CSAM-SCAM Fundamentals

# Prescription Opioid Addiction

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# Conflict of interest statement

- I received funds from Rickett Benkeiser to present on Suboxone (buprenorphine)

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# The Opioid Crisis

- Very serious (overdose deaths = deaths from MVA)
- Iatrogenic:  MD prescriptions are the major source of opioids, directly or through diversion

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# 4x increase in prescribing of strong opioids

73 per 1000

319 per 1000

Prescriptions per thousand individuals per year

| Year | Codeine | Other opioid | Oxycodone |
| --- | --- | --- | --- |
| 1991 | 385 | 50 | 23 |
| 1992 | 380 | 46 | 25 |
| 1993 | 391 | 52 | 26 |
| 1994 | 384 | 54 | 31 |
| 1995 | 386 | 59 | 35 |
| 1996 | 374 | 59 | 40 |
| 1997 | 350 | 60 | 45 |
| 1998 | 341 | 67 | 52 |
| 1999 | 335 | 72 | 62 |
| 2000 | 309 | 74 | 74 |
| 2001 | 302 | 80 | 89 |
| 2002 | 299 | 92 | 106 |
| 2003 | 288 | 95 | 129 |
| 2004 | 279 | 104 | 146 |
| 2005 | 277 | 110 | 161 |
| 2006 | 269 | 115 | 181 |
| 2007 | 272 | 122 | 197 |

Dhalla et al CMAJ 2009

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# 9x increase in oxycodone-related deaths

Before addition of OxyContin onto public drug formulary

After addition of OxyContin onto public drug formulary

| Year | Number of deaths per 1 000 000 per year |
|---|---|
| 1991 | 0.10 |
| 1992 | 0.76 |
| 1993* | 0.65 |
| 1994 | 1.02 |
| 1995 | 1.64 |
| 1996 | 1.71 |
| 1997 | 1.51 |
| 1998 | 1.94 |
| 1999 | 1.39 |
| 2000 | 2.91 |
| 2001 | 4.03 |
| 2002 | 5.78 |
| 2003 | 8.40 |
| 2004 | 7.17 |
| 2005 | 11.24 |
| 2006 | 12.93 |

Dhalla 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%) |

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# Most deaths occur in people who were *prescribed* opioids

- 56% dispensed an opioid in the 4 weeks prior to death
- 82% dispensed an opioid in the year prior to death
- Median number of opioid prescriptions in year prior to death
  → ***10 prescriptions***

*Important limitation: data only available for 1/3 of population (those eligible for public coverage)*

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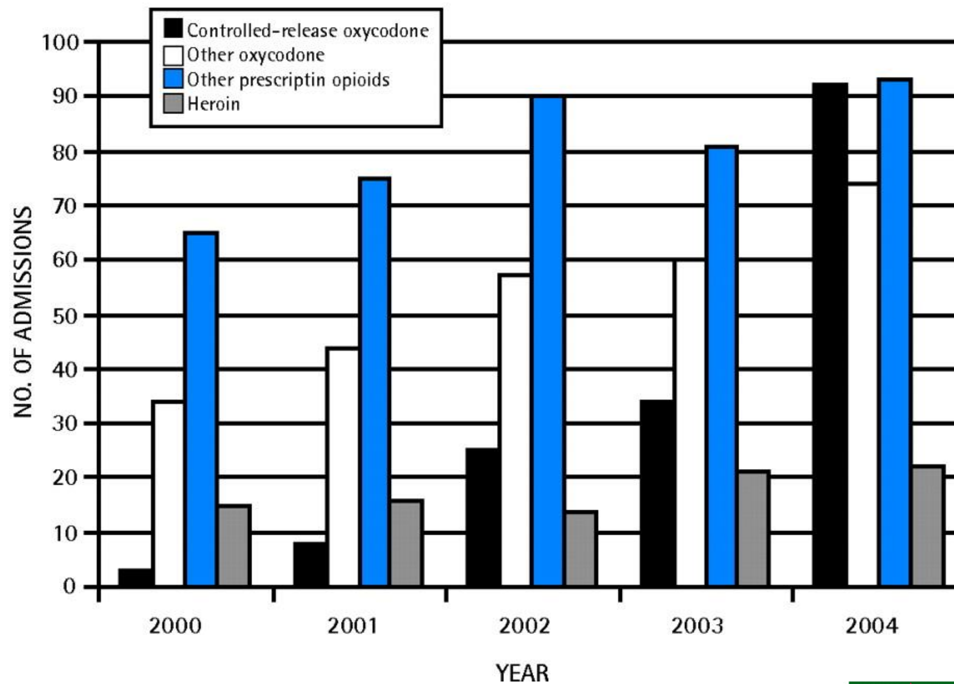
# Case-control study: opioid dose & risk of OD

| Dose (mg morphine equivalent/day) | Odds Ratio |
|---|---|
| > 200 mg | 2.9 |
| 100-199 mg | 2.0 |
| 50-99 mg | 1.9 |
| 20-49 mg | 1.3 |

