DEA Alert Conference
November 13, 2008

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Center for Substance Abuse Treatment
Substance Abuse and Mental Health Services Administration
Overview

- Opioid Assisted Treatment SAMHSA (methadone/buprenorphine)
- Methadone abuse/mortality increasing.
- National Assessments
Active Opioid Treatment Programs by State as of June 2008 (1,192)
States Where Methadone Treatment is not Available

- 2000
  - Idaho
  - Mississippi
  - Montana
  - New Hampshire
  - North Dakota
  - South Dakota
  - Vermont
  - West Virginia

- 2008
  - Montana
  - North Dakota
  - South Dakota
  - Wyoming
Modest Increase in Patients

Patients in MMTPS

Number of Patients

Year

0
50000
100000
150000
200000
250000
300000

Increase in Methadone Patients

- 2002 – 2006 (260,000)
- US – 2.3%
- TX – 27 %
- Oklahoma –114 %
- Louisiana –25 %
- Source: National Survey on Substance Abuse Treatment Services, SAMHSA
Dependence on or Abuse of Specific Illicit Drugs in the Past Year among Persons Aged 12 or Older: 2007

![Graph showing numbers of persons with drug use disorders for various substances.

- **Marijuana**: 3,932,000
- **Pain Relivers**: 1,707,000
- **Cocaine**: 1,598,000
- **Tranquilizers**: 443,000
- **Stimulants**: 406,000
- **Hallucinogens**: 368,000
- **Heroin**: 213,000
- **Inhalants**: 164,000
- **Sedatives**: 154,000

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Numbers of Persons with Drug Use Disorder

0 1,000,000 2,000,000 3,000,000 4,000,000 5,000,000
Treatment Gap?

- 260,000 methadone patients
- 305,000 buprenorphine
- Total 560,000
- Rx Pain Dependence - 1.56 million
- Heroin dependence – 0.23 million
- Total 1.9 million
- Gap ~ 1.4 million
OTP Characteristics

- Treatment capacity – average 208 patients
- Mean size—253 patients
- Range—20 to 2,000 patients
- Public/Non-profit—approximately 52% (2004)
- 44.6% non-profit; 41% for-profit, 14.4%, run by a government agency
- Less than one/third of patients without insurance
- Of patients with insurance, two-thirds covered for OTP treatment.
OTP Characteristics (2)

- Typical pt: white male, 26-50 years old
- 75% treated for heroin addiction; 14.6%, oxycodone and 5.7%, morphine addiction.
- Less than 1% treated with buprenorphine
- **Mean years in treatment:** 6.3
- **Mean length, current treatment episode:** 25.9 months
SAMHSA Regulations 42 CFR § 8

- Federal opioid treatment standards, e.g.
  - Patient Admission Criteria
  - Medication administration, dispensing
  - Unsupervised use
  - Diversion control
  - Required medical, drug testing and other services

- SAMHSA Certification
- Certification Based Upon
  - Accreditation
  - DEA Registration
  - State Approval

- SAMHSA approval of accreditation bodies
- Suspension or revocation of OTP certification
- Collaboration with State Authorities
  - Conference calls
  - Annual meeting
Federal Opioid Treatment Standards (§8.12)

- Administrative and organizational structure
- Quality assurance/improvement
- Diversion Control Plan
- Staff credentials
- Patient admission criteria
- Required services
- Record keeping and patient confidentiality
- Medication administration, dispensing
- Unsupervised use
- Interim maintenance
- Detoxification
Diversion Control Plan - Surveillance and Monitoring

• How are diversion problems addressed?
  - Change frequency of take-home reviews, if needed
  - Investigate source of diversion
  - Special/intensified groups or individual counseling sessions
  - Establish patient committee to advise on policies, procedures and problem solving
Take Home Schedule - 6

Steps

- A patient may receive a single take home dose for a day the program is closed, AND
- 0 - 90 days - patient may receive a single dose each week
- 90 - 180 days - patient may receive up to two doses per week
- 180 - 270 days - patient may receive up to three doses per week
- 270 - 365 days - patient may receive up to six doses per week
- After 1 year continuous treatment - up to a 2 week supply
- After 2 years of continuous treatment - up to a 30 day supply
Take Home Determinations

- 8 Criteria unchanged
- More reliance on clinical judgement of medical director and program physicians
- Less reliance on regulatory test results, complex probation monitoring or drug testing
- Programs must have diversion control plans
- No Federal approval necessary for TH doses above 100 mg
Solid Dosage Forms

- Permitted under new regulations
- All opioid treatment medications pose a risk of diversion
- Diskettes lower potential than tablets
- Physician determines that patient can responsibly handle diskettes
Federal Confidentiality Law

• Applies to substance abuse treatment programs, including methadone programs
• Restricts disclosure of patient information
• Court order required for undercover investigations
Is methadone effective?

