Opioid Dependence Treatment: Should substitution therapy be the management of choice?

CON

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Objectives
Helpful? For everyone?

- Discuss the concerns associated with opioid substitution therapy evidence base and outcomes.
- Identify the characteristics of patients and services that predict poor opioid substitution therapy results.
Secondary Objectives

Harmful?

• Review risk of diversion, misuse, abuse and overdose in adults

• Describe the risk to children in MAT families
Medication-Assisted Therapy

• Pharmaceuticals:
  – Methadone
  – Buprenorphine
  – Naltrexone

• Behavioral therapy
Benefits of MAT

• **Primary:**
  – Retention in treatment
  – Reduction in opioid use

• **Secondary (reduction in):**
  – Use of other illicit drugs
  – HIV-risky behaviors
  – Crime
  – Heroin craving
  – Mortality

PROBLEMS
State investigating Baltimore methadone clinic after man's death

Firm that runs clinic has recently come under scrutiny for deaths in other states

April 02, 2013 | By Carrie Wells, The Baltimore Sun

The day after her ex-husband's funeral in January, Sabrina Lumpkin started calling every public official she could think of, trying to get someone to pay attention.

Warren Lumpkin, 34, had died in a Southwest Baltimore house of heart complications related to using methadone, the prescription drug typically used to treat heroin addiction, according to an autopsy from the state medical examiner. But Sabrina Lumpkin said he had no such prescription — he took his roommate's methadone the night before he died.
Methadone - Safety

• Patient deaths – rapid escalation
• Community morbidity/mortality
  – Poisoning
    ▪ Small children
    ▪ Adults
      › Naïve users
      › Combination with CNS depressants
  – Operating under the influence

1-800-222-1222
www.nnepc.org
Addiction Treatment With a Dark Side

By DEBORAH SONTAG  NOV. 16, 2013

Dissolvable filmstrips of buprenorphine

Northern New England Poison Center

1-800-222-1222
www.nnepc.org
NYT – Buprenorphine Article
Bad Players

• Bad doctors (US national data)
  – 1,350/12,780 (>10%) sanctioned
    ▪ Excessive narcotic prescribing
    ▪ Insurance fraud
    ▪ Sexual misconduct
    ▪ Practicing impaired

• Bad patients

• Drug dealers
NYT – Buprenorphine Article
Underground Market

- Manage withdrawal
- Recreational use
  - Shooting
  - Snorting
  - Sublingual
- Prison heroin
SUCCESS?
Methadone

How successful is success? Baltimore 40-week Program

• Plan:
  – Maintenance for 30 weeks
    • Moderate-dose: 40 – 50 mg/day
    • High-dose: 80 – 100 mg/day
  – Detoxification for 10 weeks (10%/week)

• Withdrawn:
  – Maintenance: missed > 3 days, incarcerated, med/psych issues, other
  – Detoxification: missed > 3 days, transferred to treatment, other

Methadone
How successful is success? Baltimore 40-week Program

• Disappearing patients:
  – Maintenance:
    • Moderate-dose: 97 to start, 54 after this phase (56% left)
    • High-dose: 95 to start, 57 after this phase (60% left)
  – Detoxification:
    • Moderate-dose: 54 to start, 11 after this phase (11% left)
    • High-dose: 57 to start, 19 after this phase (20% left)

• Outcome?:
  – Ability to taper off methadone
    66% withdrew due to failure to show up to clinic or incarceration
  – No longer-term success measured
    5% transferred to community treatment

Methadone
How good is good? Swedish Program

- **Swedish methadone program**
  - 1988 – 2000
  - N=848

- **Strict rules:**
  - No abuse of other medications/alcohol
  - No violence toward staff/patients
  - No ongoing criminal activity

Methadone
How good is good? Swedish Program

• Results:

  – 77 deaths/1000 person years in the program
    ▪ Mostly natural causes (HIV, Hep C)
  – 74 deaths/1000 person years of those discharged
    ▪ Mostly unnatural (heroin overdose)
  – 2 deaths in the community from leakage of program methadone

Methadone

How good is good? Swedish Program

• **Notes:**
  – In-program deaths: 77/679
  – Discharged: 74/368

• **Take-home messages:**
  – Outcomes must look at all patients/all causes
  – Strictness of rules may dictate types of deaths
    - Overdose among those discharged OR
    - Overdose with program methadone diverted into community and drug abuse while in the program

Methadone and Buprenorphine
How good is good? California 52-week study

- **Methadone 80 mg (N=75):**
  - 52% retention at 26 weeks
  - 31% retention at 52 weeks
- **Methadone 30 mg (N=75):**
  - 40% retention at 26 weeks
  - 19% retention at 52 weeks
- **Buprenorphine 8 mg (N=75):**
  - 35% retention at 26 weeks
  - 20% retention at 52 weeks

