

# The History, Assessment and Treatment of Opiate Dependence

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## Disclosure

- Some slides courtesy of Chantal Laflamme, Dr. Kathryn Gill and Dr. Dara Charney
- Data courtesy of Patryk Simon
- L'Atrium
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## Opiate Dependence

- "For the drunkard and the glutton shall come to poverty; and the drowsiness shall clothe a man with rags"
- Proverbs 23:21

## Opiate Dependence

- Prescription Opioids
  - Codeine
  - Morphine
  - Dilaudid
  - Percodan/Percocet
  - Fentanyl
  - Methadone
- Street Opiates
  - Heroin
  - Opium

## Definition of Addiction

- Various accepted definitions exist, but all agree that addiction is:
  - Chronic<sup>1</sup>
  - Progressive<sup>1</sup>
  - Relapsing<sup>1,2</sup>
  - Compulsive<sup>2,3</sup>
  - Characterized by continued use despite physical or psychological problems<sup>4</sup>

1. O'Brien CP, McLellan AT. Rites about the treatment of addiction. *Lancet*. 1996;347:237-240.  
2. McLellan AT, Lewis DC, O'Brien CP, Klerman MD. Drug dependence, a chronic medical illness: implications for treatment, relapse prevention, and long-term evaluation. *JAMA*. 2000;284(13):1689-1695.  
3. Koob GF, Le Moal M, Rivier JC. The neurobiology of drug dependence: the neurobiology of addiction. *Brain Res Rev*. 1993;18(1):247-291.  
4. Koob GF, Le Moal M. Neurobiology of addiction. In: Grant KM, Schmitz TW, eds. *Principles of Addiction Medicine*, 2nd ed. Chevy Chase, MD: American Society of Addiction Medicine, Inc.; 1999:279-290.

## Components of Addictive Behavior

### Drug Abuse Has Behavioral, Cognitive, and Affective Components<sup>1-4</sup>

	Treatment Considerations
Behavioral	• Help patients find alternative nondrug re-inforcers and behaviors
Cognitive	• Help patients develop new ways of thinking about themselves and how they interact with the world • Help patients view themselves as drug nonusers
Affective	• Help patients deal with people, places, emotions, events, and things that may trigger relapse due to their close and lengthy association with drug taking

1. Haseltine PL, Henningfield JB, Epstein EE. Theories of alcohol and other drug use disorders. In: McLellan AT, O'Brien CP, eds. *Addiction: A Comprehensive Guidebook*. New York, NY: Oxford University Press; 1998:10-20.  
2. D'Amico EJ, Higgins ST, Dixon RE, Wang HC. Efficacy of relapse prevention: a meta-analytic review. *J Consult Clin Psychol*. 1996;64(1):53-57.  
3. National Institutes of Health. *Principles of Drug Addiction Treatment: A Research-Based Guide*. <http://www.nida.nih.gov/2009/07/28/2011>.  
4. Liu MD, Kadden RM, Kabela-Cormier E, Petry NK. Coping skills training and contingency management treatments for marijuana dependence: exploring mechanisms of behavior change. *Addiction*. 2008;103(4):499-509.

## What Is Opioid Dependence?

### Definition of Opioid Dependence

Considered a chronic, relapsing brain disease<sup>1</sup>

Associated with:

- Pervasive changes in cognitive and drug-rewarding circuits of the brain<sup>1,2</sup>
- Significant alterations at the molecular, cellular, and structural levels<sup>2</sup>
- Changes to brain function that persist after drug use has ceased<sup>2</sup>
- Compulsive drug-seeking and abuse<sup>3</sup>

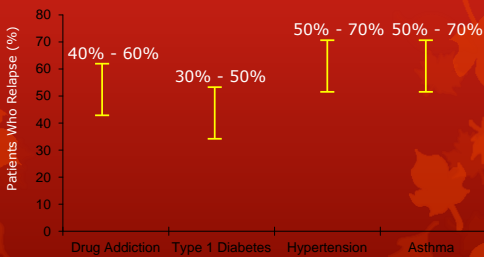
1. Carr LJ, Palani D. Mechanisms of disease: drug addiction. *N Engl J Med*. 2003;349:975-985.  
 2. Volkow ND, Alia-Smerdis I, Wang SC, et al. Neurobiological mechanisms of addiction: implications for treatment, insurance, and outcomes evaluation. *JAMA*. 2009;301(13):1589-1595.  
 3. McLellan AT, Lewis GC, O'Brien CP, Kessler RC. Drug dependence, a chronic medical illness: implications for treatment, insurance, and outcomes evaluation. *JAMA*. 2000;284(13):1689-1695.

## Comparison With Other Chronic Diseases<sup>1-3</sup>

Characteristics	Diabetes, Asthma, and Hypertension	Drug Dependence
Well studied	✓	✓
Chronic disorder	✓	✓
Predictable course	✓	✓
Effective treatments	✓	✓
Curable	NO	NO
Heritable	✓	✓
Requires continued care	✓	✓
Requires adherence to treatment	✓	✓
Requires ongoing monitoring	✓	✓
Influenced by behavior	✓	✓
Tends to worsen if untreated	✓	✓

1. McLellan AT, Metzger BJ, Barron JL, et al. Reconsidering the evaluation of addiction treatment: from retrospective follow-up to concurrent recovery monitoring. *Addiction*. 2005;100(4):414-420.  
 2. Volkow ND, Alia-Smerdis I, Wang SC, et al. Neurobiological mechanisms of addiction: implications for treatment, insurance, and outcomes evaluation. *JAMA*. 2009;301(13):1589-1595.  
 3. McLellan AT. Have we evaluated addiction treatment correctly? Implications from a chronic care perspective. *Addiction*. 2002;97(3):249-252.

## Relapse Rates Are Similar to Other Chronic Diseases<sup>1</sup>



1. National Institute on Drug Abuse. Drugs, Brains, and Behavior: The Science of Addiction. <http://www.nida.nih.gov/neuroscienceaddiction/vol04addiction.pdf>. Accessed January 3, 2009.

## Features of a Chronic, Relapsing Condition

- Limited chances of complete 'cure' or 'recovery'
- Relapse common
- Multifactorial
  - Genetic (heritable vulnerability)
  - Environmental (exposure)
  - Biological (demonstrated pathophysiology)
  - Behavioural (lifestyle aspects)

*Optimal patient care depends on accepting opioid dependence as a chronic, relapsing condition*

## The Neurobiology of Opioid Dependence

### Impact of Opioid Dependence on the Brain<sup>1</sup>

Opioid molecules attach to $\mu$ -opioid receptors	→ Changes occur in the locus ceruleus (LC) at the base of the brain
Activated LC receptors suppress release of noradrenaline (NA)	→ Symptoms of opioid intoxication
Repeated exposure of LC neurons to opioid molecules	→ LC neurons adjust by increasing NA production
When opioids are NOT present to stop LC activity	→ Neurons release excessive amounts of NA, triggering withdrawal effects

1. Koob GF, George TP. The neurobiology of opioid dependence: implications for treatment. *Soc Pharm Perspect*. 2002;1:13-20.

## The Biological Basis of Opioid Dependence

- Opioid dependence can cause drug-seeking behavior
  - The brain's reward circuit has evolved to positively reinforce behaviors essential to survival<sup>1</sup>
  - Drugs of abuse, such as opioids, manipulate the reward circuit, causing the person to feel that use of these chemicals is necessary for survival<sup>1,2</sup>

1. Tomkins DR, Sellers DR. Addiction and the brain: the role of neurotransmitters in the cause and treatment of drug dependence. *Chias*. 2002;144:817-821.  
 2. Carr LJ, Palani D. Mechanisms of disease: drug addiction. *N Engl J Med*. 2003;349:975-985.

## Neuroadaptation of Dopamine (DA) D<sub>2</sub> Receptors<sup>1</sup>

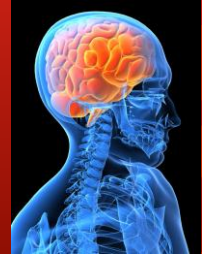


Positron emission tomography showing the effects of heroin dependence on brain DA D<sub>2</sub> receptors

<sup>1</sup> Wang G-J, Volkow ND, Fowler JS, et al. Dopamine D<sub>2</sub> receptor availability in opiate-dependent subjects before and after naloxone precipitated withdrawal. *Neuropsychopharmacology*. 1997;16(2):119-132.

