Arkansas Prescription Drug Abuse Summit
Medication Assisted Treatment for Opioid Use Disorder

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This Presentation Reviews

• Part I: The problem

• Part II: Potential solutions
Part I: The Problem

- Definitions
- Epidemiology
Part II: Potential Solutions

• Reasons for prescription drug misuse

• Factors in prescription drug misuse

• Intervention strategies

• Treatment
Part I: The Problem

• Definitions

• Epidemiology
Definitions

• Misuse
• Non-medical use
• Use disorder
  - previously abuse/ dependence
Prescriptions

Misuse
- Incorrect use
  - By patient
- Mismanaged
  - By physicians
    - D ated
    - D uped
    - D isabled
    - D ishonest

Non-medical
- Illegal use
  - Not prescribed
  - Took for euphoria
  - Most commonly used
  - In US, age 12 +:
    - Past month 2%
    - Lifetime: 14%
Use Disorder
2 or more in 12 months

- Failure to fulfill role
- Hazardous use
- Craving
- Use despite relationship problems
- Larger/Longer than intended
- Tolerance
- Withdrawal
- Can’t Quit
- Much time spent
- ↓ Activities
- Use despite medical/psychological
Part I: The Problem

• Definitions

• Epidemiology
Non-medical use

• 2013 National Survey on Drug Use and Health (NSDUH)
  - 7 % youth 12-17 lifetime non-medical use

• 2013 NSDUH
  - 20 % young adults 18-25 lifetime non-medical use
Emergency Department Visits

2009 Drug Abuse Warning Network (DAWN)

• 4.6 million drug-related ED visits
• 45 % were drug misuse
  - 27 % non-medical use of pharmaceuticals
  - 50 % of these were opioid analgesics
Prescription Opioids
Opioid Admissions in Adolescents Aged 12 to 17 Years

Source: Subramaniam G. Treatments for adolescents/young adults with opioid use disorder. Presented at: 8th National Institute on Drug Abuse Blending Conference; April 22, 2010; Albuquerque, NM.
Epidemiology

• Heroin Use
  - National Household Survey on Drug Use and Health (NSDUH 2016)
    - 948,000 Americans used heroin at least once
    - 13,000 were adolescents age 12-17

• Prescription Opioids (NSDUH 2016)
  - 11.5 million used prescription analgesics non-medically
  - 891,000 were adolescents aged 12-17
  - 641,000 misused prescription analgesics and heroin

• Opioid use disorder present in 2.4 million > age 12
Arkansas NSDUH Data

- 2006-2007 Data for ages 12 and older
- Past year non-medical use: 169,000 or 7.29% of the Arkansas population
- 66,000 (2.85%) of Arkansans reported needing but NOT receiving treatment for illicit drug use in the past year (2006-2007)
- Admissions to treatment for opiates in Arkansas (TEDS)

<table>
<thead>
<tr>
<th></th>
<th>2006</th>
<th>2008</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin</td>
<td>40</td>
<td>52</td>
<td>211</td>
</tr>
<tr>
<td>Other opiates</td>
<td>778</td>
<td>1441</td>
<td>1572</td>
</tr>
</tbody>
</table>
Opioid dependence: Treatment Gaps

- Patients with opioid use disorder (NSDUH-2013)
  - Pain relievers: 1.9 million
  - Heroin: 517,000

- Less than half received any treatment

- Detoxification: limited effectiveness

- Access to treatment restricted
Part I: The Problem

• Definitions

• Epidemiology
This Presentation Reviews

• Part I: The problem

• Part II: Potential solutions
Part II: Potential Solutions

• Reasons for prescription drug misuse

• Factors in prescription drug misuse

• Intervention strategies

• Treatment
Non-medical Use Rx Opioids

- Relieve pain – 63-79 %
- Feel good or get high – 32 %
- Experimentation – 27 %
- M 2X > F to report “get high”
- Get high ↑ other drug use
- Existing addiction/safety < 10 %
Generational Angst?

