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
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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
  • Progressive
  • Relapsing
  • Compulsive
• Characterized by continued use despite physical or psychological problems

Components of Addictive Behavior

<table>
<thead>
<tr>
<th>Drug Abuse Has Behavioral, Cognitive, and Affective Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Considerations</td>
</tr>
<tr>
<td>Behavioral</td>
</tr>
<tr>
<td>• Help patients find alternative nondrug reinforcers and behaviors</td>
</tr>
<tr>
<td>Cognitive</td>
</tr>
<tr>
<td>• Help patients develop new ways of thinking about themselves and how they interact with the world</td>
</tr>
<tr>
<td>• Help patients view themselves as drug nonusers</td>
</tr>
<tr>
<td>Affective</td>
</tr>
<tr>
<td>• Help patients deal with people, places, emotions, events, and things that may trigger relapse due to their close and lengthy association with drug taking</td>
</tr>
</tbody>
</table>
What Is Opioid Dependence?

**Definition of Opioid Dependence**
- Considered a chronic, relapsing brain disease
- Associated with:
  - Pervasive changes in cognitive and drug-rewarding circuits of the brain
  - Significant alterations at the molecular, cellular, and structural levels
  - Changes to brain function that persist after drug use has ceased
  - Compulsive drug-seeking and abuse

Relapse Rates Are Similar to Other Chronic Diseases

Comparison With Other Chronic Diseases

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Diabetes, Asthma, and Hypertension</th>
<th>Drug Dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well studied</td>
<td>✅</td>
<td>✅</td>
</tr>
<tr>
<td>Chronic disorder</td>
<td>✅</td>
<td>✅</td>
</tr>
<tr>
<td>Predictable course</td>
<td>✅</td>
<td>✅</td>
</tr>
<tr>
<td>Effective treatments</td>
<td>✅</td>
<td>✅</td>
</tr>
<tr>
<td>Curable</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Heritable</td>
<td>✅</td>
<td>✅</td>
</tr>
<tr>
<td>Requires continued care</td>
<td>✅</td>
<td>✅</td>
</tr>
<tr>
<td>Requires adherence to treatment</td>
<td>✅</td>
<td>✅</td>
</tr>
<tr>
<td>Requires ongoing monitoring</td>
<td>✅</td>
<td>✅</td>
</tr>
<tr>
<td>Influenced by behavior</td>
<td>✅</td>
<td>✅</td>
</tr>
<tr>
<td>Tends to worsen if untreated</td>
<td>✅</td>
<td>✅</td>
</tr>
</tbody>
</table>

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

- Opioid molecules attach to μ-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

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
  - Drugs of abuse, such as opioids, manipulate the reward circuit, causing the person to feel that use of these chemicals is necessary for survival
Neuroadaptation of Dopamine (DA) D₂ Receptors

Positron emission tomography showing the effects of heroin dependence on brain DA D₂ receptors

The Multiple Components of Drug Abuse

- Drug abuse has multiple components:
  - Neurobiologic
  - Behavioural, cognitive, and affective
  - Treatment must address each component

Cycle of Addiction: Neurobiological Aspects

- Acute reinforcing effects
- Tolerance and withdrawal
- Craving and relapse

Chemical Changes: Withdrawal

Withdrawal Symptoms and Associated Brain Neuroadaptation

- Symptoms: Dysphoria, Stress, Depression, Anxiety, Pain
- Brain Adaptation
- Dopamine, Opioid peptides, GABA, Serotonin, Corticotropin-releasing factor

Understanding the Scope of the Problem

Global Illicit Intravenous Opioid Use

- Estimated IDUs (000)
  - USA: 90,000-1,250,000
  - Canada: 75,000
  - Australia: 75,000
  - EU: 850,000-1,300,000

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

Prescription Opioid Use in Canada

- Worldwide ranking in per capita consumption (2005):
  - Hydromorphone: #1
  - Morphine and oxycodone: #2
  - Hydrocodone: #3
- In 2009, the International Narcotics Control Board:
  - Canada was the:
    - Largest importer of hydromorphone, the 2nd largest importer of cocaine, and the 3rd largest importer of morphine
    - 2nd largest morphine, hydromorphone, oxycodone, and fentanyl 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