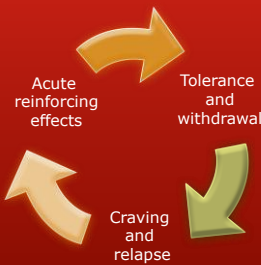
## The Multiple Components of Drug Abuse

- Drug abuse has multiple components:
  - Neurobiologic<sup>1,2</sup>
  - Behavioural, cognitive, and affective
- Treatment must address each component
- Drug abuse is learned<sup>3,4</sup>
- Long-term drug use alters:
  - The way people think about their own behaviour<sup>5</sup>
  - Emotional reactions to environmental stimuli<sup>5</sup>



<sup>1</sup> Koob GF, Le Moal M. *Neuropsychopharmacology*. 2001;24(2):97-129; <sup>2</sup> Kalivas PW, Volkow ND. *Am J Psychiatry*. 2005;162(8):1403-1413. <sup>3</sup> Hesselbrock MN et al. *Addictions: A Comprehensive Guidebook*. New York, NY: Oxford University Press; 1999:50-65. <sup>4</sup> Irvin JE et al. *J Consult Clin Psychol*. 1999;67(4):563-570. <sup>5</sup> Larimer ME et al. *Alcohol Res Health*. 1999;23(2):151-160.

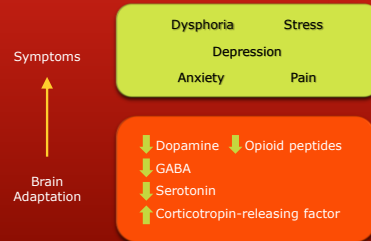
## Cycle of Addiction: Neurobiological Aspects<sup>1,2</sup>



<sup>1</sup> Koob GF, Le Moal M. Drug addiction: dysregulation of reward and distress. *Neuropsychopharmacology*. 2001;24(2):97-129; <sup>2</sup> Kalivas PW, Volkow ND. The neurobasis of addiction: a pathology of motivation and choice. *Am J Psychiatry*. 2005;162(8):1403-1413.

## Chemical Changes: Withdrawal

Withdrawal Symptoms and Associated Brain Neuroadaptation<sup>1,2</sup>



<sup>1</sup> Koob GF, Le Moal M. Drug addiction: dysregulation of reward and distress. *Neuropsychopharmacology*. 2001;24(2):97-129; <sup>2</sup> Koob GF, Le Moal M. Plasticity of reward neurocircuitry and the "dark side" of drug addiction. *Nat Neurosci*. 2005;8(11):1442-1444.

## Understanding the Scope of the Problem

## Global Illicit Intravenous Opioid Use



Fischer B et al. *Can J Psychiatry*. 2006;51(10):624-634.

## Opiate Dependence

### Illicit Heroin Use in Canada:

- Estimated Number of Heroin Users - 60,000-100,000
  - Deaths by Overdose per year - 500-1,000
  - HIV Prevalence:
    - Toronto - 9.5%
    - Montreal - 17.9%
    - Vancouver - 25%
  - Hep C in IV Drug Users - 60-95%
- Benedikt Fischer, U of T Public Health

## Epidemiology

- ECA study - 16.7 % lifetime substance abuse/dependence
- NCS study - 26.6 % lifetime substance abuse/dependence
- NCS study - 1.5% lifetime use of heroin, 0.4% lifetime heroin dependence
- NCS study - 9.7% lifetime use of Rx opiates, 7.5% developing dependence

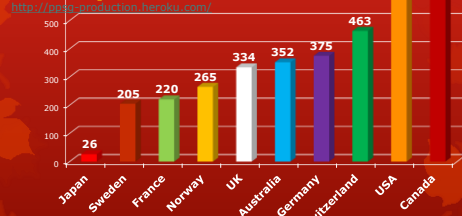
## Prescription Opioid Use in Canada

- Worldwide ranking in per capita consumption (2005)<sup>1</sup>:
  - Hydromorphone: #1
  - Morphine and oxycodone: #2
  - Hydrocodone: #3
- In 2009, the International Narcotics Control Board<sup>2</sup>
  - Canada was the:
    - Largest importer of hydromorphone, the 2nd largest importer of codeine and the 3rd largest importer of morphine
    - 2nd largest morphine, hydromorphone, oxycodone, and fentanyl consumer, and 3rd largest hydrocodone consumer per million inhabitants per day
  - In 2010, among youth, abuse of cannabis, cocaine, and MDMA (ecstasy) all declined, and prescription pain reliever abuse increased<sup>2</sup>

<sup>1</sup> Popova S. *Can J Public Health*. 2009;100(2):104-108; 2. International Narcotics Control Board. [http://www.incb.org/pdf/technical-reports/narcotic-drugs/2010/Narcotic\\_drugs\\_publication\\_2010.pdf](http://www.incb.org/pdf/technical-reports/narcotic-drugs/2010/Narcotic_drugs_publication_2010.pdf). Accessed June 8, 2011.

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## Per-Capita Consumption of Severe Pain Killers by Country in 2010



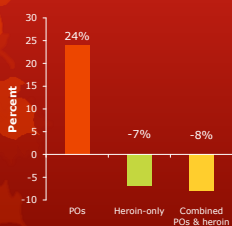
<sup>1</sup>Total mg per capita consumption of the six most common opioids used for cancer, AIDS and other end-of-life conditions.

<sup>2</sup>Source: Drug Control and Access to Medicines Consortium - <http://opsa-production.heroku.com/> using data from the International Narcotics Control Board

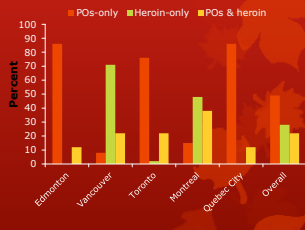
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## Nonmedical Use of Prescription Opioids

### Canada Trend 2002 to 2005



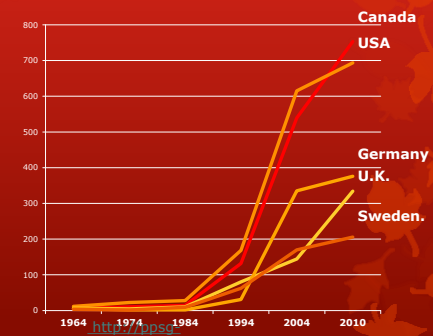
### Nonmedical Prescription Opioid Use, Heroin Use, and Both, 2005



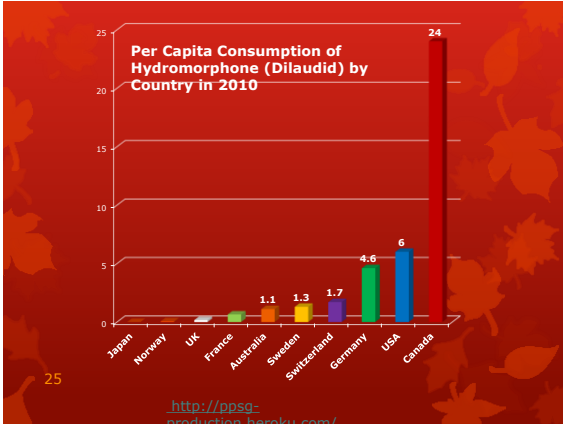
POs=prescription opioids. <sup>1</sup> Popova S. *Can J Public Health*. 2009;100(2):104-108; Reproduced with permission of the Canadian Public Health Association.

