The cost-effectiveness of diacetylmorphine compared to methadone in chronic, treatment refractory opioid dependent individuals

Nosyk B, Guh DP, Bansback NJ, Oviedo-Joekes E, Marsh DC, Brissette S, Miekleham E, Schechter MT, Anis AH. For the NAOMI Study Team
Background

- Opioid dependence is a chronic relapsing disease
- Substitution treatment is the most effective approach
- Methadone works, however not for everyone
- Available clinical evidence from European studies indicates that prescribed heroin for injection is effective, feasible and safe
- A challenge to the use of diacetylmorphine has been the increased direct costs of therapy over conventional substitution treatment
NAOMI Trial

• North American Opiate Medication Initiative (NAOMI): RCT comparing injectable diacetylmorphine (DAM) to optimized methadone maintenance treatment (MMT) in subjects with long-standing opioid dependence

• The study reported the rate of retention in addiction treatment at 12 months in DAM was 87.8%, as compared with 54.1% in MMT
Objective

• To determine the long-term cost-effectiveness of a policy to introduce DAM versus conventional MMT for chronic treatment-refractory opioid dependent individuals.
Decision Analytic Model

Allocated to MMT

Cycle = 3

Death

MMT₃

Relapse₃

Abstinence

MMT₄

Cycle, j = 4-6

Allocated to DAM

Death

DAM₁

MMT-PD₃

Relapse₃

Abstinence

DAMⱼ-₂
Primary Data Sources

- NAOMI data
  - Time to discontinuation of treatment (DAM, MPD, not MMT due to lottery effect)
  - Direct Costs of treatment, health resource use
  - EQ-5D for calculation of QALYs
  - Data on criminal activity collected alongside NAOMI study retrieved from local police departments

- BC MMT Outcome Study
  - Time to discontinuation of MMT (among those in 3rd episode)
  - Time to discontinuation of relapse
  - HRs for successive episodes
Supplementary Data Sources

• Swiss HAT cohort study
  • Probability of transition from DAM to relapse, MMT, abstinence, death (Rehm, 2001)
  • Mortality: SMR during HAT (Rehm, 2005)

• Other key references
  • Rate of HIV seroconversion: Bayoumi & Zaric, 2008
  • Duration in abstinence state: Termorshuizen et al, 2005
Key Parameter Inputs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DAM state</th>
<th>MMT state</th>
<th>Relapse State</th>
</tr>
</thead>
<tbody>
<tr>
<td>12m retention</td>
<td>88%</td>
<td>54%</td>
<td>62%</td>
</tr>
<tr>
<td>Mortality (SMR)</td>
<td>9.7</td>
<td>9.2</td>
<td>30.1</td>
</tr>
<tr>
<td>QALYs</td>
<td>0.852</td>
<td>0.852</td>
<td>0.750</td>
</tr>
<tr>
<td>Treat. cost (mo)</td>
<td>$1415.21</td>
<td>$329.48</td>
<td>--</td>
</tr>
<tr>
<td>Criminal cost (mo)</td>
<td>$1349.34</td>
<td>$1349.34</td>
<td>$9571.33</td>
</tr>
</tbody>
</table>
Movement within Model: proportion of cohort in each state by time

Time in years

Percentage of hypothetical patient cohort (%)
Results: Lifetime Hoziron

<table>
<thead>
<tr>
<th></th>
<th>DAM</th>
<th>MMT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Years alive</strong></td>
<td>15.25</td>
<td>14.03</td>
</tr>
<tr>
<td><strong>In Treatment</strong></td>
<td>10.07 (66%)</td>
<td>7.44 (53%)</td>
</tr>
<tr>
<td>In DAM</td>
<td>8.23</td>
<td></td>
</tr>
<tr>
<td>In MMT/MPD</td>
<td>1.84</td>
<td>7.44</td>
</tr>
<tr>
<td><strong>In Relapse</strong></td>
<td>4.26 (28%)</td>
<td>6.34 (45%)</td>
</tr>
<tr>
<td><strong>Total QALYs</strong></td>
<td>9.180</td>
<td>8.332</td>
</tr>
<tr>
<td><strong>Total Costs</strong></td>
<td>$1,195,164</td>
<td>$1,230,037</td>
</tr>
<tr>
<td><strong>Difference in QALYs</strong></td>
<td>0.848</td>
<td></td>
</tr>
<tr>
<td><strong>Difference in Total Costs</strong></td>
<td>$ -54,853</td>
<td></td>
</tr>
</tbody>
</table>

DAM was a dominant strategy across 1, 5, 10 year and lifetime time horizons.
Results: Sensitivity Analysis

• Selection of scenarios tested:
  – DAM not available after initial relapse
  – Assumed no change in tx/relapse episode lengths after first cycle
  – Alternative mortality, criminal cost, HRU cost estimates
  – HIV Seroconversion = 0
  – Threshold analysis on DAM retention, costs of criminal activity

• One-way and probabilistic sensitivity analysis confirmed baseline results for a wide range of valuations of societal willingness to pay to achieve a gain of one QALY
Probabilistic Sensitivity Analysis

Threshold value of willingness to pay ($000s)

Probability of being cost-effective

DAM

MMT
Conclusions

• By keeping opioid-dependent individuals retained in treatment for longer periods, our results suggest that DAM is a cost-effective treatment option for those unable to benefit from MMT.

• It is important to emphasize that the NAOMI trial, and subsequently this economic analysis was a test of the effectiveness and cost-effectiveness of treatment options for opioid dependence after initial unsuccessful treatment with methadone.
Acknowledgements

• The NAOMI study was supported by grants from the Canadian Institutes of Health Research, 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, and the BC Centre for Disease Control.

• BN is a CIHR Bisby Fellow and also supported by a Postdoctoral Fellowship from the Michael Smith Foundation for Health Research, MTS is a Tier I Canada Research Chair

• Technical, editorial assistance of H. Sun, X. Wang and S. Harvard.
NAOMI Team

- Suzanne Brissette
- Jill Chettiar
- Bohdan Nosyk
- Paul-André Guevremont
- Martin Schechter
- Pascal Schneeberger
- Serge Brochu
- David Marsh
- Kurt Lock
- Daphne Guh
- Julie Schneiderman
- Jeff Lawlor
- Aslam Anis
- Nancy Laliberte
- Candice Gartry
- Eugenia Oviedo-Joekes
- Pierre Lauzon

***and a large dedicated staff***