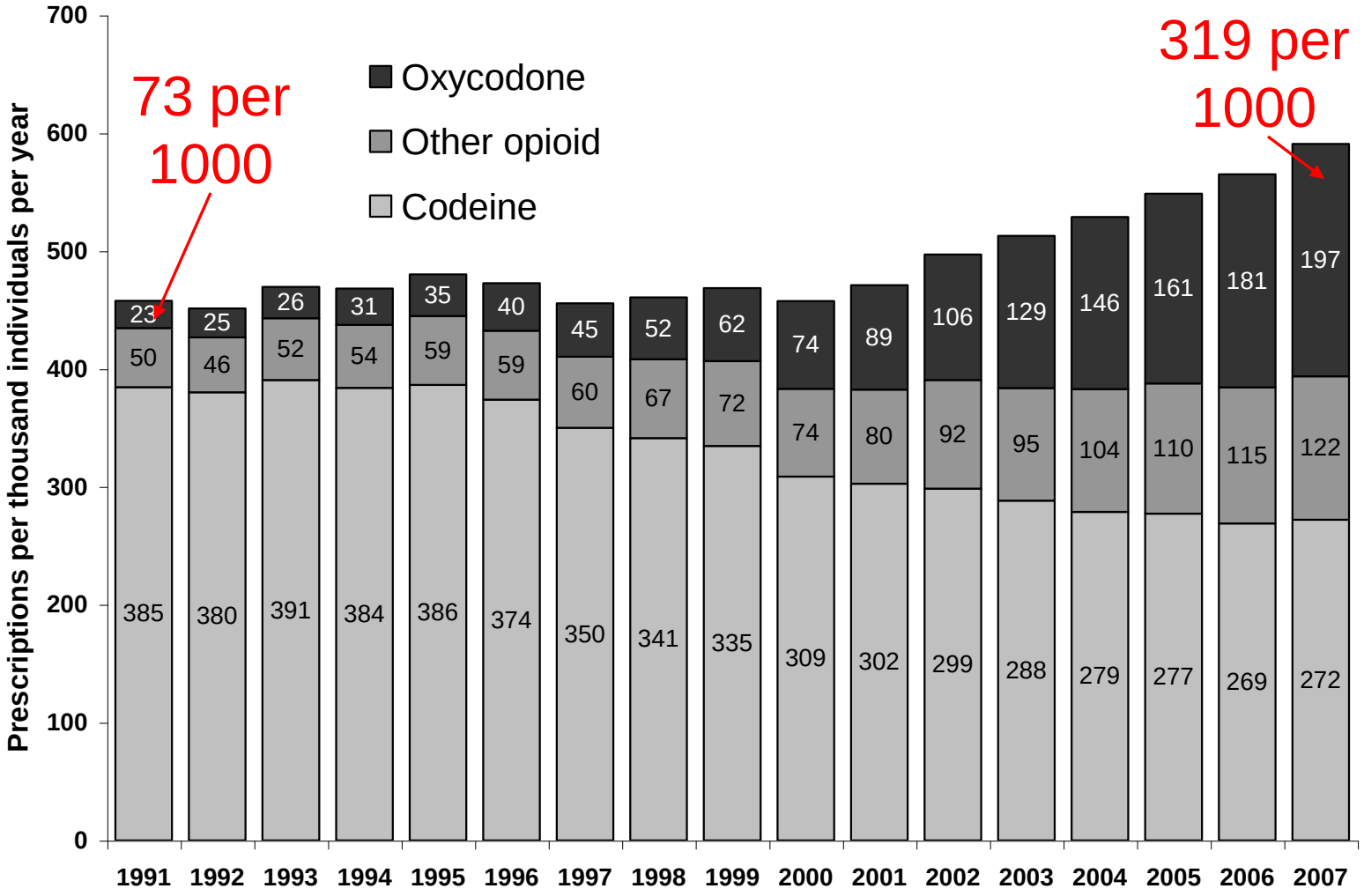
Methods: Data

- Prescribing data obtained from IMS Canada from 1991 to 2007 for all of Ontario
- ICES Administrative Datasets used to conduct linked analyses among ODB-eligible Ontarians
- Manual file review at Coroner's office for deaths between 1991 and 2006
  - All deaths flagged as involving drugs, alcohol or both were reviewed