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## Per-Capita Consumption of Severe Pain Killers by Country 1964 – 2010



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## Prevalence of Prescription Opioid Use in Québec<sup>1</sup>

- 25% of the Québec Public Prescription Drug Insurance Plan were surveyed in 2005
  - 11% (~300,660) people were dispensed an opioid in 2005
- A 2003 study estimated that 38,307 to 109,058 people in Québec used prescription opioids for nonmedical purposes<sup>2</sup>
- Estimates suggest that >10% of the people in Québec who are dispensed opioids may use them for nonmedical purposes

1. Williams RE et al. Pain Res Manage 2008;13(5):395-400; 2. Popova S. Can J Public Health. 2009;100(2):104-108

## Provincial comparison: Primary dependency

	Percentage of discharges		Provincial rate (N=7569)
	DHA 1-8 (N=5852)	CDHA (N=1717)	
Primary dependency			
Alcohol	54.9%	50.4%	53.9%
Opioids	34.0%	35.3%	34.3%
Cocaine/Crack cocaine	3.2%	8.6%	4.5%
Cannabis	3.9%	3.0%	3.7%
Benzodiazepines	2.2%	1.6%	2.0%
Other	1.8%	1.2%	1.7%
Total	100.0%	100.0%	100.0%

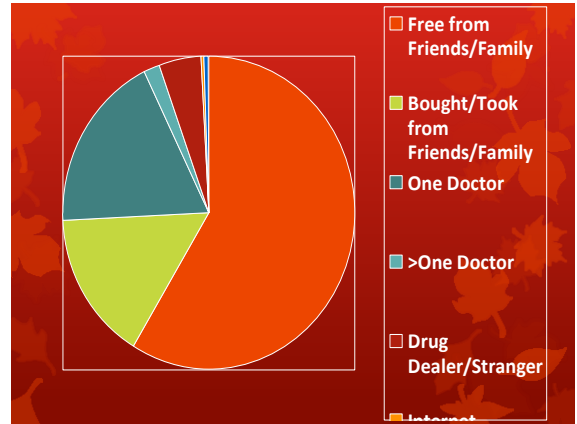
Other - includes over the counter items, other prescription medications, Gambling, hallucinogens, MD  
 Note: No statistically significant differences noted

## Average length of stay on WM Inpatient by primary treatment issue, FY2008-2011

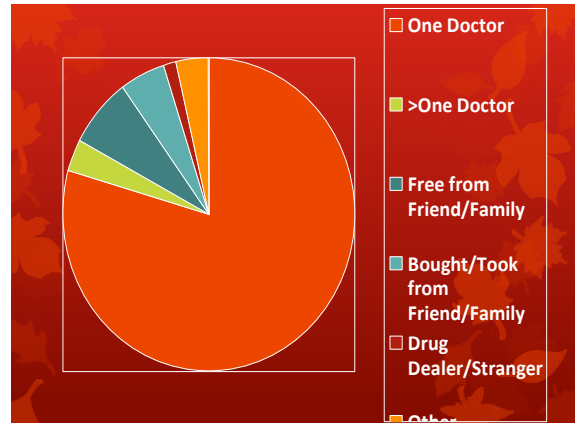
Primary Treatment Issue	FY2008			FY2009			FY2010			FY2011		
	# Discharges	Avg LOS	%	# Discharges	Avg LOS	%	# Discharges	Avg LOS	%	# Discharges	Avg LOS	%
Alcohol	562	6.4	49.9	519	5.1	55.4	499	4.0	55.1	442	4.1	50.3
Opioids	178	6.6	15.8	171	5.6	18.3	262	4.3	29.0	303	4.2	34.5
Cocaine/Crack cocaine	323	5.5	28.7	180	4.7	19.2	100	3.4	11.0	79	3.5	9.0
Cannabis	40	9.4	3.5	46	4.7	4.9	26	3.6	2.9	25	3.0	2.8
Benzodiazepines	14	11.9	1.2	14	7.6	1.5	11	5.9	1.2	16	4.3	1.8
Other	10	6.1	0.9	6	3.7	0.6	7	4.4	0.8	13	3.8	1.5
Grand Total	1127	6.3	100.0	936	5.1	100.0	905	4.0	100.0	878	4.0	100.0

## Source Where Pain Relievers Were Obtained for Most Recent Nonmedical Use Amongst Past Year Users Aged 12 or Older: NSDUH 2010

## Source Where Respondent Obtained



## Source Where Friend/Relative Obtained



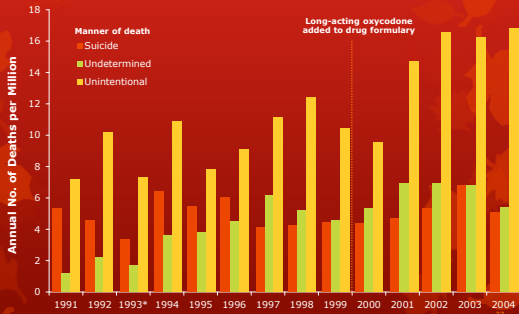
## Opiate Dependence

- Administration
  - oral
  - snorting
  - smoking
  - subcutaneous
  - intravenous

## Opiate Dependence

- Consequences
  - crime to support habit (stealing, dealing, prostitution)
  - inability to sustain work
  - loss of significant relationships (partners, children, family)
  - downward social drift
  - medical sequelae (Hep C, HIV, cellulitis)

## Deaths Related to Opioid Analgesics Use in Ontario, 1991 to 2004 (Dhalla et al., 2009)



\*The value for 1993 is an underestimate owing to missing data.  
Dhalla JA et al. CMAJ. 2009;181(12):891-896.

## The History of Opiates and Opioids

### The History of Opiates

"Her eyes closed in spite of herself,  
and she forgot where she was and fell  
among the poppies, fast asleep.

"What shall we do?" asked the Tin  
Woodman.

"If we leave her here she will die," said  
the Lion. "The smell of the flowers is  
killing us all, I myself can scarcely  
keep my eyes open and the dog is  
asleep already."

-L. Frank Baum, The Wonderful Wizard of Oz

### The History of Opiates

- 3300 BC – Sumerians cultivate opium poppy (*Papaver somniferum*) called "hul gil" or "plant of joy"
- 700-140 BC – Opium poppy spreads through Middle East and Mediterranean
- 500 BC – appears in Greek pharmacopeia
- 400 BC – Hippocrates prescribes for insomnia
- 100 AD - Dioscorides' *De Materia Medica* – used for insomnia, diarrhea, nausea and aphrodisiac

### The History of Opiates

- 1275 – Marco Polo arrives in China by sea
- 1497-98 – Vasco de Gama established sea route to India via Africa
- 1513 – Portugese control trade from Calcutta to Canton
- Portugese introduce smoking pipe to China, begin to trade opium, take back spices, silk, tea, porcelain

### The History of Opiates

- Opium dens flourish in China
- 1600's – Dutch, French and British get involved in Opium trade
- 1770-1833 – British controlled opium trade
- 1796 – Emperor banned opium
- 1840 – 3 million Chinese opium addicts

## The History of Opiates

- Opium shipments to China
  - 1660: 1,350 pounds
  - 1720: 15 metric tons
  - 1773: 75 metric tons
  - 1800: 250 metric tons
  - 1840: 2,555 metric tons

## The History of Opiates

- 1838 – Chinese gov't seizes 95 metric tons of British opium, beginning of first Opium War
- 1842 – China surrenders, cedes Hong Kong to British, but refuses to legalize opium
- 1856-60 – Second Opium War between China and Britain/France, treaty imposes legalized opium in China
- 1900 – 13.5 million Chinese opium addicts
- 1906 – 27% Chinese men opium smokers

## The History of Opiates as Medicine

- 1541 – Paracelsus develops odorless liquid Laudanum
- 1803 – Seturner discovers Morphine, named after Morpheus the Greek God of Dreams
- 1827 – Merck begins commercial production of morphine, codeine in 1836 and cocaine in 1862

## The History of Opiates

- 1878-1885 – 50-70% of addicts middle class women who bought legal opium
- Addiction rate 4.59/1000 compared to current 2.04/1000
- US Civil War produced large number of morphine dependent men
- 1852-70 – large Chinese immigration to work on railroads bringing opium to West Coast

## The History of Opiates as Medicine

- 1874 – Wright discovers heroin, introduced by Bayer in 1898 without prescription
- 1887 – prohibition of opium importation
- 1914 – Harrison Narcotic Act – designed to eliminate non-medical use of opiates, lead to involvement of Organized Crime
- 1930-62 – Anslinger & Federal Bureau of Narcotics - 200,000 addicts in 1924 to 20,000 in 1945

