North American Opiate Medication Initiative (NAOMI)

Multi-Centre, Randomized Controlled Trial of Heroin-Assisted Therapy for Treatment-Refractory Injection Opioid Users

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Funding: Canadian Institutes of Health Research with additional support from the Canada Foundation for Innovation, the Canada Research Chairs Program, the University of British Columbia, Providence Health Care, the University of Montreal, Centre de Recherche et Aide aux Narcomanes, the Government of Quebec, Vancouver Coastal Health Authority and the BC Centre for Disease Control.
Opioid dependence is a **chronic** relapsing disease.

**Substitution** treatment is the most effective approach.

**Methadone** works, however not for everyone.

**More formulations** need to be tested and made available to reach people that is not attracted/retained/responding to methadone (i.e. buprenorphine, morphine, diacetylmorphine, etc.)

Available clinical evidence from European studies indicates that **prescribed heroin for injection** is effective, feasible and safe.
Design: Randomised controlled trial

Setting: Vancouver and Montreal

Participants: 251

Treatment period: 12 months (+ 3 months transition)

Interventions:

- Injected diacetylmorphine (or hydromorphone) (plus oral methadone if deemed appropriate)
- Optimized oral methadone

Recruitment started: March 2005

Last patient finishing active treatment: June 2008
Study Design

Total Sample

Randomization

Oral Methadone (45%)

Injectable DAM (45%)

Injectable HMO (10%)

Double blind

12 months evaluation

Treatment efficacy
Between groups comparison

Validation of reported illicit heroin use
Within group comparison
Inclusion Criteria

“chronic injection opioid users who did not benefit previously from the available therapies”:

› DSM-IV opioid dependence
› ≥ 25 yrs old
› ≥ 5 yrs opioid dependence
› regular predominant use of heroin in prior year
› at least 2 prior treatment attempts including at least one MMT reaching ≥ 60 mg for at least 30 days in a 40 day period
› no opioid maintenance treatment in the prior 6 months

Two Primary Outcome Measures

Treatment Retention

- received study medication (DAM, HMO, and/or MMT) on at least 10 of the 14 days prior to the 12-month date; or
- confirmed to be enrolled in a detoxification program at the 12-month date; or
- confirmed to be enrolled in a drug-free program at the 12-month date; or
- confirmed to be abstinent at the 12-month date.

Treatment Response

- based on European Addiction Severity Index scores, displays a 20% improvement in illicit drug use or legal status scores or both from baseline; and
- a deterioration of 10% or greater on at most one of the seven remaining composite scores

all those not meeting these criteria or lost will be “not retained” and “not responders”.
Screening and Recruitment

Pre-Screening

• 1587 individuals contacted the study
  • 1053 Vancouver
  • 534 Montreal
• pre-screened on telephone
• 1006 (63%) ineligible on pre-screen
  • 85% due to MMT criteria
• 581 invited to full screening
Equivalent of downtown Eastside
1. Profile of the Participants

<table>
<thead>
<tr>
<th></th>
<th>Vancouver (n=192)</th>
<th>Montreal (n=59)</th>
<th>Total (n=251)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Yrs)</td>
<td>40.9</td>
<td>35.6</td>
<td>39.7</td>
</tr>
<tr>
<td>Female</td>
<td>38.5%</td>
<td>39.0%</td>
<td>38.6%</td>
</tr>
<tr>
<td>Unstable Housing</td>
<td>88.5%</td>
<td>22.0%</td>
<td>72.9%</td>
</tr>
<tr>
<td>Aboriginal</td>
<td>31.3%</td>
<td>-</td>
<td>23.9%</td>
</tr>
<tr>
<td>Charged for Crime (Lifetime)</td>
<td>97.9%</td>
<td>83.1%</td>
<td>94.4%</td>
</tr>
<tr>
<td>Spent on Drugs (Median in Past 30 Days)</td>
<td>$1500</td>
<td>$1200</td>
<td>$1500</td>
</tr>
</tbody>
</table>

## 2. Profile of the Participants

<table>
<thead>
<tr>
<th>Mean</th>
<th>Vancouver (n=192)</th>
<th>Montreal (n=59)</th>
<th>Total (n=251)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin (Days in last 30)</td>
<td>26.8</td>
<td>25.4</td>
<td>26.5</td>
</tr>
<tr>
<td>Crack (Days in last 30)</td>
<td>16.9</td>
<td>2.3</td>
<td>13.4</td>
</tr>
<tr>
<td>Cocaine Powder (in last 30)</td>
<td>5.1</td>
<td>4.9</td>
<td>5.1</td>
</tr>
<tr>
<td>Speedball (Days in last 30)</td>
<td>3.2</td>
<td>1.1</td>
<td>2.7</td>
</tr>
<tr>
<td>Times Injecting per Day</td>
<td>5.1</td>
<td>3.6</td>
<td>4.8</td>
</tr>
<tr>
<td>Years of Injecting Drugs</td>
<td>17.4</td>
<td>13.4</td>
<td>16.5</td>
</tr>
</tbody>
</table>
### 3. Profile of the Participants

<table>
<thead>
<tr>
<th></th>
<th>Vancouver (n=192)</th>
<th>Montreal (n=59)</th>
<th>Total (n=251)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis C Positive</td>
<td>66.1%</td>
<td>52.5%</td>
<td>62.9%</td>
</tr>
<tr>
<td>HIV Positive</td>
<td>9.9%</td>
<td>8.6%</td>
<td>9.6%</td>
</tr>
<tr>
<td>Attempted Suicide Ever</td>
<td>28.1%</td>
<td>40.7%</td>
<td>31.3%</td>
</tr>
<tr>
<td>Prior MMT Attempts (median)</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Prior Other Treatments (median)</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Overdoses (lifetime)</td>
<td>3.5</td>
<td>5.9</td>
<td>4.1</td>
</tr>
</tbody>
</table>
Follow-up of the Participants