Methods: Deaths

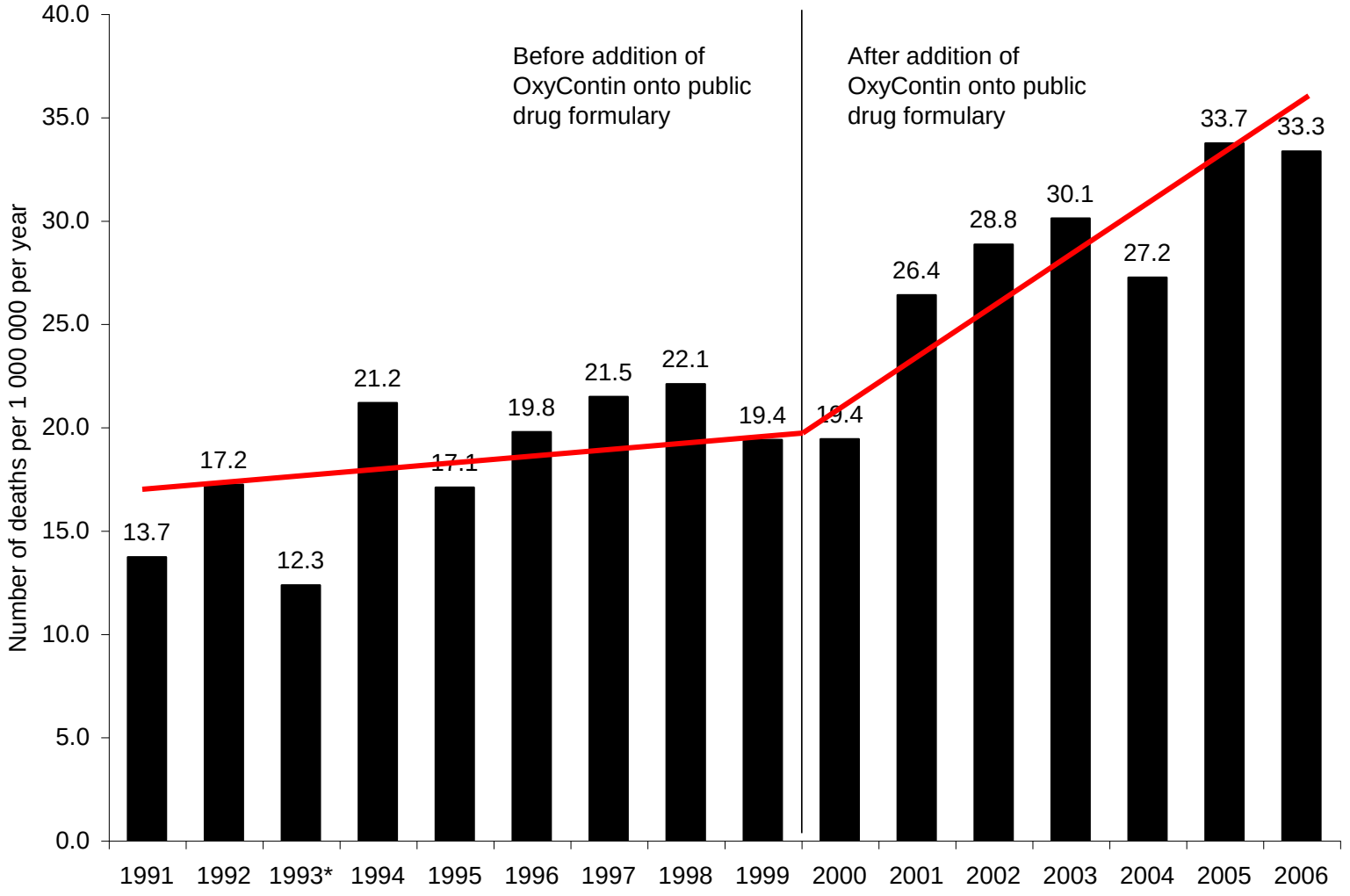
- Deaths were deemed to be related to opioids based on coroner's investigation
  - Post-mortem toxicological analysis revealed an opioid at high enough level to cause death
  - Post-mortem toxicological analysis revealed a combination of drugs including opioids that resulted in death
- Deaths were deemed to be unrelated to opioids if:
  - Opioid at therapeutic levels and another drug at levels high enough to cause death (e.g., tricyclic antidepressant)
- Single physician abstractor
  - Double abstraction of 20 charts x 2 → no significant differences
  - Difficult cases flagged → agreements resolved by consensus
- Overall 4,119 opioid-related deaths abstracted