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

Nonmedical Use of Prescription Opioids

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

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

Nonmedical Use of Prescription Opioids

Canada Trend 2002 to 2005

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

Canada

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

205 220 285 334 352 375 463 693 753

26 28 30 32 34 36 38 40 42

0 50 100 150 200 250 300 350 400 450 500

0 10 20 30 40 50 60 70 80 90 100

0 10 20 30 40 50 60 70 80 90 100

0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0

- POs=prescription opioids.
Per Capita Consumption of Hydromorphone (Dilaudid) by Country in 2010

Opioid Dependence

Prevalence of Prescription Opioid Use in Québec

- 25% of the Quebec Public Prescription Drug Insurance Plan were surveyed in 2005.
- A 2003 study estimated that 38,307 to 109,058 people in Quebec used prescription opioids for nonmedical purposes.
- Estimates suggest that >10% of the people in Quebec who are dispensed opioids may use them for nonmedical purposes.

Provincial comparison: Primary dependency

Note: No statistically significant differences noted

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

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

- Free from Friends/Family
- Bought/Took from Friends/Family
- One Doctor
- >One Doctor
- Drug Dealer/Stranger
- Internet

Source Where Friend/Relative Obtained

- One Doctor
- >One Doctor
- Free from Friend/Family
- Bought/Took from Friend/Family
- Drug Dealer/Stranger
- Other

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 sequelia (Hep C, HIV, cellulitis)
Deaths Related to Opioid Analgesics Use in Ontario, 1991 to 2004 (Dhalla et al., 2009)

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 pharmacopoeia
- 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 – Portuguese control trade from Calcutta to Canton
- Portuguese 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 government 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 as Medicine

- 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-medicinal 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)

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

<table>
<thead>
<tr>
<th>Cost per Individual ($)</th>
<th>Cost ($) (million) per 15,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>$6,000</td>
<td>$10</td>
</tr>
<tr>
<td>$44,000</td>
<td>$650</td>
</tr>
<tr>
<td>$55,000</td>
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</tbody>
</table>

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 1st 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

- 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

- 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

- 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 process 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

Components of Treatment: Pharmacotherapy and Psychosocial Intervention

**Pharmacotherapy**
- Can control symptoms by normalizing brain chemistry

**Psychosocial Intervention**
- Essential to change behaviors 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

The Importance of Counseling

- Counseling is the cornerstone of opioid dependence treatment
- Patients may benefit from combined pharmacotherapy and counseling
- 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
- 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
- Adding counseling support to medically assisted withdrawal improves treatment completion and decreases opioid use

Treatment Goals

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

Treatment Components and Considerations

<table>
<thead>
<tr>
<th>Treatment Component</th>
<th>Treatment Considerations</th>
</tr>
</thead>
</table>
| **Pharmacotherapy** | - Can control symptoms by helping to normalise brain chemistry\(^1,2\)  
- Not sufficient treatment alone and has a higher risk of relapse compared with patients receiving contingency-based counseling\(^1,2\) |
| **Counseling Intervention** | - Essential to change behaviors and responses to environmental and social cues that significantly impact relapse  
- Can be equally effective as an adjustment in medication dose in response to renewed instability during treatment\(^4\) |
Counseling Improves Outcomes in Other Chronic Diseases

- Depression\textsuperscript{1-3}
- Panic disorder\textsuperscript{4}
- Nicotine dependence\textsuperscript{5,6}
- Alcohol dependence\textsuperscript{6,7}
- Obesity\textsuperscript{8}

Counseling Techniques

- Counselors can use a variety of evidence-based approaches\textsuperscript{1}:
  - Cognitive behavioral therapy
  - Individualised drug counseling
  - Motivational enhancement therapy
  - Supportive-expressive therapy
  - Contingency management

Importance of Pharmacotherapy

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

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 narcan challenge test\textsuperscript{*} 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)

\textsuperscript{*}See next page for Narcan Challenge Test

RATIONAL 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

Percentage Completing Inpatient Detoxification

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

Fraser et al., unpub.