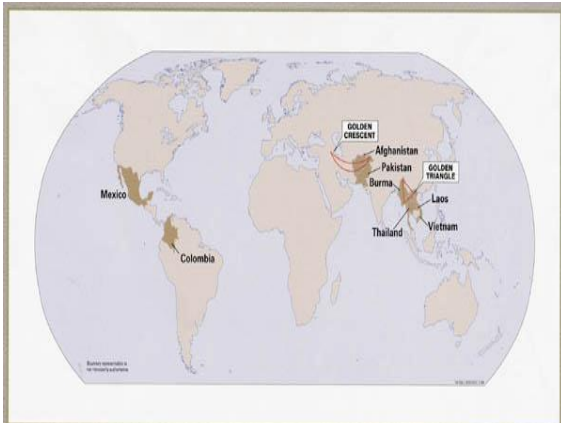
## The History of Opiates as Medicine

- Charlie "Lucky" Luciano and the rise of Organized Crime (1930's) from Mafia
- End of Prohibition, development of prostitution (1,200 women in 200 NYC brothels)
- 1945 – 20,000 addicts
- 1965 -150,000 addicts

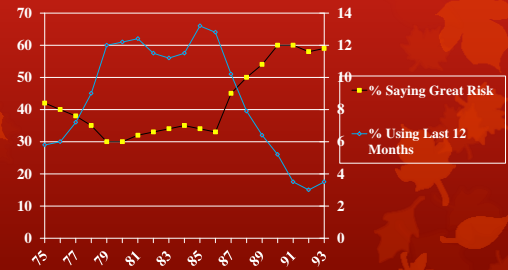


## The History of Opiates

- 1950's – Cold War begins
- 1960-75 – CIA involvement in South East Asia, heroin production to fund weapons created The Golden Triangle; American soldiers in Vietnam using heroin
- 1979 – CIA involvement with Afghanistan, heroin production to buy weapons for rebels
- 1990 – Colombia begins to enter heroin production and distribution using existing cocaine network
- 1980 – 500,000 heroin addicts

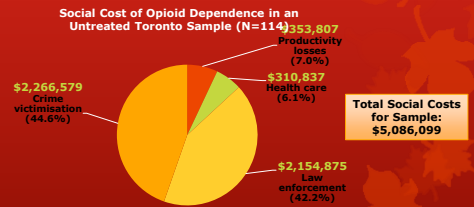


## Trends in Perceived Risk and Use of Cocaine (1975-93)



## Treatment of Opioid Dependence

## Social Costs of Untreated Opioid Dependence



- Survey was completed between June 1996 and March 1997
- \$105 to 171 million per annum (\$43 to \$69 per capita)
- Costs arise from opioid dependence and environment, including measures limiting availability of opioids

## Treatment Benefits Outweigh Costs



Hart WA.  
[http://www.health.gov.on.ca/english/public/pub/ministry\\_reports/methadone\\_taskforce/methadone\\_taskforce.pdf](http://www.health.gov.on.ca/english/public/pub/ministry_reports/methadone_taskforce/methadone_taskforce.pdf)  
 Accessed September 9, 2011.

## Early Treatment of Opiate Addiction

- Legislation and regulation to limit the availability of opiates was started in 1908 in Canada (Narcotic Control Act) and in 1914 in the U.S. (Harrison Act)
- Physicians were able to prescribe heroin for addicted patients – however, government made many attempts to prosecute these doctors
- In 1918, the U.S. government established clinics in 14 U.S. cities to treat addiction – morphine and other drugs were prescribed for opiate addicts. (This could be considered the 1<sup>st</sup> wave of opiate maintenance programs.) These programs were discontinued in 1923.

## Early Treatment of Opiate Addiction

- After 1923 the main treatments available for opiate addiction were prison-like hospitals in Lexington, Kentucky as well as in Texas and New York. These programs involved drug-free detoxification (cold-turkey) and appeared to have very high failure rates
- Riverside Hospital opened in mid-1950s in NYC for detox and abstinence based treatment, but follow-up showed 90% relapse rate

## Early Treatment of Opiate Addiction

- By early 1960's, heroin-related mortality was leading cause of death for young adults (ages 15-35)
- Jails overcrowded with drug-related offences
- Marked increase in hepatitis
- NYC viewed heroin as a public health emergency (half of all US addicts lived in NYC)

## Early Treatment of Opiate Addiction

- In 1963 Dole and Nyswander first started testing patients with methadone.
- Methadone is a long-acting opiate that could be administered through the oral route, that suppressed withdrawal symptoms with single daily dose (80-120mg)
- Early reports of the use of this therapy indicated that there could be a considerable amount of rehabilitation of opiate addicts following regular methadone administration

## Early Treatment of Opiate Addiction

- At Manhattan General Hospital, they enrolled a 120 patients in a pilot program
- By 1967, 107 remained in treatment
- 71% employed in steady jobs, attending school or both
- "To date we have seen no indication to remove the blockade from any patient in the treatment program since all of them are still in the proces of rehabilitation and no patient has been limited by intolerance of the medication."

## Early Treatment of Opiate Addiction

- Ten year follow-up data revealed:
  - Decreased antisocial behaviour as measured by arrests/incarceration
  - Increase in social productivity
  - Relief in heroin cravings, measured by negative urines
  - Greater willingness to accept help, both medical and psychiatric

## Treatment Goals

- Retain patients
- Minimise withdrawal symptoms and cravings
- Provide medical, social and psychological treatment

## Components of Treatment: Pharmacotherapy and Psychosocial Intervention<sup>1,2</sup>

**Pharmacotherapy**

Can control symptoms by normalizing brain chemistry

↔

**Psychosocial Intervention**

Essential to change behaviours and responses to environmental and social cues that so significantly impact relapse

Both are necessary to normalise brain chemistry, change behaviour, and reduce risk for relapse; neither alone is sufficient

## Treatment Components and Considerations

Treatment Components	Treatment Considerations
Pharmacotherapy	<ul style="list-style-type: none"> <li>• Can control symptoms by helping to normalise brain chemistry<sup>1,2</sup></li> <li>• Not sufficient treatment alone and has a higher risk of relapse compared with patients receiving contingency-based counseling<sup>3-5</sup></li> </ul>
Counseling intervention	<ul style="list-style-type: none"> <li>• Essential to change behaviors and responses to environmental and social cues that significantly impact relapse</li> <li>• Can be equally effective as an adjustment in medication dose in response to renewed instability during treatment<sup>1</sup></li> </ul>

## The Importance of Counseling

- Counseling is the cornerstone of opioid dependence treatment
- Patients may benefit from combined pharmacotherapy and counseling<sup>1</sup>
- An effective matrix of care consists of:
  - The patient
  - The physician; provides pharmacotherapy, support, and referral for counseling
  - The counselor; trained to assist patients with psychosocial aspects of recovery

## Counseling Improves Outcomes: Opioid Dependence

- McLellan et al (1993 and 1998) demonstrated a "dose response" for counseling services in addiction treatment<sup>1,2</sup>
- Most recent updates of Cochrane Database reviews of pharmacological interventions for opioid dependence and medical withdrawal
  - Adding psychosocial support to maintenance treatments improves abstinence at follow-up<sup>3</sup>
  - Adding counseling support to medically assisted withdrawal improves treatment completion and decreases opioid use<sup>4</sup>

## Counseling Improves Outcomes in Other Chronic Diseases

- Depression<sup>1-3</sup>
- Panic disorder<sup>4</sup>
- Nicotine dependence<sup>5,6</sup>
- Alcohol dependence<sup>6,7</sup>
- Obesity<sup>8</sup>

1. Robinson, J.L. Improving the quality of antidepressant care. *Psychosomatics*. 2004;45(2):119-23. 2. Robinson, J.L. Improving the quality of antidepressant care. *Psychosomatics*. 2004;45(2):119-23. 3. Robinson, J.L. Improving the quality of antidepressant care. *Psychosomatics*. 2004;45(2):119-23. 4. Robinson, J.L. Improving the quality of antidepressant care. *Psychosomatics*. 2004;45(2):119-23. 5. Robinson, J.L. Improving the quality of antidepressant care. *Psychosomatics*. 2004;45(2):119-23. 6. Robinson, J.L. Improving the quality of antidepressant care. *Psychosomatics*. 2004;45(2):119-23. 7. Robinson, J.L. Improving the quality of antidepressant care. *Psychosomatics*. 2004;45(2):119-23. 8. Robinson, J.L. Improving the quality of antidepressant care. *Psychosomatics*. 2004;45(2):119-23.