4-fold increase in prescribing of opioids



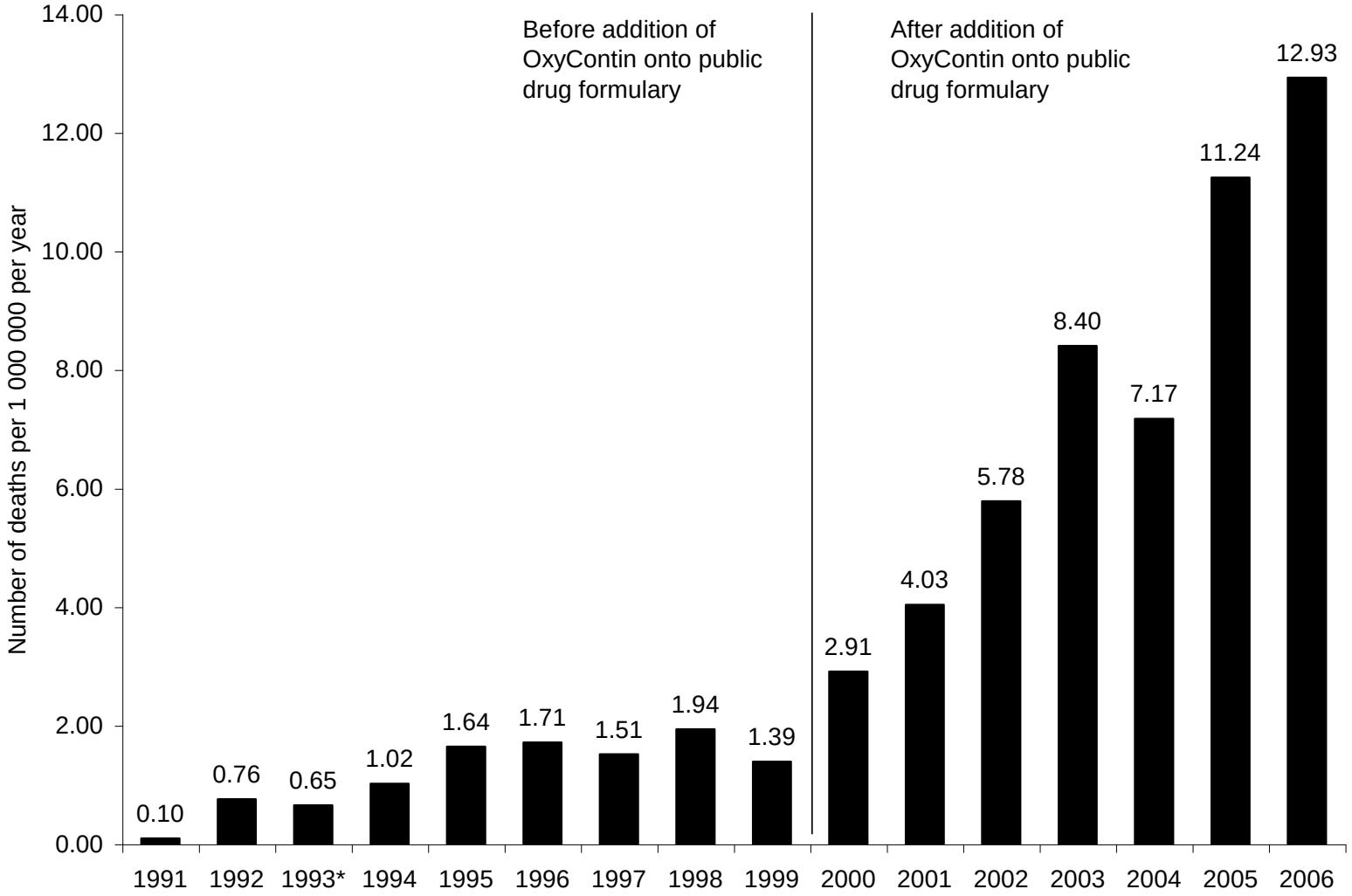
Dhalla I et al, Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone. CMAJ. 2009. 181(12):891-6.