- Methadone maintenance treatment is safe and effective when used appropriately, when treatment is individualized to each patient, and when provided with counseling and other services.
- Has saved thousands of lives from overdose, HIV-AIDS
- NIH concluded most effective for opiate addiction.
Emerging Issues Methadone Treatment

• Program Closures
  – Georgia, Texas, Illinois, New Mexico
  – Failure to comply with regulations

• Civil fines for failing to adhere to Federal dispensing schedule. ($25,000 each, under CSA)

• Cardiac Conductivity – TDP

• FDA Labeling Revision
Is Methadone Abused?
Nonmedical Use of Pharmaceuticals, Selected Opiates/Opioids, 2006

Visits (thousands)

- Fentanyl*
  - CI lower bound: 7
  - CI upper bound: 16
  - Estimate: 15

- Hydrocodone*
  - CI lower bound: 25
  - CI upper bound: 44
  - Estimate: 26

- Morphine*
  - CI lower bound: 71
  - CI upper bound: 58
  - Estimate: 58

- Oxycodone*
  - CI lower bound: 80
  - CI upper bound: 65
  - Estimate: 65

* Single- & multi-ingredient formulations

Source: National estimates from DAWN, 2006

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Nonmedical Use of Pharmaceuticals, Selected Opiates/Opioids, 2006

![Graph showing the nonmedical use of selected opiates/opioids in 2006. The graph includes visits data for Opiates/opioids not specified, Buprenorphine, and Methadone.]

- Opiates/opioids not specified: 64 (95% CI: 51, 77)
- Buprenorphine: 8 (95% CI: 4.1, 10.4)
- Methadone: 54 (95% CI: 45, 63)

* Single- & multi-ingredient formulations

Source: National estimates from DAWN, 2006
Nonmedical Use of Specific Pain Relievers in Lifetime, Numbers in Thousands, 2007

- Darvocet, Darvon, or Tylenol with Codeine
- Percocet, Percodan, or Tylox
- Vicodin, Lortab, or Lorcet
- Codeine
- Demerol
- Dilaudid
- Hydrocodone
- Oxycontin
- Methadone
- Morphine

Source: NSDUH 2007
Past Month Illicit Drug Use among Persons Aged 12 or Older: 2007

Numbers in Millions

- Illicit Drugs: 19.9
- Marijuana\(^1\): 14.4
- Psychotherapeutics: 6.9
- Cocaine: 2.1
- Hallucinogens: 1.0
- Inhalants: 0.6
- Heroin: 0.2

\(^1\) Illicit Drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically.
Past Month Use of Selected Illicit Drugs among Persons Aged 12 or Older: 2002-2007

Percent Using in Past Month

- Illicit Drugs
- Marijuana
- Psychotherapeutics
- Pain Relievers
- Cocaine
- Methamphetamine

\(^+\) Difference between this estimate and the 2007 estimate is statistically significant at the .05 level.
Past Month Use of Selected Illicit Drugs among Youths Aged 12 to 17: 2002-2007

Percent Using in Past Month

- Illicit Drugs
- Marijuana
- Psychotherapeutics
- Inhalants
- Hallucinogens

+ Difference between this estimate and the 2007 estimate is statistically significant at the .05 level.
Past Month Use of Selected Illicit Drugs among Young Adults Aged 18 to 25: 2002-2007

Percent Using in Past Month

Marijuana
Illicit Drugs
Psychotherapeutics
Cocaine
Hallucinogens

+ Difference between this estimate and the 2007 estimate is statistically significant at the .05 level.
Methadone Associated Mortality?

- 2003-2007 National Assessments
- NCHS Data – National/West Virginia
Methadone Kills.

The use of methadone can lead to respiratory depression, coma and death.

Need Help? Call 800-342-5653

A Public Service Announcement of the Kenosha County Health Department
NCHS Data

- Crude Death Rates, methadone-related unintentional deaths/100M
- 1999 – 2004
- WV – 25 fold (4 to 99 deaths)
- KY – 15 fold (8 to 121 deaths, decr in 2004)
- NC -  7 fold (34 to 245)
- US -  5 fold (623 to 3202) 4462 in 2005
Nearly all poisoning deaths in the United States are attributed to drugs, and most drug poisonings result from the abuse of prescription and illegal drugs.


NCHS Methadone Mentions increased 390% between 1999-2004.

Methadone Distribution (ARCOS) Increased 390% between 1990-2004.
Figure 2.

Poison Control Data, 2001 - 2005: Number of Drug Exposures

Source: American Association of Poison Control Centers (AAPCC)
Figure 3.