6

## Counseling Techniques

- Counselors can use a variety of evidence-based approaches<sup>1</sup>:
  - Cognitive behavioral therapy
  - Individualised drug counseling
  - Motivational enhancement therapy
  - Supportive-expressive therapy
  - Contingency management

1. National Institutes of Health. *Principles of Drug Addiction Treatment: A Research-Based Guide*. NIH publication 09-4180. <http://www.nida.nih.gov/publications/Principles>. Released April 2009. Accessed July 28, 2011.

6

## Importance of Pharmacotherapy

- Two types of pharmacotherapy:
  - Agonist Therapies
    - Methadone, Buprenorphine
    - ? Heroin, Dilaudid
  - Antagonist Therapies
    - Naltrexone

## NALTREXONE

- Who might benefit from naltrexone ?
  - Highly motivated individuals
  - Former opiate-dependent individuals who are employed and socially functioning
  - Those recently detoxed from methadone/buprenorphine maintenance
  - Those who are leaving prison
  - Those who are leaving residential treatment settings
  - Those who sporadically use opiates but are not on methadone/buprenorphine maintenance
  - Those not eligible for methadone/buprenorphine maintenance
  - Those in a long waiting period for methadone/buprenorphine maintenance
  - Those wishing to prevent relapse
  - Adolescents not wishing to go on methadone/buprenorphine maintenance
  - Healthcare professionals not wishing to go on methadone/buprenorphine maintenance

## NALTREXONE

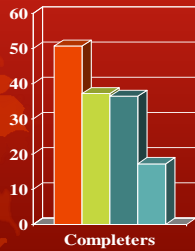
- For opiate-dependent patients
  - Dosing
    - Must wait 5 – 7 days after last use of a short-acting opiate (heroin) or 7 – 10 days after a long-acting opiate to prevent withdrawal.
    - Can perform a naran challenge test\* to see if withdrawal can be induced, thus not safe to start naltrexone yet
    - Should always have a negative urine drug screen for opiates before starting
    - Start with 25 mg first day, then 50 mg per day thereafter.
    - Can dose for 3 times a week (100mg – 100mg – 150 mg on Monday, Wednesday and Friday)

\*See next page for **Narcan Challenge Test**

## RATIONALE FOR OPIOID AGONIST MEDICATIONS

- OPIOID AGONIST TREATMENT
  - Most effective treatment for opioid dependence
  - Controlled studies have shown significant
    - Decreases in illicit opioid use
    - Decreases in other drug use
    - Decreases in criminal activity
    - Decreases in needle sharing
    - Improvements in prosocial activities
    - Improvements in mental health

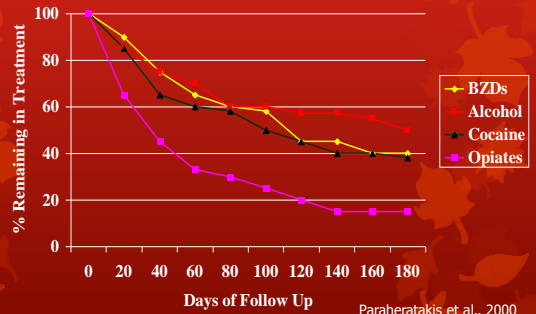
### Percentage Completing Outpatient Treatment



- Alcohol - 50.7%
- Cocaine - 37.1%
- BZDs - 36.4%
- Opiates - 17.2%

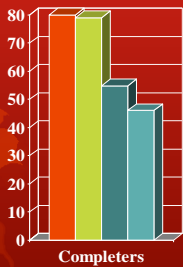
Paraheratakis et al., 2000

### Retention - Outpatient Treatment



Paraheratakis et al., 2000

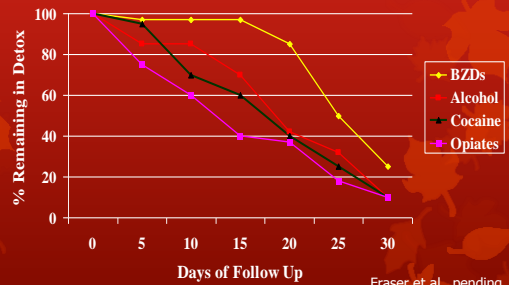
### Percentage Completing Inpatient Detoxification



- Sedatives-Hypnotics - 80%
- Alcohol - 79%
- Cocaine - 54.8%
- Opiates - 46%

Fraser et al., unpub.

### Retention - Inpatient Detoxification



Fraser et al., pending

Experimental Studies of Heroin Detoxification

AUTHOR	N	DETOX METHOD	OUTCOME
Hunt & Odoroff, 1962	1912	Non-opiate	90% re-addicted at 6 months follow-up
Berle & Nyswander, 1964	53	Non-opiate, 2-4 weeks, outpatient	98% readdicted at 2 years follow-up
Bewley & Ben-Arie, 1968	100	Heroin, outpatient	86% re-addicted at 3 months follow-up
Katon et al., 1972	232	Methadone, 21-90 days, outpatient	97% failed to complete detox protocol
Canada, 1972	157	Methadone, 30-60 days, outpatient	93% re-addicted at 6 months follow-up
Stimmel et al., 1977	335	Methadone, 2 months - 1 year, outpatient	72% re-addicted at 2 years follow-up
Del Campo et al., 1977	91	Methadone + sedatives, 21 days, outpatient	Only 4% completed detox. 100% re-addicted at 3 mo
Gossop et al., 1986	50	Methadone, inpatient vs outpatient	Outpatient- 17% completion, Inpatient- 81%. No follow-up
San et al., 1989	170	Methadone or clonidine, inpatient	Methadone- 75% completion, clonidine- 44%. No follow-up
Ball & Ross, 1991	?	Methadone, outpatient	82% re-addicted at 10 month follow-up

ORIGINAL ARTICLE

### A 33-Year Follow-up of Narcotics Addicts

Yih-Ing Hser, PhD; Valerie Hoffman, PhD; Christine E. Grella, PhD; M. Douglas Anglin, PhD

**Backgrounds:** This study examined longitudinal patterns of heroin use, other substance use, health, mental health, employment, criminal involvement, and mortality among heroin addicts.

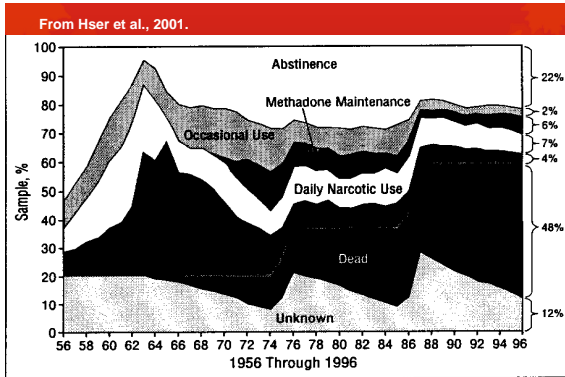
**Methods:** The sample was composed of 581 male heroin addicts admitted to the California Civil Addict Program (CAP) during the years 1962 through 1964. CAP was a compulsory drug treatment program for heroin-dependent criminal offenders. This 33-year follow-up study updates information previously obtained from admission records and 2 face-to-face interviews conducted in 1974-1975 and 1985-1986; in 1996-1997, at the latest follow-up, 284 were dead and 242 were interviewed.

**Results:** In 1996-1997, the mean age of the 242 interviewed subjects was 57.4 years. Age, disability, years since first heroin use, and heavy alcohol use were significant correlates of mortality. Of the 242 interviewed

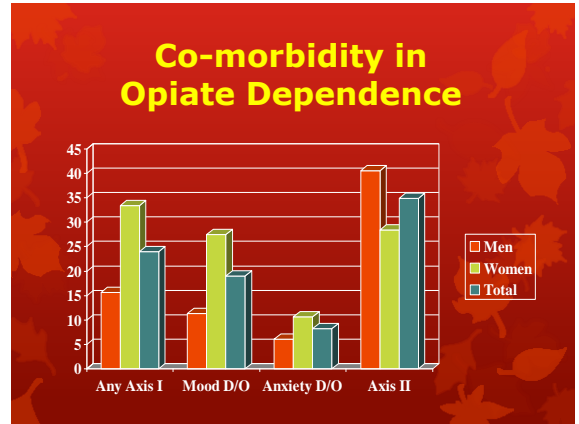
subjects, 20.7% tested positive for heroin (with additional 9.5% urine refusal and 14.0% incarceration, for whom urinalyses were unavailable), 66.9% reported tobacco use, 22.1% were daily alcohol drinkers, and many reported illicit drug use (eg, past-year heroin use was 40.5%; marijuana, 35.3%; cocaine, 19.4%; crack, 10.3%; amphetamine, 11.6%). The group also reported high rates of health problems, mental health problems, and criminal justice system involvement. Long-term heroin abstinence was associated with less criminality, morbidity, psychological distress, and higher employment.