2-fold increase in opioid-related deaths



Dhalla I et al, CMAJ, 2009

9-fold increase in oxycodone-related deaths



Dhalla I et al, CMAJ, 2009

Details of 423 Ontario deaths in 2006

Manner of death	
Accident	285 (67%)
Suicide	65 (15%)
Undetermined	71 (17%)
Other or missing	2 (0%)
Opioids associated with death	
Single opioid	297
Oxycodone	119 (40%)
Morphine or heroin (or both)	66 (22%)
Methadone	55 (19%)
Fentanyl	14 (5%)
Codeine	10 (3%)
Other	33 (11%)

92% of deaths involve a non-opioid central nervous system depressant

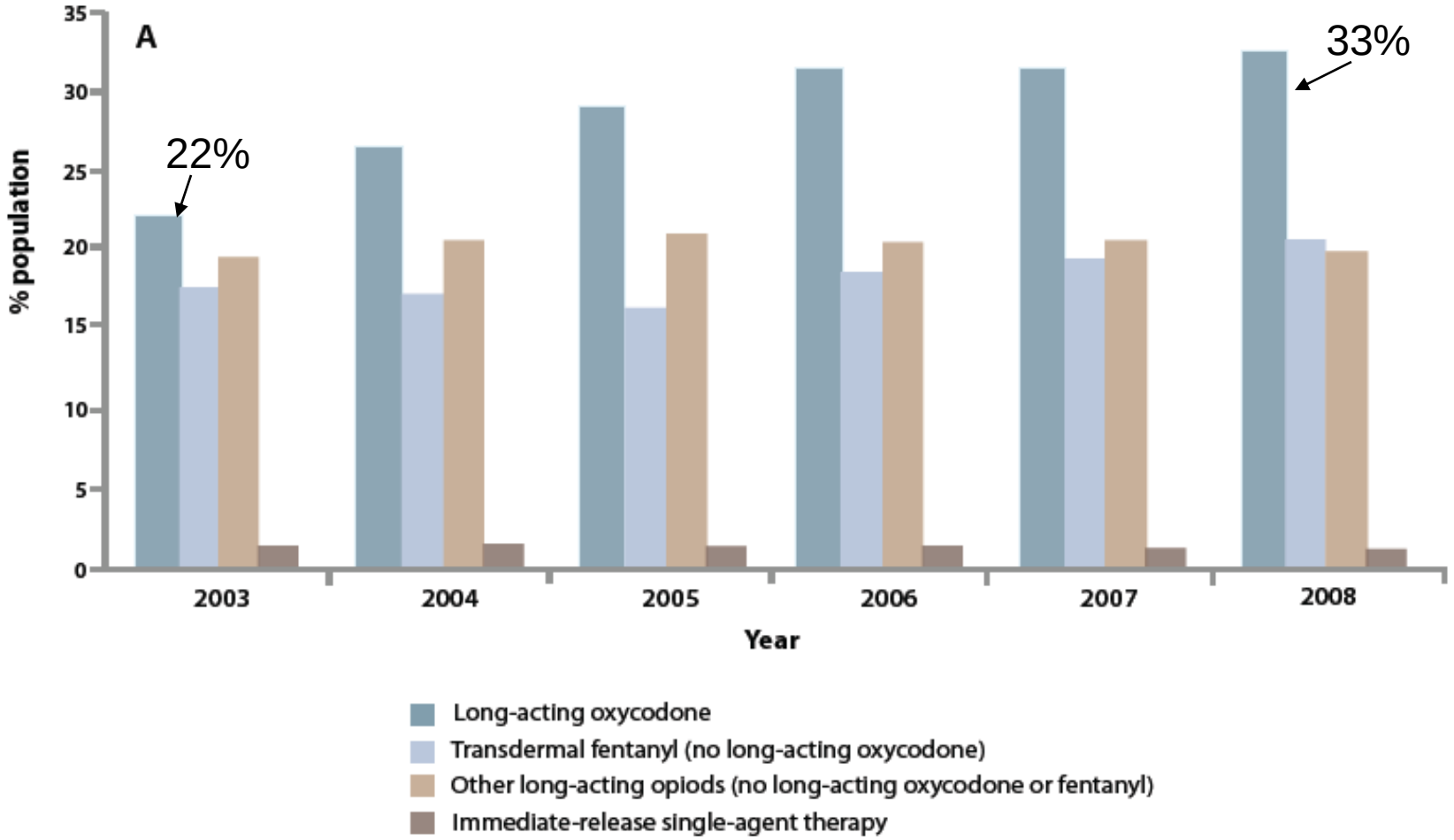
- 60% involved benzodiazepines
- 44% involved alcohol
- Also, antipsychotics, antihistamines, anticholinergics, antidepressants, etc.