Poison Control Data, 2005: Number of Deaths Per 100 Exposures

Source: American Association of Poison Control Centers (AAPCC)
<table>
<thead>
<tr>
<th></th>
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<tr>
<td>Total US</td>
<td>623</td>
<td>3,202</td>
<td>5.1</td>
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<tr>
<td>West Virginia</td>
<td>4</td>
<td>99</td>
<td>24.8</td>
</tr>
<tr>
<td>Ohio</td>
<td>7</td>
<td>122</td>
<td>17.4</td>
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<tr>
<td>Louisiana</td>
<td>4</td>
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<td>10.5</td>
</tr>
<tr>
<td>Maine</td>
<td>5</td>
<td>52</td>
<td>10</td>
</tr>
</tbody>
</table>
Manners of Death for Cases Reported
(Accidental, Homicide, Natural, Suicide or Undetermined)

Oxycodone Deaths
- Accident 65%
- Suicide 18%
- Natural 17%
- Homicide 1%

Hydrocodone Deaths
- Accident 62%
- Suicide 18%
- Natural 29%
- Homicide 5%

Naloxone Deaths
- Accident 82%
- Suicide 8%
- Natural 8%
- Homicide 2%

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Reasons for methadone toxicity
Pharmacology

- Slow onset
- Long duration of action
  - Half life 24-36 hours
  - Steady state 4-5 days
  - Half of each day's dose remains to be added to next day's dose.
- Accumulation
- Tolerance – respiratory depression slower than pain relief
- Interactions with depressants
Methadone Toxicity Varies Greatly Across Individuals –100x

- Enhanced by other drugs/alcohol – interactions not fully quantified.
- Enhanced by natural disease – e.g., pathology due to history of drug use, sleep apnea, heart, lung, or liver disease.
- Enhanced by circumstances – e.g., airway position, temperature, food.

Source: Sorg 2002
• Has methadone distribution increased in recent years?
• If so, how?
Methadone Prescriptions

- 1998-2003 Rx for hydrocodone, oxycodone, methadone increased.
- Methadone Rx increased 0.5-1.8 million
- Unique Patient Rx methadone increased 80% from 2005-2006
- Correlation between increases in methadone dispensed by pharmacies and increases in methadone associated mortality
Figure 8.

Increase in Number of Prescriptions for Methadone and 3 Other Opioids

(Source: IMS Health Prescription Audit)

Note: In 2006, there were about 35 times more prescriptions dispensed for hydrocodone, 10 times more prescriptions for oxycodone, and twice as many prescriptions for fentanyl as for methadone.
Methadone Rx Increases - 2006

• Out of all strengths of methadone, the largest growth in sales is seen with methadone 40mg with a 240% growth in combined sales since 2001. (10mg 150%, 5mg 91%).

• Sales of methadone 40mg to chain stores and independent pharmacies have increased 700% and 450%, respectively since 2001.
Sales of opioids by type, US, 1997 thru 3rd quarter, 2006 (DEA ARCOS data)
Patient-level data: Total number of unique patients receiving a prescription for methadone in U.S. outpatient retail pharmacies, Years 2002 - 2006, Verispan, Total Patient Tracker (TPT)
Pain Reliever Cost Comparison

- Estimated Monthly Drug Costs

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<thead>
<tr>
<th>Agent</th>
<th>Dosage</th>
<th>Cost*</th>
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<tbody>
<tr>
<td>Methadone</td>
<td>90 pills</td>
<td>$ 8.00</td>
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<tr>
<td>SR morphine</td>
<td>60 pills</td>
<td>101.50</td>
</tr>
<tr>
<td>MS Contin</td>
<td>60 pills</td>
<td>113.50</td>
</tr>
<tr>
<td>Oxycontin</td>
<td>60 pills</td>
<td>176.50</td>
</tr>
<tr>
<td>Duragesic</td>
<td>10 patches</td>
<td>154.00*</td>
</tr>
</tbody>
</table>

-Estimated cost to the pharmacist based on average wholesale prices, rounded to the nearest half dollar, in Red book. Montvale, N.J.: Medical Economics Data, 2004. Cost to the patient will be higher, depending on prescription filling fee.
Opioid Treatment and Mortality

- Texas
- North Carolina
- Maine
- West Virginia

• Compared to general population NTP patients:
  • 4.6 x drug overdose
  • 3.4 x liver disease
  • 1.7 x respiratory disease
  • 1.5 x cancer
Maxwell – NTP Patient Deaths –
Texas – 1994-2002 - 2

- Older cohort – chronic disease
- Younger cohort – trauma, overdose
- Knowledge of Toxicity
  - 14% aware of overdose risk during 1st 2 weeks
  - 15% aware of risks of starting patients at 30 mg or higher
Activities – Education/Training

- FDA Revised Labeling
- **Black-box warning**
  - Methadone for pain, second line
  - accidental overdose
  - death due to respiratory depressant effects
  - death due to cardiac conduction effects
- **Dosing revision**
  - lower starting dose and greater inter-dose interval
  - conversion from other opioids
  - stresses unique pharmacology and caution during initiation and conversion from other opioids
Patients should take methadone exactly as prescribed. Taking more methadone than prescribed can cause breathing to slow or stop and can cause death. A patient who does not experience good pain relief with the prescribed dose of methadone, should talk to his or her doctor.