“"We’re living in a time that seems decidedly more apocalyptic, especially since 9/11 and all the recent natural disasters. Maybe we need something to slow down”

- Friedman, 2006
Part II: Potential Solutions

- Reasons for prescription drug misuse
- Factors in prescription drug misuse
- Intervention strategies
- Treatment
Contributing Factors

- Parents don’t talk about Rx drugs
- Pain management: late 1980’s
- New pain meds: early 1990’s
  - Hydrocodone RX ↑ 376 %
  - Oxycodone Rx ↑ 380 %
- Media changes
  - DTCA
  - Internet
Protective Factors

• Parental discussion about risks
• Gatekeeper access to Rx drugs
• School based programs
  - Science curriculum
  - Media awareness training
• Pharmaceutical approaches
Awareness of Teens “Lingo”

- Pharming
- Pilz
- Pharm parties
- Trail mix or M & M’s
- Chill pills
- Big boy
Part II: Potential Solutions

• Reasons for prescription drug misuse

• Factors in prescription drug misuse

• Intervention strategies

• Treatment
Prevention

- Exposure

- Target high-risk
  - Adolescents
  - Genetically vulnerable
  - Cognitive probs (schizophrenia, brain injury)
  - Stress reactive (depressed/anxious)
Intervention

• School Nurses
• Computerized, involve parents
• Cognitive Behavioral Therapy
• Motivational Interviewing
• Medication Assisted Treatment
Questions?
Part II: Potential Solutions

• Reasons for prescription drug misuse

• Factors in prescription drug misuse

• Intervention strategies

• Treatment
"I medicate first and ask questions later."
"Sorry, no water. We’re just a support group."
Opiate Withdrawal

**Early**
- Lacrimation
- Yawning
- Rhinorrhea
- Sweating

**Middle**
- Restless Sleep
- Dilated Pupils
- Anorexia
- Piloerection (term cold turkey)
- Irritability
Late Opiate Withdrawal

- ↑ all previous S/S
- Tachycardia
- Hypertension
- Nausea/vomiting
- Diarrhea
- Abdominal cramps
- Labile mood
- Depression
- Muscle spasm
- Weakness
- Bone pain
Diagrammatic summary of functional state of typical "mailine" heroin user. Arrows show the repetitive injection of heroin in uncertain dose, usually 10 to 30 mg but sometimes much more. Note that addict is hardly ever in a state of normal function ("straight").

From "Narcotic Blockade," by V. P. Dole, M. E. Nyswander, and M. J. Kreek, 1966, Archives of Internal Medicine, 118, p. 305.
Stabilization of patient in state of normal function by blockade treatment. A single daily oral dose of methadone prevents him from feeling symptoms of abstinence ("sick") or euphoria ("high"), even if he takes a shot of heroin. Dotted line indicates course if methadone is omitted.

From "Narcotic Blockade," by V. P. Dole, M. E. Nyswander, and M. J. Kreek, 1966, Archives of Internal Medicine, 118, p. 305.
GOALS FOR PHARMACOTHERAPY

• Prevention or reduction of withdrawal symptoms
• Prevention or reduction of drug craving
• Prevention of relapse to use of addictive drug
• Restoration toward normalcy

Source: MJ Kreek, Rationale for Maintenance Pharmacotherapy of Opiate Dependence, 1992
Medications for Opioid Dependence

- Naltrexone
- Methadone
- Buprenorphine
Medications for Opioid Dependence

- Naltrexone
- Methadone
- Buprenorphine
Rationale for Naltrexone
Block Pleasurable Drug Effects

- Extinction paradigm: no pleasure → no use
- Craving ↓ if heroin “not available”
- Naltrexone ↓ cue-induced craving
- Naltrexone ↓ priming-induced craving
Naltrexone