High Dose Prescribing is Common

- In 2008, among ODB eligible Ontarians aged 15 to 64:
  - 180 974 (26%) of 686 307 eligible individuals were dispensed an opioid
  - OxyContin accounted for nearly one-fifth (18.8%) of all opioid prescriptions dispensed through the ODB
  - 18 096 received OxyContin through the ODB
    - The mean daily dose was 223 mg ME daily
    - 5903 (33%) received more than 200 mg of morphine equivalent per day

Gomes T, Juurlink DN, Dhalla IA, Mailis-Gagnon A, Paterson JM, Mamdani MM. Trends in Opioid Use and Dosing in the Socioeconomically Disadvantaged. Open Medicine. 2011;5(1):E13-E22.

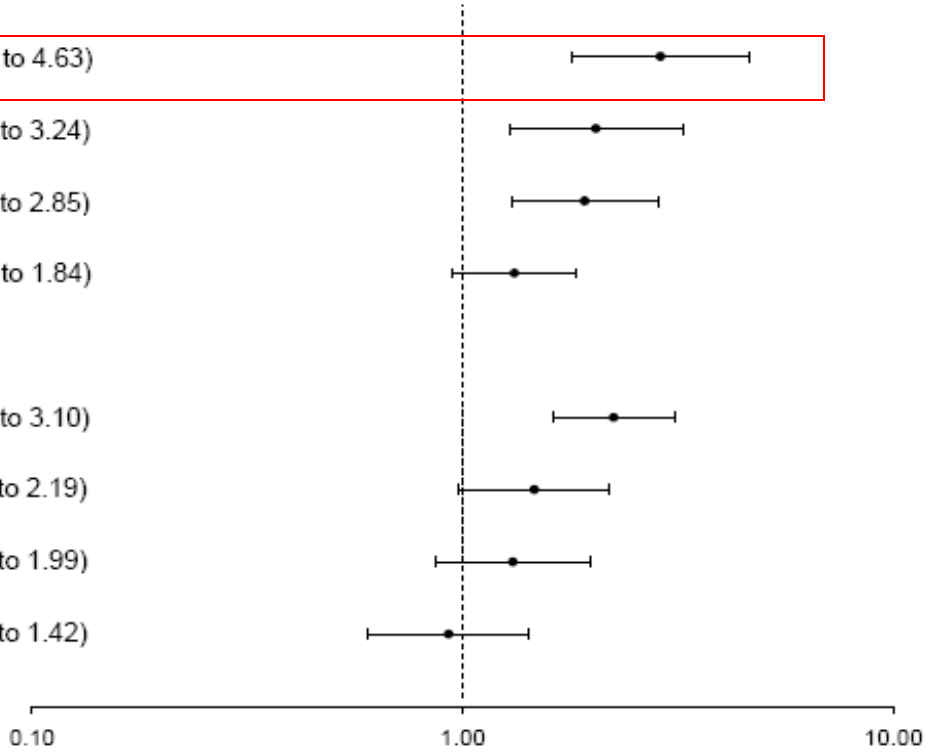
Proportion of People prescribed >200mg ME daily



Gomes T et al Open Medicine 2011

High-dose prescribing is associated with a 3-fold increase risk of opioid-related death

	Cases n/N	Controls n/N	Adjusted Odds Ratio* (95% CI†)
Primary Analysis: Overlapping Opioid Prescriptions (Reference: 1 to 19 mg morphine equivalents)			
≥200mg	116/498	223/1714	2.88 (1.79 to 4.63)
100 to 199 mg	82/498	181/1714	2.04 (1.28 to 3.24)
50 to 99 mg	97/498	273/1714	1.92 (1.30 to 2.85)
20 to 49 mg	118/498	514/1714	1.32 (0.94 to 1.84)
Secondary Analysis: 120 Day Exposure Window (Reference: 1 to 19 mg morphine equivalents)			
≥200mg	557/781	1319/2804	2.24 (1.62 to 3.10)
100 to 199 mg	64/781	303/2804	1.47 (0.98 to 2.19)
50 to 99 mg	52/781	300/2804	1.31 (0.86 to 1.99)
20 to 49 mg	41/781	366/2804	0.93 (0.60 to 1.42)



Gomes T, Mamdani MM, Dhalla IA, Paterson JM, Juurlink DN. Opioid dose and drug-related mortality in patients with nonmalignant pain. Arch Int Med. 2011. 171(7):686-691.

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Strategies to Reduce Opioid-related Harm

- Education (patients, physicians, pharmacists, etc.)
- Better treatment for chronic pain and addiction
- Electronic databases accessible at the point-of-care
- Marketing restrictions

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Educational interventions?

What will be the impact of educational interventions?