**Conclusions:** While the number of deaths increased steadily over time, heroin use patterns were remarkably stable for the group as a whole. For some, heroin addiction has been a lifelong condition associated with severe health and social consequences.

Arch Gen Psychiatry. 2001;58:503-508



The natural history of narcotics addiction among a male sample (N=581).



## Opioid-Dependence Treatment in Canada: A History of Expansion and Contraction

### A History of Polarised Perspectives

Criminal Model	Medical Model
<ul style="list-style-type: none"> <li>Opioid addicts subjected to mandatory treatment until abstinence achieved</li> <li>Promoted by law enforcement and government sector</li> </ul>	<ul style="list-style-type: none"> <li>Treatment rather than punishment</li> <li>Promoted by addiction treatment sector</li> </ul>

Fischer B. J Public Health Policy, 2000;21(2):187-210.

### Phases of Drug Treatment in Canada

1900-1940s	1950s-1960s	1970s	1980s	1990s	2000s
Limited treatment options for opioid dependence <sup>1</sup>	Maintenance treatment programs introduced <sup>2</sup>	Federal regulations increased; treatment options reduced <sup>2</sup>	Enforced restrictive federal regulations and MMT declined <sup>2</sup>	Decentralised regulatory authority and expanded treatment <sup>2</sup>	Continued treatment expansion and introduction of "SUBOXONE" (buprenorphine and naloxone) Sublingual Tablets

MMT=metadone maintenance treatment.  
 1. Roberts G, Ogborn AC. Profile Substance Abuse Treatment and Rehabilitation in Canada. <http://publications.gc.ca/site/eng/97504/publication.html>. Accessed September 9, 2011; 2. Fischer B. J Public Health Policy, 2000;21(2):187-210.

### 1900 to 1940s: Opioid Dependence and Limited Treatment Options

1900-1940s 1950s-1960s 1970s 1980s 1990s 2000s

- Moralistic attitudes, limited understanding, little attention or access to treatment<sup>1</sup>
- Post-World War II: opiate addiction replaces opium and cocaine addiction, led to<sup>2</sup>:
  - Increased drug law enforcement
  - New drug scare in Vancouver driven by media sensationalising
- 2 main treatment models emerged
  - Criminal: addicts subjected to mandatory treatment until abstinence achieved; promoted by law enforcement and government sector
  - Medical: treatment vs punishment; promoted by addiction treatment sector

1. Roberts G, Ogborn AC. Profile Substance Abuse Treatment and Rehabilitation in Canada. <http://publications.gc.ca/site/eng/97504/publication.html>. Accessed September 9, 2011; 2. Fischer B. J Public Health Policy, 2000;21(2):187-210.

## 1950 to 1960s: Introduction and Expansion of Maintenance Treatment Programs

1900-1940s 1950s-1960s 1970s 1980s 1990s 2000s

- Disillusionment over effective treatment strategies for opioid dependence sparked a drug treatment movement
- Law enforcement was at odds with medical sector over benefits of opiate maintenance treatment
- MMT proposed and established as an alternative treatment in opiate addiction management
- MMT programs began to expand in the late 1960s

Fischer B. J Public Health Policy. 2000;21(2):187-210.

## 1970s: Opposing Goals and Their Impact

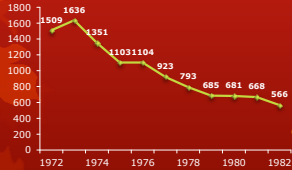
- The Le Dain Commission recommended MMT expansion while acknowledging issues
- 1971: Special Joint Committee of health, law enforcement, and Canadian Medical Association officials investigated misuse of MMT
- 1972: federal guidelines (amendments to the Narcotic Control Act; [NCA]) made MMT unattractive to physicians
- Before the 1972 NCA
  - ~1700 opiate addicts in MMT
  - ~136 active MMT prescribers
  - Under the NCA: a 5-fold increase in convictions for heroin offenses between 1966 and 1973
- After NCA, substantive decline in MMT
  - 65% decline in addicts in MMT in 10 years
  - By 1982, only 62 physicians providing MMT to 577 patients

Fischer B. J Public Health Policy. 2000;21(2):187-210.

## 1970s to 1980s: Restrictive Federal Regulations Cause MMT to Continue to Decline

1900-1940s 1950s-1960s 1970s 1980s 1990s 2000s

Opiate Users in Methadone Treatment in Canada, 1972 to 1982



1983: 38,000 to 80,000 opiate addicts living in Canada

- Results of 1982 survey of Canadian physicians
  - Number of physicians actively prescribing MMT dropped to 56 in 1982
  - A daily dose of >60 mg is minimum needed for positive results
    - <33% received >60 mg (none in Ontario or Manitoba)
    - 28% received 40 to 60 mg
    - Remainder received <40 mg
- Explanations for decline in MMT after new treatment restrictions disregarded recent treatment restrictions

Fischer B. J Public Health Policy. 2000;21(2):187-210.

## 1987 to 1990s: A Time of Change

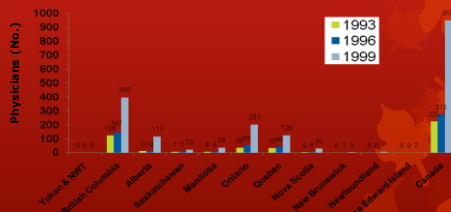
1900-1940s 1950s-1960s 1970s 1980s 1990s 2000s

- 1987: Canada's drug strategy launched<sup>1</sup>
  - The International Working Group on Substance Abuse published Canada's drug strategy, endorsed MMT and stated the following goals<sup>2</sup>:
    - Reduce demand for drugs and related morbidity/mortality
    - Increase accessibility to substance abuse information and intervention
    - Reduce the drug supply
    - Reduce costs to society
  - Treatment reforms occurred<sup>3</sup>
    - Diversification and specialisation of substance abuse treatment services and increase in services for women, children, and aboriginal people
  - Provincial control
1. Roberts G, Ogilvie AC. <http://publications.gc.ca/site/eng/97604/publication.html>. Accessed September 9, 2011.  
2. Minister of Public Works and Government Services Canada. <http://www.hc-sc.gc.ca/hppb/alcohol-otherdrugs>. Accessed September 14, 2011.

Fischer B. J Public Health Policy. 2000;21(2):187-210.

## Physicians in Canada and Provinces Authorised for Methadone Prescription Treatment, 1993 to 1999

1900-1940s 1950s-1960s 1970s 1980s 1990s 2000s



Fischer B. J Public Health Policy. 2000; 21(2):187-210.

## Mid 2000s: SUBUTEX® (buprenorphine hydrochloride) and SUBOXONE® (buprenorphine and naloxone) Sublingual Tablets Introduced

1900-1940s 1950s-1960s 1970s 1980s 1990s 2000s

- 2005: Canadians gained a new and safe treatment program for opiate addiction, SUBUTEX in combination with medical, social, psychological support<sup>1</sup>
  - Physician training in SUBUTEX use
  - Maintenance of a list of SUBUTEX National Education Program trained physicians
  - Daily dosing supervised by a healthcare professional
- 2007: SUBOXONE approved by Health Canada for medication-assisted treatment of opioid drug dependence in adults under careful monitoring within a framework of medical, social and psychological support<sup>2</sup>
  - Contains buprenorphine plus naloxone to deter intravenous misuse
  - SUBOXONE prescribed by physicians with experience in substitution treatment and have completed the accredited SUBOXONE Education Program

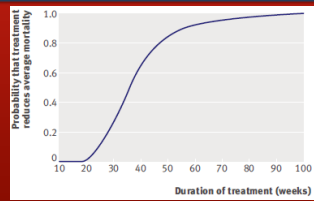
1. Press release. February 14, 2005. Schering Canada, Inc. <http://www.docufile.com/press/20050214/05-0214-01>. Accessed September 9, 2011; 2. Press Release. Kirkland, Quebec: Schering-Plough; December 11, 2007. <http://www.schering-plough.ca/English/news/media%20room/product%20news/default.aspx?18ItemID=348&Item=Virology>. Accessed September 9, 2011.