60 dropped from program for 0 opioid-negative urines after 12 urinalyses

Buprenorphine
How Good is Good?  Sweden 7-year Study

- **Patients (N=170):**
  - 148 left after 30 days - 22 (13%) dropped out
  - 94 left after 7 years – 54 (45% of the original 170)

- **Outcomes:**
  - Drug- and alcohol-free
  - Retention in the program (continuous)
  - Employment (69% regular, 29% supplemented wages, 2% studying)
  - Psychosocial conditions favorable
  - No criminal convictions

DIVERSION AND MISUSE
Diversion and Misuse
Australia Survey of People Misusing MAT Opioids (N=544)

- Removal of supervised doses:
  - Buprenorphine 19 – 33%
  - Methadone 5%
- Diversion of doses:
  - Buprenorphine >> methadone
- Injection of doses:
  - Injection once in last 6 months (buprenorphine = methadone)
  - Regular injection (at least weekly):
    - Buprenorphine – 11%
    - Buprenorphine/naloxone tablet – 9%
    - Buprenorphine/naloxone film – 3%
    - Methadone – 3%

Diversion and Misuse
Australia Survey of out-of-treatment People Who Inject Drugs (N=541)

• Most injected in rank order:
  1. Buprenorphine or methadone (recent 16 – 17%)
  2. Buprenorphine/naloxone tablet > film (recent 5 –10%)

• Reasons for injection:
  – Mostly self treatment (withdrawal) – 56 to 71%
  – Also:
    • Substitution for other opioids (methadone, buprenorphine) - 6 to 21%
    • Intoxication (methadone) – 16%
    • Other (financial stress, needing higher dose, faster onset, prefer injection, difficulty not injecting (methadone, buprenorphine/naloxone) - 12 – 21%

Diversion and Misuse

New South Wales Australia Community Pharmacy Survey
Methadone and Buprenorphine Patients (508/931 responded)

- 442 methadone
  - 12% ever sneaked
  - 43% ever injected
- 66 buprenorphine
  - 32% ever sneaked
  - 15% ever injected
- For both, injectors 10 x more likely to divert/attempt to divert

POISONING
Buprenorphine and Methadone Exposures
NPDS Data from 2000 - 2008

- **Methadone (N=2,186)**
  - All exposures (6,171, 9 deaths)
  - Children < 6 years of age (2,186, 20 deaths)

- **Buprenorphine (N=1,786)**
  - All exposures (31,609, 654 deaths)
  - Children < 6 years of age (1,786, no deaths)

Opioid Childhood Exposures
RADARs Data in children < 6 years of age exposed to 7 opioids
#9,179 over 3.5 years

• **Methadone (N=415)**
  - 4th most common
  - 2nd effects of moderate or greater severity
  - 2 deaths (25% of deaths)
    ▪ 4 oxycodone (N=2,036) and 2 hydrocodone (N=6,003)

• **Buprenorphine (N=176)**
  - 5th most common
  - 1st effects of moderate or greater severity
  - No deaths

Methadone Pediatric Exposures

French Poison Centers Data in children < 18 years of age exposed 2008 – 2014 since solid form methadone available

- **87 patients:**
  - Children < 6 years (69 accidental, 6 intentional)

- **Clinical Outcomes (N=87):**
  - 5 deaths (4 syrup, 1 capsule)
  - 20 moderate to severe
  - 62 no effect to mild effects

- **Important Points:**
  - Nearly all packages opened by parents first
  - Better outcomes associated with faster parent reaction

Methadone
206 methadone deaths from 2001 – 2005 in Victoria, Australia

• Legality:
  – 161 (78%) legally prescribed
    • Mostly maintenance (N=123)
      – Many in long-term treatment (N=72 > 2 weeks)
      – Take-home doses (N=42)
  – 36 (17%) diverted maintenance and pain management
  – 9 (4%) unknown

Methadone
206 methadone deaths from 2001 – 2005 in Victoria, Australia

• Problems:
  – Combination with CNS depressants (98%)
  – Dosing in MAT
    • Initial high dose
    • Rapid dose escalation
  – Failure to reduce deaths?
    • Methadone deaths equaled/exceeded heroin deaths
      ▪ Heroin use decreased (↓heroin supply, ↑stimulant abuse)