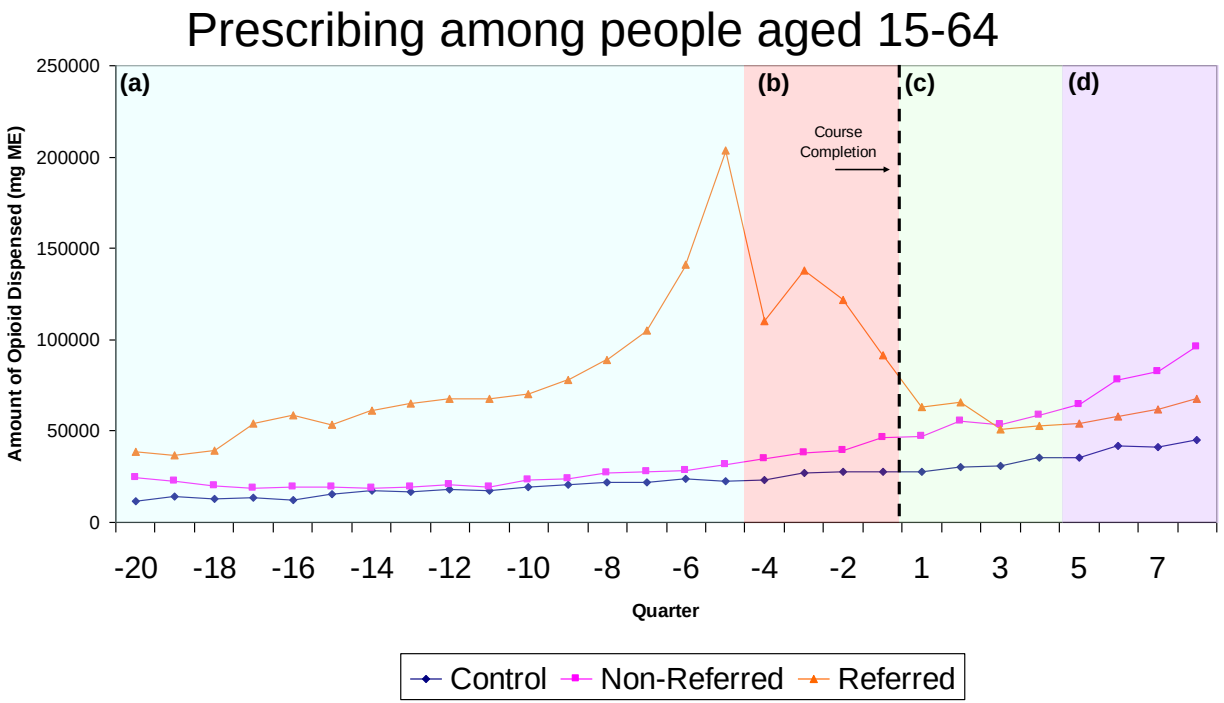
- What was the effect of a course-based intervention on physicians' opioid prescribing

Where should they be targeted?

- How does opioid prescribing and related mortality vary geographically in Ontario?

Would educating physicians reduce opioid-related harm?

- Collaboration with the CPSO to evaluate the effectiveness of a CME course offered to Physicians focused on prescribing of drugs for chronic non-cancer pain