Fischer B. J Public Health Policy. 2000;21(2):187-210.

## Long-Term Treatment Is Associated With Positive Outcomes

- Patients (n=5577) receiving medication-assisted treatment with either methadone or buprenorphine in the United Kingdom

Probability That Treatment Reduces Overall Mortality



Cornish R et al. *BMC*. 2010; 31:1-5475.

## Prolonged Medication-Assisted Treatment Sustains Improvement

4 Studies of Various Treatment Lengths

<b>After 6 Months<sup>1</sup></b> (buprenorphine-only; n=690)	<b>After 12 Months<sup>2</sup></b> (buprenorphine-only; n=40)
<ul style="list-style-type: none"> <li>Heroin use decreased by 81%</li> <li>Codeine use decreased by 83%</li> <li>Benzodiazepine use decreased</li> </ul>	<ul style="list-style-type: none"> <li>32% improvement in occupational problems</li> <li>90% improvement in drug-related problems</li> <li>90% improvement in crime-related problems</li> </ul>
<b>After 18 Months<sup>3</sup></b> (buprenorphine/naloxone; n=176)	<b>After 2 to 5 Years<sup>4</sup></b> (buprenorphine/naloxone; n=53)
<ul style="list-style-type: none"> <li>Less likely to report using any substance or heroin</li> <li>More likely to be employed</li> <li>Improved on several psychosocial parameters</li> </ul>	<ul style="list-style-type: none"> <li>91% of urine samples were opioid negative</li> <li>96% of urine samples were cocaine negative</li> </ul>

1. Lavigne P et al. *Ann Med Interne (Paris)*. 2002; 153(suppl 3):1520-1526; 2. Kakko J et al. *Lancet*. 2003; 361(9368):682-688; 3. Paron TV et al. *Drug Alcohol Depend*. 2010; 109(1):56-62; 4. Fathi DA et al. *Am J Addict*. 2006; 117(2):116-120.

## CDHA Opioid Treatment Program

- One of our strongest programs!
- 92% retention at 1 year
- Capped at 75 patients
- Previous program evaluation (2003) showed:
  - Decreased use of drugs and alcohol (80% abstinent),
  - Decreased high risk behaviors (95% no longer using iv drugs, 98% not sharing needles)
  - Improved housing (84%)
  - Improved employment (61%)
  - Increased family support (81%)
  - Decreased criminal behavior (only 2% had committed a crime)

## 2011: Continuing Challenges

### CECA Report on MMT Policy Developments

- All provinces deliver MMT, but degree of access varies. Access is very limited among First Nations and in territories
  - Models range from comprehensive programs to private clinics
  - Funding sources are generally derived from provinces and fee-for-service, which operate in isolation from each other
  - Payment systems are inconsistent, confusing, and may not encourage best practices
- Current MMT system is overburdened
  - Too many patients, not enough physicians
  - Waitlists predominate
- Stigmatisation inhibits acceptance of pharmacotherapy by governments, physicians, the public, and patients

CECA=Canadian Executive Council on Addiction.  
Luce J, Strike C. <http://www.ccsa.ca/ceca/pdf/CECA%20MMT%20Policy%20Scan%20April%202011.pdf>. Accessed September 9, 2011.

## 2011: Continuing Challenges (cont)

### CECA Report on MMT Policy Developments

- Buprenorphine/naloxone use has not become widespread in Canada
- Inhibiting factors include:
  - Cost
  - CEDAC Common Drug Review recommendation for use only when methadone is contraindicated
  - Availability limited to only physicians licensed to prescribe methadone (except in Ontario)
  - Lack of practitioner experience

CEDAC=Canadian Expert Drug Advisory Committee.  
Luce J, Strike C. <http://www.ccsa.ca/ceca/pdf/CECA%20MMT%20Policy%20Scan%20April%202011.pdf>. Accessed September 9, 2011.

## Safe injection sites

- Safe injection facilities provide sterile injection equipment, information about drugs and health care, treatment referrals
- Clean environments where IDUs can inject drugs + access to medical staff (resuscitation from overdoses)



Country	Number of supervised consumption facilities	Number of cities with supervised injecting facilities	Number of consumption facilities for injectors only	Number of facilities with injecting and inhalation areas
Switzerland	12	7	4	8
Germany	25	14	11	13
The Netherlands	22	12	0	22
Spain	3	3	3	0
Total	62	36	18	43

- First site opened in Berne, Switzerland in the early 1980's.
  - Currently approximately 90 around the world (mostly Europe)
- (European report on drug consumption rooms, European Monitoring Centre for Drugs and Addiction, 2004)





## Are the facilities being used?

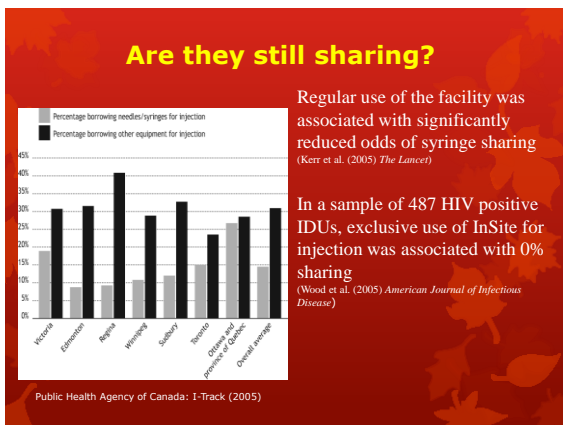
- Pre-InSite interview of 587 IDUs in Vancouver's Downtown Eastside: 36.6% reported that they would be willing to use the facility, 49% said they would not go (Wood et al. (2003) *Journal of Acquired Immune Deficiency Syndromes*)
- After a year of InSite operation: 45% of a 400 IDU sample ever used the facility (Wood et al. (2005) *American Journal of Preventative Medicine*)

~12,000 IDUs in Vancouver (~4000 Downtown Eastside)  
InSite has an average of 491 injections per day  
([http://supervisedinjection.vch.ca/research/supporting\\_research/user\\_statistics](http://supervisedinjection.vch.ca/research/supporting_research/user_statistics))

Rate of InSite use among a sample of 400 IDUs:

- 11 used it for all their injections (0.02%)
- 19 used it for >75% of injections (0.05%)
- 102 for <25% of their injections (25%)

(Wood et al. (2005) *American Journal of Preventative Medicine*)



## Overdoses?

- March 1, 2004 - February 6, 2008: 766,486 injections, 1004 overdose events (1.31 per 1,000 injections). None resulted in death (Milroy et al. (2008) *PLoS ONE*)
- Prospective study with the SEOSI cohort: At baseline pre-InSite, 638 (58.53%) reported a history of non-fatal overdose. 3 follow-ups interviews, every 6 months from 2003 to 2005. The proportion of individuals reporting non-fatal overdose in the last six months remained approximately constant (Milroy et al. (2008) *The American Journal of Drug and Alcohol Abuse*)

**No decrease in non-fatal overdoses suggests that safer injection techniques are not being learned**

## Blood-borne disease?

- Scientific Evaluation of Supervised Injecting (SEOSI) cohort at InSite - 17% HIV+ and 87.6% HCV+ (Tyndall et al. (2006) *Harm Reduction Journal*; Wood et al. (2005) *Journal of Public Health*)
- There have been **NO** prospective studies with this population to assess changes in HIV and HCV infection
- Cost-benefit analysis of InSite used mathematical modeling to explore the number of new HIV infections and deaths that have been prevented each year since InSite opened in 2003

Estimated that InSite prevents **35 new cases of HIV** and almost 3 HIV-related deaths each year

(Andresen & Boyd (2010) A cost-benefit and cost-effectiveness analysis of Vancouver's supervised injection facility. *International Journal of drug policy*, 21(1):70-6)