- Oral FDA 1984; Injectable FDA 2010
- Derivative of naloxone
- Displaces bound agonists
- Receptor affinity 20 X morphine
- Blocks heroin/opioids
- Peak plasma concentrations in 1hr
- Minimum 7 days abstinence before induction
Figure 2. Probability of opioid use by week by treatment group (N = 127), result of random regression analyses, using a linear model. All subjects were taking naltrexone 3 times a week as maintenance therapy. CM indicates contingency management; SO + CM, significant other involvement and CM.
Figure 1. Retention by week by treatment group (N=127). All subjects were taking naltrexone 3 times a week as maintenance therapy. CM indicates contingency management; SO+CM, significant other involvement and CM.
Injectable Naltrexone

Fig. 1 Efficacy of intramuscular extended-release naltrexone in patients with opioid dependence who had undergone opioid detoxification in a randomized, double-blind, multicentre trial [8]. Patients received extended-release naltrexone 380 mg (n = 126) or placebo (n = 124) once every 4 weeks for 24 weeks in combination with biweekly psychosocial support. Error bars are 95% confidence intervals. a Median proportion of weeks of confirmed abstinence during weeks 5–24. b Proportion of patients with total confirmed opioid abstinence during weeks 5–24. c Median proportion of self-reported opioid-free days on timeline follow-back survey over 24 weeks. d Mean change from baseline in self-reported need for opioids assessed on a visual analogue scale at week 24; see Table 1 for scale description and baseline scores. XR-NTX extended-release naltrexone, VAS visual analogue scale. *p < 0.05, **p < 0.001, ***p < 0.0001 vs. placebo.
Naltrexone Side Effects

- Nausea/Diarrhea
- Headache
- Insomnia
- Dizziness
- Possible liver toxicity
- Opioid analgesics NOT effective
Medications for Opioid Dependence

• Naltrexone

• Methadone

• Buprenorphine
One year outcome randomized controlled trial
Dole et al., 1969

<table>
<thead>
<tr>
<th>Reincarcerated?</th>
<th>Daily Heroin Use?</th>
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<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
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<tr>
<td>No</td>
<td>Yes</td>
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<td></td>
<td>No</td>
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<table>
<thead>
<tr>
<th>Methadone</th>
<th>Control</th>
</tr>
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<tbody>
<tr>
<td>6(37%)</td>
<td>10</td>
</tr>
<tr>
<td>4(25%)</td>
<td>12</td>
</tr>
<tr>
<td>16(100%)</td>
<td>0</td>
</tr>
<tr>
<td>16(100%)</td>
<td>0</td>
</tr>
</tbody>
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From Key Issues in MMT - Ward, Mattick, and Hall - 1992
Colonial Management Group - Payte - 2004
DEATH RATES IN TREATED AND UNTREATED HEROIN ADDICTS


Opioid Agonist Treatment of Addiction - Payte - 1998
Crime among 491 patients before and during MMT at 6 programs

Adapted from Ball & Ross - The Effectiveness of Methadone Maintenance Treatment, 1991

Opioid Agonist Treatment of Addiction - Payte - 1998
<table>
<thead>
<tr>
<th>Groups</th>
<th>Proportion Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone maintenance outpatients</td>
<td>21/74 (28.4%)</td>
</tr>
<tr>
<td>Therapeutic Community residents</td>
<td>12/28 (42.9%)</td>
</tr>
<tr>
<td>Held in custody</td>
<td>27/66 (40.9%)</td>
</tr>
<tr>
<td>Not in treatment</td>
<td>25/51 (52.9%)</td>
</tr>
</tbody>
</table>

Source: Bourne, AIDS and Drug Use: An International Perspective, 1988

Opioid Agonist Treatment of Addiction - Payte - 1998
Relapse to IV drug use after MMT
105 male patients who left treatment

Adapted from Ball & Ross - The Effectiveness of Methadone Maintenance Treatment, 1991

Opioid Agonist Treatment of Addiction - Payte - 1998
Impact of Medication Assisted Treatment