THE COLLEGE OF PHYSICIANS AND SURGEONS OF ONTARIO

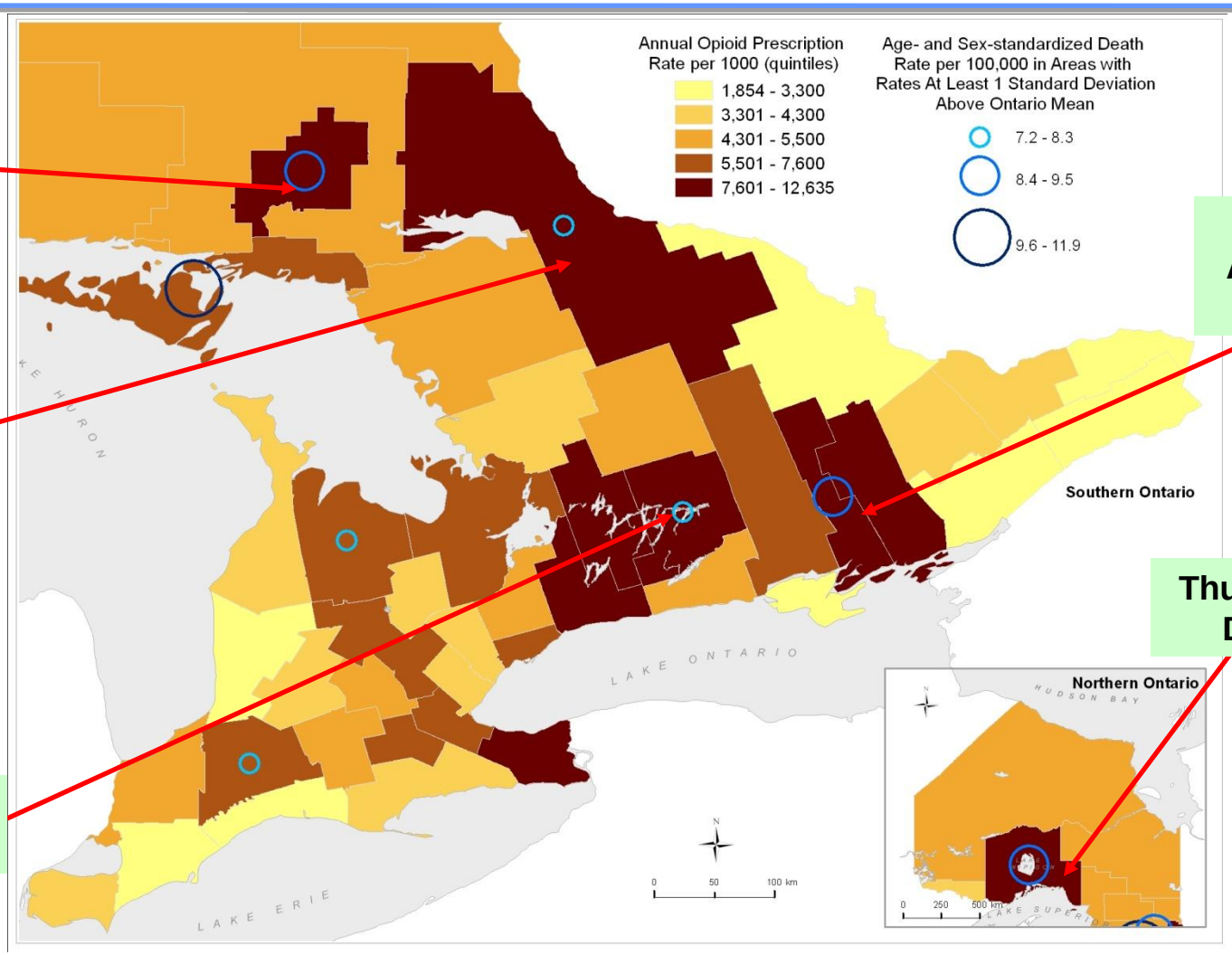
The Physicians' Prescribing Skills Course

A Focus on the Prescribing of Addictive and Psychoactive Drugs

Purpose:

This two day course has been created to assist physicians in acquiring knowledge and learning new skills in the field of pain management, especially in the area of chronic non-malignant pain.

Would targeted interventions work?



Sudbury Regional Munic.

Nipissing District

Peterborough County

Lennox & Addington County

Thunder Bay District

Gomes T, Juurlink DN, Moineddin R, Gozdyra P, Dhalla IA, Paterson JM, Mamdani MM. Geographic Variation in Opioid Prescribing and Opioid-related Mortality in Ontario. Healthcare Quarterly. 2011;14(1):22-24.

Should we Target Physicians?

Table 1. Physician characteristics across physician prescribing quintiles: *Male sex (P=.003), older age (P<.001), and a greater number of years in practice (P<.001) were associated with greater opioid prescribing.*

CHARACTERISTIC	LOWEST VOLUME QUINTILE (N = 1977)	SECOND-LOWEST VOLUME QUINTILE (N = 1978)	MIDDLE QUINTILE (N = 1980)	SECOND-HIGHEST VOLUME QUINTILE (N = 1979)	HIGHEST VOLUME QUINTILE (N = 1978)
Male sex, %	58	65	66	68	71
Mean age, y	48.4	47.0	47.1	49.0	50.5
Mean no. of years in practice	22.8	21.4	21.5	23.4	24.9
Mean no. of patients eligible for public drug plan coverage	343	374	404	433	424

Physicians prescribing high numbers of prescriptions tend to be male, older and have been practicing longer than those prescribing lower amounts of opioids

Dhalla I, Gomes T, Juurlink DN, Mamdani M. Clustering of opioid prescribing and opioid-related mortality among family physicians in Ontario. Can Fam Phys. 2011. 57(3):e92-6.