# Rise in prescription 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 Can Fam Phys 2009

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# Number of patients on opioids causing concerns

Wenghofer 2010

| | |
|---|---|
| **Number of Patients Causing Concerns for FP** | **Percent of FPs (%)** |
| None | 15.1 |
| 1 – 3 | 47.9 |
| 4 – 6 | 23.4 |
| 7 – 9 | 6.4 |
| 10 or more | 7.2 |

# FPs very concerned about…

| Concerns | Very concerned (%) |
|---|---|
| Running out early, demanding fit-in appointments, lost scripts | 44.8 |
| Lack of specialized pain clinics | 42.2 |
| Getting patient addicted (n=641) | 38.4 |
| Patients getting high doses | 28.0 |
| Lack of addiction treatment resources | 26.4 |
| Disagreements with patients about opioids | 22.0 |

# ADDICTION: KEY CONCEPTS

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# Addiction: Clinical Features

- Repeated drug reinforcement -> patient has trouble controlling use
- Opioids & all drugs of abuse acts on 'reward centre' – medial forebrain bundle
- Tolerance and withdrawal develop quickly

# Addiction (2): 4 Cs of Addiction

- **C**ompulsive drug use
- **C**raving
- **C**onsequences: Use despite harm
- Inability to **C**ut down

# Tolerance

- Neurobehavioural adaptation
- Tolerance to analgesic effects develops slowly
- Rapid tolerance to psychoactive effects
- Highly tolerant patients can function on massive amounts of opioids
- Tolerance disappears within days

# Withdrawal

- Usually mild, transient in patients taking moderate doses for analgesia
- More severe in patients taking higher doses for psychoactive effects
- No serious medical complications, except in pregnant women and neonates

# Withdrawal: Time Course

- Begins 6-24 hours after last use
- Peaks at 2-3 days
- Physical symptoms largely resolve by 5-10 days
- In severe withdrawal, insomnia and dysphoria may last weeks-months

# Withdrawal: Symptoms

**Psychological:**

- Intense anxiety
- Craving for opiates
- Restlessness, insomnia, fatigue

**Physical:**

- Myalgias
- Nausea, vomiting, cramps, diarrhea, sweating
- Signs (not usually seen): Agitation, dilated pupils, chills, goosebumps

# Withdrawal-mediated Pain

- Pain magnified as opioid wears off
- Pain "all over" (myalgia)
- Dysphoria
- Symptoms quickly relieved with opioids

# Prescription Opioid Addiction

**Most pain patients don't become addicted:**

- Tolerance to analgesic effects develops slowly
- Patients often remain on same dose for years
- Most do not experience euphoria

# PRESCRIPTION OPIOID ADDICTION: PREVENTION

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# Prevalence of Addiction to Prescription Opioids

- Recent meta-analysis: 3% in pain patients
- 14% show aberrant drug behaviours
- Usually associated current/past history of substance dependence

Fishbain 2008

# Prevalence of Opioid Abuse and Addiction

- Rates of prescription opioid abuse and addiction are increasing rapidly
- Based on data from surveys of general population, high school students, drug overdoses, methadone programs

# Major cause of the increase…

- **Prescribing higher doses of opioids to greater numbers of high risk people**
- High risk patients more likely to experience euphoria or anxiety relief with opioids
  - This may lead to tolerance, dose escalation, withdrawal and addiction
- Euphoric and anxiolytic effects of opioids are dose related

# Cause of crisis (2)

- Addiction risk of high opioid doses not counterbalanced by better pain relief:
  - Other complications of opioids are also dose related (overdose, sleep apnea etc)
  - The effectiveness of high opioid doses has not been demonstrated
  - Patients receiving high doses have **milder** biomedical pain conditions, are younger and have greater psychiatric comorbidity

# Prevention

- Don't prescribe opioids to high risk patients (younger, male, personal or strong family hx of addiction, active psychiatric disorder) unless:
  - Has condition for which opioids shown to improve functional status (generally NOT low back pain or fibromyalgia)
  - Failed trial of first line medications and non-medical approaches

# Prevention (2)

- If opioids are used, titrate slowly with codeine/tramadol first
- Avoid hydromorphone
- Keep maintenance dose << 200 mg MED
- Taper if dose above this
- Careful monitoring for aberrant behaviour and UDS

# When to taper

- Severe pain and poor function despite high dose
- Complication:  Depression, fatigue, sleep apnea, sexual dysfunction, falls
- High dose may no longer be necessary
- Addiction – discussed later

# How to taper

- Explain that tapering improves pain, mood and function
  - During taper, ask about positive effects not just withdrawal
- Use scheduled doses
  - Frequent dispensing with no early refills
- Taper by no more than 10% of dose q 2 weeks
- Negotiate with patient re rate of taper
- Endpoint not necessarily abstinence
- Also taper benzodiazepines

# PRESCRIPTION OPIOID ADDICTION: DIAGNOSIS

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# Addiction:  Typical history