Methadone Deaths
36 autopsies from Italy 2005 - 2013

• 20 long-term methadone maintenance patients
  – 9 take-home
    • 2 apparently selling their methadone
    • 1 took an excessive dose
  – 11 in-clinic (more mixing with ethanol and drugs of abuse)
• 4 induction deaths (3/4 post incarceration)
• 12 diverted/illegal (3 naïve)
  – 2 toddler deaths (1/2 possibly intentional)
  – 4 partiers

Predicting Success
Short-term of Stabilization and Detox with Buprenorphine

Positive Predictors
- Non-daily opiate use in past 30 days
- Employment in past 30 days

Negative Predictors
- Past criminal history

Stabilization Completion – 4 wks
- No opiate use in last 30 days

Retention - # wks in tx
- No opiate use in last 30 days
- Past criminal history

Predicting Success
Buprenorphine over 3 Months

Positive Predictors
• COMPLIANCE
• Older
• Male
*Compliance = taking 22/28 (80%) of days

Negative Predictors
• ↑ Addiction Severity Index Score
  – Psychiatric
  – Legal
  – Family/social

Predicting Success
Methadone, Buprenorphine, Other

Positive Predictors
• Prescription opioids (v. heroin)

Negative Predictors
• ↑ Heroin injection rate
• ↑ Number of prior treatments


Measuring Success
Physician Survey on Successful MAT (Switzerland)

• Break off as reason for terminating MAT*
• Psychological improvement
• Wish for abstinence from MAT
• Social improvement
• Medical improvement
• Social integration index**

*Patient, physician or loss of contact
**Job, earning a living, flat, partnership, family relations, friends outside drug scene

## Cost

Table ES2. Two-year costs among 1,000 hypothetical patients treated for opioid dependence.

<table>
<thead>
<tr>
<th>Outcome/Cost</th>
<th>MMT</th>
<th>BMT</th>
<th>SUB/VIV Taper</th>
<th>SUB/Oral NTX Taper</th>
<th>Vivitrol Alone</th>
<th>Oral NTX Alone</th>
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<tbody>
<tr>
<td>Treatment outcome (per 1,000):</td>
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<tr>
<td>In treatment</td>
<td>630</td>
<td>523</td>
<td>550</td>
<td>500</td>
<td>416</td>
<td>277</td>
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<tr>
<td>Relapsed</td>
<td>185</td>
<td>292</td>
<td>265</td>
<td>315</td>
<td>400</td>
<td>538</td>
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<tr>
<td>Drug –free</td>
<td>177</td>
<td>176</td>
<td>177</td>
<td>176</td>
<td>173</td>
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<td>Died</td>
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<td>9</td>
<td>8</td>
<td>9</td>
<td>12</td>
<td>16</td>
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<tr>
<td>Cost ($, per patient):</td>
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<tr>
<td>Drug therapy</td>
<td>699</td>
<td>3,655</td>
<td>8,553</td>
<td>1,249</td>
<td>6,585</td>
<td>665</td>
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<td>Other SA services</td>
<td>14,017</td>
<td>7,043</td>
<td>4,146</td>
<td>4,297</td>
<td>2,985</td>
<td>2,446</td>
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<tr>
<td>Other health care</td>
<td>23,926</td>
<td>25,993</td>
<td>25,454</td>
<td>26,441</td>
<td>28,109</td>
<td>30,844</td>
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<tr>
<td>SUBTOTAL</td>
<td>38,642</td>
<td>36,691</td>
<td>38,153</td>
<td>31,988</td>
<td>37,679</td>
<td>33,954</td>
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<tr>
<td>Social costs</td>
<td>92,068</td>
<td>102,337</td>
<td>98,033</td>
<td>105,917</td>
<td>119,239</td>
<td>141,076</td>
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<td>TOTAL</td>
<td>130,710</td>
<td>139,028</td>
<td>136,187</td>
<td>137,905</td>
<td>156,918</td>
<td>175,030</td>
</tr>
</tbody>
</table>

MMT: methadone maintenance treatment; BMT: buprenorphine maintenance treatment; NTX: naltrexone; SUB: Suboxone; VIV: Vivitrol

The Best Outcome
Are the goals sufficient?

- **Harm reduction only:**
  - Fewer overdoses
  - Not dead yet
  - Fewer infectious disease issues
    - Cellulitis/vasculitis
    - Endocarditis/heart valves
    - Hepatitis C, HIV
  - No additional heart valve replacements

- **Return to a nl life:**
  - Reasonably happy
  - Not using
  - Not demonstrating addictive behaviors
  - Maintaining a job
  - Maintaining a family life/relationships
Conclusion

What is good enough?

• What are the goals?
  – Not dead yet and lower cost to society
  – Functioning well at work and home

• What is the harm to bystanders?
  – Children
  – Naïve drug users
  – Clients and families