Retention - Inpatient Detoxification

Fraser et al., pending

Retention - Outpatient Treatment

Paraheratakis et al., 2000

Experimental Studies of Heroin Detoxification

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Detox Method</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hunt &amp; Odhner, 1962</td>
<td>1912</td>
<td>Non-opioid</td>
<td>95% re-addicted at 6 months follow-up</td>
</tr>
<tr>
<td>Berke &amp; Noyce, 1964</td>
<td>53</td>
<td>Non-opioid, 2-4 weeks, outpatient</td>
<td>66% re-addicted at 2 years follow-up</td>
</tr>
<tr>
<td>Dewey &amp; Ben-Aria, 1968</td>
<td>100</td>
<td>Heroin, outpatient</td>
<td>86% re-addicted at 6 months follow-up</td>
</tr>
<tr>
<td>Kate et al., 1972</td>
<td>325</td>
<td>Methadone, 10-40 days, outpatient</td>
<td>97% failed to complete detox protocol</td>
</tr>
<tr>
<td>Canada, 1972</td>
<td>157</td>
<td>Methadone, 30-40 days, outpatient</td>
<td>93% re-addicted at 6 months follow-up</td>
</tr>
<tr>
<td>Stimmel et al., 1977</td>
<td>355</td>
<td>Methadone, 2 months - 1 year, outpatient</td>
<td>72% re-addicted at 2 years follow-up</td>
</tr>
<tr>
<td>Del Campo et al., 1977</td>
<td>91</td>
<td>Methadone + sedatives, 21 days, outpatient</td>
<td>Only 4% completed detox, 100% re-addicted at 3 mo</td>
</tr>
<tr>
<td>Grush et al., 1986</td>
<td>50</td>
<td>Methadone, inpatient or outpatient, detox</td>
<td>Outpatient - 17% completion, Inpatient - 81% No follow-up</td>
</tr>
<tr>
<td>Stine et al., 1989</td>
<td>170</td>
<td>Methadone or clonidine, outpatient</td>
<td>Methadone - 75% completion, clonidine - 44% No follow-up</td>
</tr>
<tr>
<td>Hall &amp; Ross, 1991</td>
<td>?</td>
<td>Methadone, outpatient</td>
<td>82% re-addicted at 10 month follow-up</td>
</tr>
</tbody>
</table>

A 33-Year Follow-up of Narcotics Addicts

Tilting Hart, PhD, Valentina Hofman, PhD; Christine E. Grella, PhD; M. Douglas Anglin, PhD

Background: 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 85 male heroin addicts admitted to the California state penal system from 1955 to 1974. The study used a longitudinal design, with data collected at 6-month intervals over 33 years. The sample was representative of the California prison population and included a mix of prisoners who had served short or long sentences, as well as those who had been convicted of multiple offenses.

Results: The study found that, on average, the percentage of heroin use decreased over time. The percentage of heroin use was highest in the first year after release from prison, but it decreased sharply in the following years. By the end of the 33-year follow-up, the percentage of heroin use was less than 10%.

Conclusions: The study provides evidence that long-term follow-up is necessary to understand the impacts of prison on heroin use and other substance use. The findings suggest that prisons can play a role in reducing heroin use, but further research is needed to understand the mechanisms through which this occurs.
From Hser et al., 2001.

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

Co-morbidity in Opiate Dependence

<table>
<thead>
<tr>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Axis I Mood D/O Anxiety D/O Axis II</td>
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</tr>
</tbody>
</table>

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

A History of Polarised Perspectives

Criminal Model
- Opioid addicts subjected to mandatory treatment until abstinence achieved
- Promoted by law enforcement and government sector

Medical Model
- Treatment rather than punishment
- Promoted by addiction treatment sector

Phases of Drug Treatment in Canada

1900 to 1940s: Opioid Dependence and Limited Treatment Options
- Moralistic attitudes, limited understanding, little attention or access to treatment
- Post-World War II: opiate addiction replaces opium and cocaine addiction, led to:
  - 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
Disillusionment over effective treatment strategies for opioid dependence sparked a drug treatment movement.