Educational Interventions?

- One-time education (even if intensive) is likely to have little impact
  - Intervention by Colleges may be more impactful

- Given geographic variation, targeting of education (patients, prescribers and pharmacists) in specific regions should be considered

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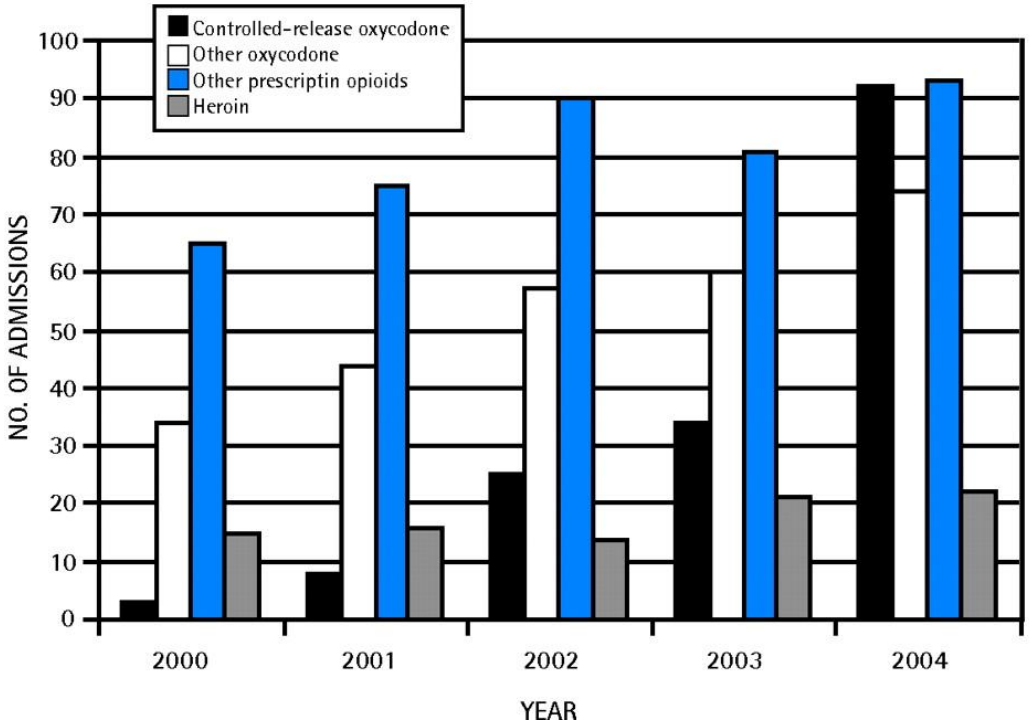
Methadone and Opioid Addiction

Figure 1. Admissions to the Medical Withdrawal Management Service for opioid detoxification, 2000–2004: *The number of admissions increased over the 5 years (2000, n=78; 2001, n=96; 2002, n=120; 2003, n=111; and 2004, n=166). Of the 571 admissions, 295 involved 1 opioid, 204 involved 2 opioids, 68 involved 3 opioids, and 4 involved 4 opioids.*



Sproule B et al. Changing patterns in opioid addiction: characterizing users of oxycodone and other opioids. Can Fam Phys. 2009. 55(1):68-69

Methadone and Opioid Addiction

- 18,759 ODB eligible people aged 15 to 64 were treated with methadone in Ontario (2003-2010)
- 18.4% received non-methadone opioids with ≥7 day duration (after allowing for 30 day titration period)
- On average, they received **12** non-methadone opioid prescriptions each year
- Almost **half** of these prescription originated from non-MMT prescribers and pharmacies

Kurdyak P, Gomes T, Yao Z, Mamdani MM, Hellings C, Fischer B, Rehm J, Bayoumi AM, Juurlink DN. Use of Other Opioids During Methadone Therapy: A Population-Based Study. Addiction. 2011. [Epub]

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- **Electronic databases accessible at the point-of-care**
- **Marketing restrictions**

Other Strategies

- **Electronic databases accessible at the point-of-care**
  - Current disconnect between prescribers and pharmacies regarding patient prescribing history
  - Access to real-time data could allow for more rapid identification of double-doctoring, potential diversion and drug-seeking behaviour
- **Marketing/Funding restrictions**
  - Maximum daily dose
  - Maximum quantity of medication
  - Removal of high dose formulations that are particularly dangerous
  - Funding of patients through special programs (e.g. Exceptional Access Program)

Questions?

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