- Reduction death rates (Grondblah, ‘90)
- Reduction IVDU (Ball & Ross, ‘91)
- Reduction crime days (Ball & Ross)
- Reduction rate of HIV seroconversion (Bourne, ‘88; Novick ‘90; Metzger ‘93)
- Reduction relapse to IVDU (Ball & Ross)
- Improved employment, health, & social function
Methadone Side Effects

- Minimal sedation once tolerance achieved
- Constipation
- Increased appetite/weight gain
- Libido; May ↓ gonadal hormone levels
- Exhaustively studied: no evidence of harm
Medications for Opioid Dependence

- Naltrexone
- Methadone
- Buprenorphine (BUP)
Potential for Abuse and Dependence

- Buprenorphine is abusable
- Diversion and illicit use (by injection)
- Low abuse potential vs other opioids

Average Number of Cases of Abuse of Buprenorphine Products, Methadone, Tramadol, and Oxycodone per Drug-Abuse Expert

Combination of Buprenorphine plus Naloxone

- Sublingual buprenorphine good bioavailability
- Sublingual naloxone relatively poor bioavailability
- Combination ratio is 4/1 (buprenorphine/naloxone)
- Suboxone (2/0.5, 4/1, 8/2, 12/3 mg films)
- Generic BUP and BUP/naloxone available
- Sublingual naloxone has a bitter taste
- New brands available
  - Minty flavored tablet (Zubsolv®)
  - Buccal film (Bunavail®)
Combination of Buprenorphine plus Naloxone

- Sublingual use $\rightarrow$ predominantly BUP effect

- Dissolves/injects $\rightarrow$ predominantly naloxone effect
Efficacy and Safety of Buprenorphine
BUP Maintenance/Withdrawal: Retention

(Kakko et al., 2003)
Buprenorphine Safety

• Highly safe medication
  - Acute dosing
  - Chronic dosing

• Primary side effects:
  - Nausea
  - Constipation
  - Headaches

• No disruption in cognitive or psychomotor performance

• No evidence of organ damage with chronic dosing
Overdose Risk Minimal

- Very low risk
- High dose BUP → no respiratory depression
- No respiratory depression BUP vs methadone
- Overdose BUP + other CNS depressants:
  - Benzos
  - Etoh
  - Barbs
Buprenorphine

- Partial mu agonist
- Effects similar to other mu agonists
- ↓ risk of respiratory depression
- Lower physical dependence
- BUP/naloxone combination preferred
  - Unsupervised dosing
  - ↓ diversion
## Opiate Addiction Treatment Outcome*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Methadone Maintenance</td>
<td>50 – 80%</td>
</tr>
<tr>
<td>Naltrexone Maintenance</td>
<td>10 – 20%</td>
</tr>
<tr>
<td>“Drug Free” (non-pharmacotherapeutic)</td>
<td>5 – 30%</td>
</tr>
<tr>
<td>LAAM Maintenance</td>
<td>50 – 80%**</td>
</tr>
<tr>
<td>Buprenorphine-Naloxone Maintenance</td>
<td>40-50%</td>
</tr>
<tr>
<td>Short-term Detoxification (any mode)</td>
<td>5 – 20% (limited data)</td>
</tr>
</tbody>
</table>

*One year retention in treatment and/or follow-up with significant reduction or elimination of illicit use of opiates

**Maximum effective dose (24mg/s) equal to 60 to 70 mg/d methadone. Data base on 6 month follow-up only.

*Kreek, 1996; 2001*
This Presentation Covered

• Part I: The problem

• Part II: Potential solutions
  • Reasons for prescription drug misuse
  • Factors in prescription drug misuse
  • Intervention strategies
  • Treatment
Opioid Agonist Therapy

For Some Patients OAT Can Be An Effective and Durable Band-Aid..... But More Is Usually Needed For Stable Remission—”Recovery”
MEDICATION ASSISTED ADDICTION TREATMENT

“All Treatments Work For Some People/Patients”

“No One Treatment Works for All People/Patients”

Alan I. Leshner, Ph.D
Former Director NIDA
Questions?