Law enforcement was at odds with medical sector over benefits of opioid maintenance treatment.

MMT proposed and established as an alternative treatment in opioid addiction management.

MMT programs began to expand in the late 1960s.


After NCA, substantive decline in MMT.

By 1982, only 62 physicians providing MMT to 177 patients.

The Le Dain Commission recommended MMT organization 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: About 1,200 opiate addicts in MMT.

After the NCA, substantive decline in MMT.

66% decline in addicts in 1990s.

0.20% received 0–40 mg.

Suboxone approved by Health Canada for medication-assisted treatment.

The International Working Group on Substance Abuse published their impact.

Explanations for decline in MMT after 1970s:

- Results of 1982 survey of Canadian physicians.
- Number of physicians actively prescribing MMT dropped to 50 in 1992.
- For opioid dependence, there is no evidence of a dose threshold effect.
- For opioid dependence, the daily dose is not predictive of effectiveness or relapse.
- By 1982, only 62 physicians providing MMT to 177 patients.

1940s: Treatment reforms occurred to reduce costs to society.

1972: Federal guidelines (amendments to the Narcotic Control Act [NCA]) made MMT unattractive to physicians.


1990s: Increase accessibility to substance abuse information and intervention needs for positive results.

1970: Canada’s drug strategy launched.

The International Working Group on Substance Abuse published their impact.

Opiate Users in Methadone Treatment in Canada, 1972 to 1982

- Results of 1982 survey of Canadian physicians.
- Number of physicians actively prescribing MMT dropped to 50 in 1992.
- A daily dose of >60 mg is minimum needed for positive results.
- 22% received >60 mg (now is 60% in Prairies, 54% in Ontario, and >60 mg in West).
- 24% received <40 mg.
- 56% received <20 mg.

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

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Long-Term Treatment Is Associated With Positive Outcomes

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

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

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)

2011: Continuing Challenges (cont)

CECA Report on MMT Policy Developments (cont)

- 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

Prolonged Medication-Assisted Treatment Sustains Improvement

4 Studies of Various Treatment Lengths

- After 6 Months:
  - Heroin use decreased by 81%
  - Cocaine use decreased by 53%
  - Benzodiazepine use decreased

- After 12 Months:
  - 32% improvement in occupational problems
  - 90% improvement in drug-related problems
  - 90% improvement in crime-related problems

- After 2 to 5 Years:
  - 91% of urine samples were opioid negative
  - 96% of urine samples were cocaine negative

2011: Continuing Challenges (cont)

- First site opened in Berne, Switzerland in the early 1980's.
- Currently approximately 90 around the world (mostly Europe)
- (European report on drug consumption, European Monitoring Centre for Drugs and Addiction, 2004)
North-America’s first safe injection facility opened in Vancouver’s Downtown Eastside in 2003

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. (2005) 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://www.supervisedinjection.vch.ca/research/supporting_research/user_statistics)

Are they still sharing?
Regular use of the facility was associated with significantly reduced odds of syringe sharing (Kerr et al. (2005) The Lancet)

Overdoses?
* March 1, 2004 - February 6, 2008: 766,486 injections, 1004 overdose events (1.31 per 1,000 injections). None resulted in death (Milloy 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 (Milloy et al. (2008) The American Journal of Drug and Alcohol Abuse)

Blood-borne disease?
- Scientific Evaluation of Supervised Injecting (SEOSI) cohort at InSite - 17% HIV+ and 87.6% HCV+ (Tyndall et al. (2006) HIV 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

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

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-retroviral medications
- Physician, nursing, social work, aftercare 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 (e.g., 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 96 mg/day

The NAOMI Project - Results

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)
1) retention in treatment (*But not necessarily in the trial)
2) response – 20% improvement on ASI scores for illicit drug use or crime

Results – A closer look

Illicit Drug Use

Drug Acquisition

Figure 5: Money spent on drugs in the prior 30 days

Figure 6: Days of illegal activity in the prior 30 days
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 it’s 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