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

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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

Cycle = 3

Allocated to MMT

Death

MMT₃

Relapse₃

Abstinence

MMT₄

Cycle, j = 4-6

Allocated to DAM

Death

DAM₁

MMT-PD₃

Relapse₃

Abstinence

DAM_{j-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>
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Movement within Model: proportion of cohort in each state by time
Results: Lifetime Hoziron

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

The graph shows the probability of being cost-effective as a function of the threshold value of willingness to pay, depicted for two different models: DAM and MMT. The x-axis represents the threshold value of willingness to pay ($000s), while the y-axis shows the probability of being cost-effective. As the threshold value increases, the probability of being cost-effective decreases for both models, with DAM showing a higher probability at higher thresholds compared to 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.
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***and a large dedicated staff***