## Conclusions

- InSite attracts primarily "high risk" users – low % of daily injections:

Reduction in blood-borne disease: Mathematical modeling suggests this is the case but prospective data is lacking

Preventing overdoses: non-fatal overdose remains prevalent but consequences are controlled

- Referral for treatment does occur, but clients are not followed up



# Heroin-Assisted Therapy (HAT) \$8,115,661 study

## HAT Studies

Lead investigator (funding period)	Canada	Germany	The Netherlands	Spain (Andalusia)	Spain (Catalonia)	Switzerland	United Kingdom	
Schroten et al 2009	Schroten et al 2009	Naber, D 2003-2004	van den Brink, W 1999-2002	March, JC 2003-2004	Casas, R 2004-2005	Boehm, J 1996-2000	String, J 2006-2008	
Design	RCT, multicenter	RCT, multicenter, stratified	2 RCTs, multicenter	RCT	RCT	RCT, prospective cohort, cohort follow up	RCT, multicenter	
Intervention/ main study period	Injected heroin + oral methadone vs. oral methadone (open-label) + oral methadone vs. oral methadone 12 months	Injected heroin + oral methadone (open-label) vs. oral methadone 12 months	Injected heroin + oral methadone vs. oral methadone (open-label) vs. oral methadone 12 months	Injected heroin + oral methadone vs. oral methadone 9 months	Oral heroin (HT) vs. oral methadone vs. oral methadone	Injected heroin + oral methadone, oral methadone, oral morphine 2 years (ongoing)	Injected heroin vs. oral methadone vs. oral methadone 8 months	
Participants	Opium-dependent persons, predominantly using injected heroin on regular basis, and were not reached by the health care system. Sample 340	Heroin addicts, with concurrent health problems, who had not responded sufficiently to methadone treatment or were not reached by the therapeutic system. Sample 1,832	Heroin-dependent patients in MMT with severe concurrent problems related to drug misuse, not responding to methadone. Sample 349	Regular opium-injecting people, with severe concurrent problems related to drug misuse, not responding to methadone. Sample 62	Regular heroin users, not responding to MMT in the past, not currently using methadone. Sample 62	Severe heroin dependent persons to whom other therapies had failed or the health care system or other another level of therapy. Sample 1,273 (247)	Regular heroin users, currently in methadone, who do not benefit from conventional substitution treatment. Sample 100	Regular injecting heroin users, currently in methadone, who do not benefit from conventional substitution treatment. Sample 100
Outcomes	Retention	Improvement by 20% in physical or mental health and 20% reduction of street heroin use (and no increase in cocaine use)	Improvement by 40% in physical, mental or social health and no increase in cocaine use	Physical health, Drug related problems, Street drug use, Risk behavior, Psychosocial adjustment, Criminal activities	Retention	Treatment retention	Reduction of illicit heroin and other substance use	

**Conclusions:** Statistically positive outcome measures favouring HAT over methadone, however results are difficult to interpret, due to designs, and definition of good outcomes

## The NAOMI Project

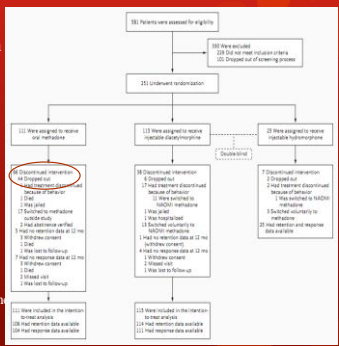
- Components of treatment
- HIV and anti-microbial medications
  - physician, nursing, social work, addiction counselling
  - pain management in cases of acute or chronic pain

- High-quality medical services
- low patient-to-staff ratio
  - highly trained and specialized medical team
  - outreach support (eg.: accompaniment to specialty care)
  - on call and weekend support

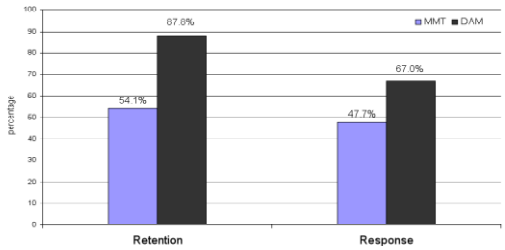
Mean heroin dose 392.3 mg/day, 27% received supplements of methadone 34 mg/day; MMT group – mean methadone dose of 96mg/day

## Reaching the Hardest-to-Reach Treating the Hardest-to-Treat

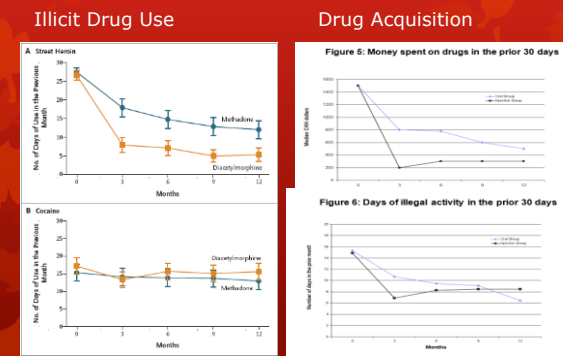
- Selection Criteria - long-term user, significant health and social problems, minimum 2 prior unsuccessful treatment attempts
- ITT analysis
- Outcomes: (\*beware unusual definitions)



## The NAOMI Project - Results



## Results - A closer look



## Adverse Events

79 Serious Adverse Events (Overdoses, Infections, Seizures)

- 18 in MMT in which 0 were related to the study drug
- 51 in Heroin group in which 24 were related to the study drug
  - 11 overdoses (11/24 = 46%)
  - 7 seizures (7/24 = 29%)
- 10 in HMO in which 5 were related to the study drug
  - 2 overdoses (2/5 = 40%)
  - 2 abscesses and cellulitis (2/5 = 40%)

## Limitations & Implications

- difficult to conclude that HAT is more effective than MMT in this sample (NB: trial was biased towards HAT due to design - high drop-out from MMT in ITT analysis)
- high cost, specialized injection rooms and security
- risk for severe adverse events requires on site medical supervision, unlike MMT
- high polysubstance abuse in most IDU populations – increased risk for seizures, overdoses and poor outcomes
- repeated cycles of intoxication and withdrawal, hypoxia with unknown neurocognitive consequences. Multiple daily visits to the HAT site – implications for rehabilitation? employment?
- little information on psychological status, and differential outcome for patients with *concurrent disorders*

## Concerns in relation to HAT

Failure to convincingly demonstrate effectiveness of the interventions, as well as the use of procedures that maintain high dose administration of short-acting, potent drugs of abuse among vulnerable populations:

- What harms are being reduced? Harm to whom? Trade-offs?
- The use of short-acting drugs like heroin are not optimal substitution or maintenance strategies
  - frequent need for re-administration, repeated cycles of intoxication and withdrawal are disruptive to brain and behaviour
- There is no disengagement from the rush (euphoria or intoxication) and little change in addiction (cycle of drug seeking, drug using, intoxication, and withdrawal.....)

## Concerns continued...

- For those that don't do well in HAT, what then? Do we understand why treatment fails?
- Overall there is a very high prevalence of concurrent disorders (Axis I and Axis II) among addicts
  - hyperalgesia and hypersensitivity to sensory stimuli?
  - poor affect regulation, intolerance of emotions?
- Concurrent mental disorders are associated with poorer outcomes, including lower rates of treatment retention and higher rates of relapse to drug use during and following treatment (Compton et al., 2003; Mason et al., 1998; Rounsaville et al., 1986; Havard et al., 2006; Mills et al., 2007)

## Coming Soon

**salome**  
Study to Assess Long-term Opioid Maintenance Effectiveness

Heroin versus dilaudid - injectable

## Conclusions

- Opioid Dependence is a significant serious public health problem in Canada that is growing steadily
- There are effective evidence based interventions combining pharmacotherapy and psychosocial treatments, but both are required for success
- Ideally, treatment teams should be multi-disciplinary (physicians, nurses, social work, psychology, OT and RT)
- Buprenorphine should be used initially due to its superior side effect profile, safety profile and lower abuse/diversion risk
- Patients failing buprenorphine should then be treated with methadone
- There should be provincial oversight and accountability for treatment programs