Patients taking methadone should not start or stop taking other medicines or dietary supplements without talking to their health care provider. Taking other medicines or dietary supplements may cause less pain relief. They may also cause a toxic buildup of methadone in the body leading to dangerous changes in breathing or heart beat that may cause death.
FDA Advisory - 2

- Health care professionals and patients should be aware of the signs of methadone overdose. Signs of methadone overdose include trouble breathing or shallow breathing; extreme tiredness or sleepiness; blurred vision; inability to think, talk or walk normally; and feeling faint, dizzy or confused. If these signs occur, patients should get medical attention right away.
Methadone Physician Training - 1

- Explain the criteria for determining when methadone is appropriately used in the management of pain.
- Describe approaches to devising an appropriate dosing regimen.
- Describe the considerations involved in patient selection and monitoring.
- Discuss the special precautions to be taken during the induction phase of methadone use.
Methadone Rx Training - 2

- Explain the special issues involved in managing pain in the methadone-maintained patient.
- Describe the legal and administrative requirements for the use of methadone to treat pain.
- Discuss steps that can be taken to minimize the risks of drug diversion and abuse.
Dear Colleague Letter - Dosing

- SAMHSA cannot emphasize strongly enough that determining the admitting diagnosis, admitting the patient, and setting the initial dose must only be done by the OTP physician who possesses the demonstrated competency to diagnose and treat patients with opioid intoxication, dependency.

- "steady-state concentrations are not usually attained until 3 to 5 days of dosing,"

Center for Substance Abuse Treatment
Methadone Induction

• Dose “holding” (first few weeks)
  – Judge dose by how the patient feels during the peak period (2 to 4 hrs after dosing) rather than during the trough period (just prior to the next dose) generally 24 hrs after ingestion
  – Patients waking up “sick” during the first few days of induction are often convinced that they need a dose increase, when in fact more time is needed to reach steady state.
## Comparison - Methadone Dosing Schedules

<table>
<thead>
<tr>
<th>Dose Schedule</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
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<tr>
<td><strong>A</strong></td>
<td>30</td>
<td>30</td>
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<tr>
<td>50%</td>
<td>15</td>
<td>22.5</td>
<td>26.25</td>
<td>28.125</td>
<td>29.0625</td>
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<tr>
<td><strong>Effect</strong></td>
<td>45</td>
<td>52.5</td>
<td>56.25</td>
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<td><strong>Effect</strong></td>
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<td>50%</td>
<td>15</td>
<td>27.5</td>
<td>38.75</td>
<td>49.375</td>
<td>54.6875</td>
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<tr>
<td><strong>Effect</strong></td>
<td>55</td>
<td>77.5</td>
<td>98.75</td>
<td>109.375</td>
<td>114.688</td>
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<td><strong>D</strong></td>
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<td><strong>Effect</strong></td>
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<td><strong>L</strong></td>
<td>Day 1</td>
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<td>77.5</td>
<td>98.75</td>
<td>119.375</td>
<td>139.688</td>
<td></td>
</tr>
</tbody>
</table>
George B

- 37 yo, opioid dependence, heroin, age first use 27; cocaine, age first use 21; ETOH age first use 12
- Intake, reported daily heroin, for past 3 yrs, varying amounts, based upon how much money available; denied cocaine
- UDS + opiates
- +HCV, HBV
George B

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
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<td>1/13/07</td>
<td>1/14/07</td>
<td>1/15/07</td>
<td>1/16/07</td>
<td>1/17/07</td>
<td>1/22/07</td>
</tr>
</tbody>
</table>

Dose Schedule:
- **30**
- **40**
- **50**
- **60**
- **70**
- **80**

COWS not available Physiological dependence
- No Follow up

Father called clinic, advised of patient’s demise on 1/17/07; funeral was at 1:00 pm.
How Are States Responding-

- programs are required to be open 7 day a week
- Programs must check the PMP periodically.
- Programs must assess for tapering, withdrawal, detox
- Take home revoked for positive drug test
- Moratorium on new programs.
Other Recommendations ??

- Induction period dangerous and should only be carried out inpatient
- Programs must be open seven days per week.
- Patients who continue to abuse illicit substances should not continue treatment
- No take homes - trust
Summary/conclusions

- Methadone and Buprenorphine treatment expanding.
- Methadone associated mortality continues to be an increasing problem.
- Increases not associated with addiction treatment source.
  - However, cases of deaths during induction are not uncommon
  - SAMHSA will emphasize caution in induction process for OTPs
Opioid Treatment Issues
CSAT

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