- Current, past or family history of addiction
- On a high dose for underlying pain condition
- Strong resistance to changing opioid
- Reports severe pain, little evidence of benefit from opioid
- Withdrawal symptoms
- Depression, irritability, anxiety
- Social isolation, deteriorating functioning

# Laboratory Findings

- Elevated AST, ALT (viral or alcoholic hepatitis)
- Gamma GT, MCV (alcohol)
- Hepatitis B, C

# Other Sources of Information

- **Often critical**
- **Addiction is longitudinal diagnosis**
  - Other physicians
  - Spouse, family

# Behaviours

- Binge use ("unsanctioned dose escalations")
- Alters route of entry
  - bite, crush, snort, inject
- Accesses opioids from other sources
  - Other doctors, the 'street'

# Why do they act like this?

- Overcome tolerance
- Achieve psychoactive effect
- Avoid withdrawal

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# Limitations of behaviour monitoring

- Patients will hide these behaviours
- These behaviours not always seen if physician prescribes higher doses
  - Some patients take oral opioids without running out early yet experience psychoactive effects, withdrawal, dysphoria and decreased function

# Urine Drug Screening

- Pain patients have high prevalence of unauthorized drug use on UDS
- Patients usually don't object if it's routine
- Used for detection of:
  - Diversion and non-compliance
  - Double-doctoring
  - Abuse of other drugs eg cocaine, benzodiazepines

# Types of UDS: Immunoassay

- Opioids, cocaine, benzodiazepines etc.
- Detects use for up to five days
- False +ve: Poppy seeds
- False –ve:
  - Often misses semisynthetic opioids (oxycodone)
  - Usually misses synthetic opioids (methadone, fentanyl)

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# Chromatography

- Detects specific opioids
- Shorter window of detection (1-2 days)
- More sensitive for oxycodone & other synthetics
- Codeine metabolized to morphine

# Limitations

- Not quantitative
- Easy to tamper
- Influenced by a variety of factors
- False +ve, -ve common

**To order:**

- Specify drugs you wish to detect
- Or specify "broad spectrum" toxicology

# PRESCRIPTION OPIOID ADDICTION: TREATMENT

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# Management of Suspected Opioid addiction

- Trial of structured opioid therapy
- Methadone or buprenorphine
- Abstinence-based treatment

# Structured opioid therapy: Indications

- Has biomedical pain condition that hasn't responded to non-opioid therapy
- Is not injecting or crushing opioids
- Is not acquiring opioids from other sources
- Is not currently abusing other drugs
  - Limited evidence of effectiveness so view as therapeutic trial

# Structured opioid therapy

- Frequent visits, regular UDS, faxed scripts
- Daily or alternate day dispensing
- Long-acting scheduled opioids
- Avoid opioids with higher addiction liability eg hydromorphone
- Taper if on high dose (> 200 mg MED)

# Methadone treatment: Indications

- Failed trial of structured opioid therapy
- Injecting or crushing tablets
- Double doctoring or acquiring opioids from other sources
- Currently addicted to other drugs

# Methadone treatment

- Slow onset, long duration of action
- Relieves withdrawal, cravings without sedation or euphoria
- Can be monitored with UDS

# Methadone Rx (2)

- Three components:
  - Daily dispensing with gradual introduction of take-home doses
  - Regular UDS
  - Counselling and medical care
- Provincial College guidelines about methadone Rx
  - who prescribes & how

# Limitations of methadone treatment

- High risk of overdose early in treatment
  - Optimal candidate is highly tolerant to opioids
- Not all communities have methadone providers
- Major commitment of time for patient and provider

# Buprenorphine

- Suboxone (buprenorphine + naloxone)
- Sublingual partial opioid agonist
- Long duration of action
- As effective as 60-80 mg of methadone
- Lower risk of overdose than methadone (ceiling effect because partial agonist)

# Buprenorphine: ODB criteria

- Three-month wait for methadone Rx
- Methadone failed or contraindicated
- High risk for toxicity
  - > 65
  - Not fully opioid tolerant eg codeine or binge user
  - Heavy drinker
  - Benzodiazepine use
  - COPD

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# Abstinence-based treatments

- Medical detoxification
  - Buprenorphine, clonidine, opioid tapering, methadone tapering
  - Usually fails with heroin users but may be more effective with prescription use
- NA, AA, self-help groups
- Naltrexone (opioid antagonist)
- Residential or outpatient treatments

# Addiction and pain: Paradigm shift

- MDs see pain treatment is in opposition to addiction treatment
  - 'Patient is addicted but also has severe pain – if I stop opioids his/her pain will be unbearable'
- Yet evidence shows this is false:
- Opioid addiction increases pain perception and depression, worsens function
- Patient's pain, mood and functioning improves with treatment, by resolving withdrawal-mediated pain and opioid-induced depression

# What if patient refuses to enter treatment?

- If you're prescribing the opioid:
  - Explain that ongoing opioid prescribing is unsafe and will make patient feel worse
  - Pain, mood and function improves with treatment
- Give a firm start date for treatment: Structured opioid therapy, methadone or buprenorphine
- If patient refuses, taper and discontinue BUT do not 'fire' the patient