- critically important to achieve maximal follow-up
- independent of treatment retention
- of 251 people
  - only 11 did not complete 12-month assessment
- research completion rate = 95.6%
- tribute to the dedication
  - of the participants
  - of the NAOMI staff
# The Primary Outcomes

<table>
<thead>
<tr>
<th>Outcome Description</th>
<th>MMT (n=111)</th>
<th>DAM (n=115)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in illicit drug use or other illegal activity – n (%)</td>
<td>53 (47.7)</td>
<td>77 (67.0)</td>
<td>1.40 (1.11-1.77; p=0.004)</td>
</tr>
<tr>
<td>Reduction in illicit drug use alone – n (%)</td>
<td>15 (13.5)</td>
<td>26 (22.6)</td>
<td></td>
</tr>
<tr>
<td>Reduction in other illegal activities alone – n (%)</td>
<td>6 (5.4)</td>
<td>1 (0.9)</td>
<td></td>
</tr>
<tr>
<td>Reduction in both illicit drug use and other illegal activities – n (%)</td>
<td>32 (28.8)</td>
<td>50 (43.5)</td>
<td></td>
</tr>
<tr>
<td>Retention in addiction treatment – n (%)</td>
<td>60 (54.1)</td>
<td>101 (87.8)</td>
<td>1.62 (1.35-1.95; p&lt;0.001)</td>
</tr>
<tr>
<td>NAOMI DAM – n (%)</td>
<td>-</td>
<td>77 (67.0)</td>
<td></td>
</tr>
<tr>
<td>NAOMI MMT – n (%)</td>
<td>45 (40.5)</td>
<td>21 (18.3)</td>
<td></td>
</tr>
<tr>
<td>Other MMT – n (%)</td>
<td>13 (11.7)</td>
<td>2 (1.7)</td>
<td></td>
</tr>
<tr>
<td>Other treatments – n (%)</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Abstinence – n (%)</td>
<td>2 (1.8)</td>
<td>1 (0.9)</td>
<td></td>
</tr>
</tbody>
</table>

“Street” Heroin Use

![Graph showing the decrease in mean days of heroin use in the prior month over 12 months, comparing Oral Group and Injection Group.

- **Oral Group**: The line for the Oral Group is shown in purple and starts high at around 30 days in the first month, then decreases sharply to around 5 days by the end of 12 months.
- **Injection Group**: The line for the Injection Group is shown in black and starts lower than the Oral Group, around 5 days in the first month, and decreases gradually to around 3 days by the end of 12 months.

The graph indicates a significant reduction in heroin use over time, with the Injection Group showing a more consistent decrease compared to the Oral Group.
Cocaine Use

Number of days in the prior month

Months

Oral Group
Injection Group
MAP Physical Health

MAP-PHH mean score over time for two groups:
- Oral Group
- Injection Group

Months: 0, 3, 6, 9, 12
MAP Psychological Health

- Oral Group
- Injection Group

MAP-PSH mean score vs Months

- 0 months
- 3 months
- 6 months
- 9 months
- 12 months
Safety

- addiction medicine specialists
- nursing
- safety procedures
  - pre and post-injection assessments
  - time and identifier bar codes
  - pharmaceutical GMP
  - emergency protocols
Adverse Events

• 109,171 treatment injections
• common expected side effects:
  – drowsiness
  – local histamine reaction (itchiness, pins and needles)
• 7 episodes of serious seizures
  – previous history of seizures
  – often associated with cocaine use
• 13 episodes of serious over-sedation
  – treated with O₂ and narcan
  – no hospitalization
  – often associated with benzodiazepines
Hydromorphone

- Over the 12 month period at which no use of illicit heroin was reported in the prior 30 days in 46 research visits (17 different individuals), none of the 46 urine samples obtained at these visits tested positive for monoacetylmorphine or morphine.

- Of 23 participants in the HDM group who were asked at 12 months which drug they thought they were receiving, none reported that it was definitely HDM.

- Urine test show higher percentage of positive test for monoacetylmorphine and morphine in the MMT group compared with HDM

<table>
<thead>
<tr>
<th></th>
<th>MMT</th>
<th>HDM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>MONOACETYLMPHINE*</td>
<td>Negative</td>
<td>264</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>83</td>
</tr>
<tr>
<td>MORPHINE*</td>
<td>Negative</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>212</td>
</tr>
</tbody>
</table>

*<0.001

Conclusions

- Heroin-assisted therapy
  - Safe
  - Highly effective
    - very high retention
    - decreased illicit heroin use
    - decreased criminal activity
    - decreased spending on drugs
    - improved physical health
    - improved psychological health

- High retention and response
  - difficult-to-treat group
  - heroin assisted therapy and optimized MMT
  - both have important roles to play
  - Hydromorphone may be an option
NAOMI Team

• Suzanne Brissette
• Bohdan Nosyk
• Paul-André Guevremont
• Martin Schechter
• Serge Brochu

• Jill Chettiar
• Jeff Lawlor
• Nancy Laliberté
• David Marsh
• Pascal Schneeberger

• Julie Schneiderman
• Kurt Lock
• Aslam Anis
• Candice Gartry
• Eugenia Oviedo-Joekes
• Daphne Guh

and a large dedicated staff

most of all, thank you to all our participants