

# DEA Alert Conference

## November 13, 2008

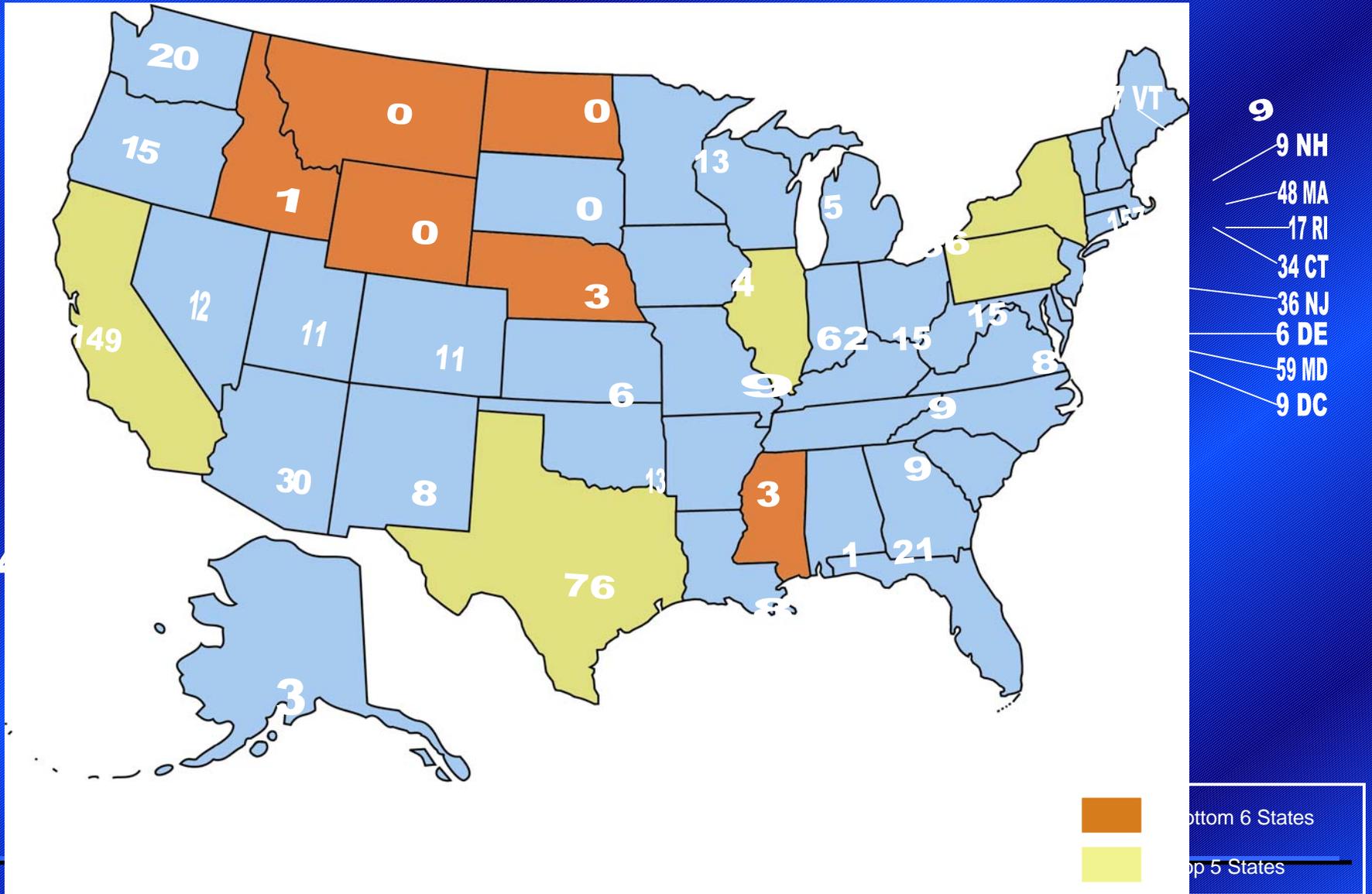
Nick Reuter

Division of Pharmacologic Therapy  
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

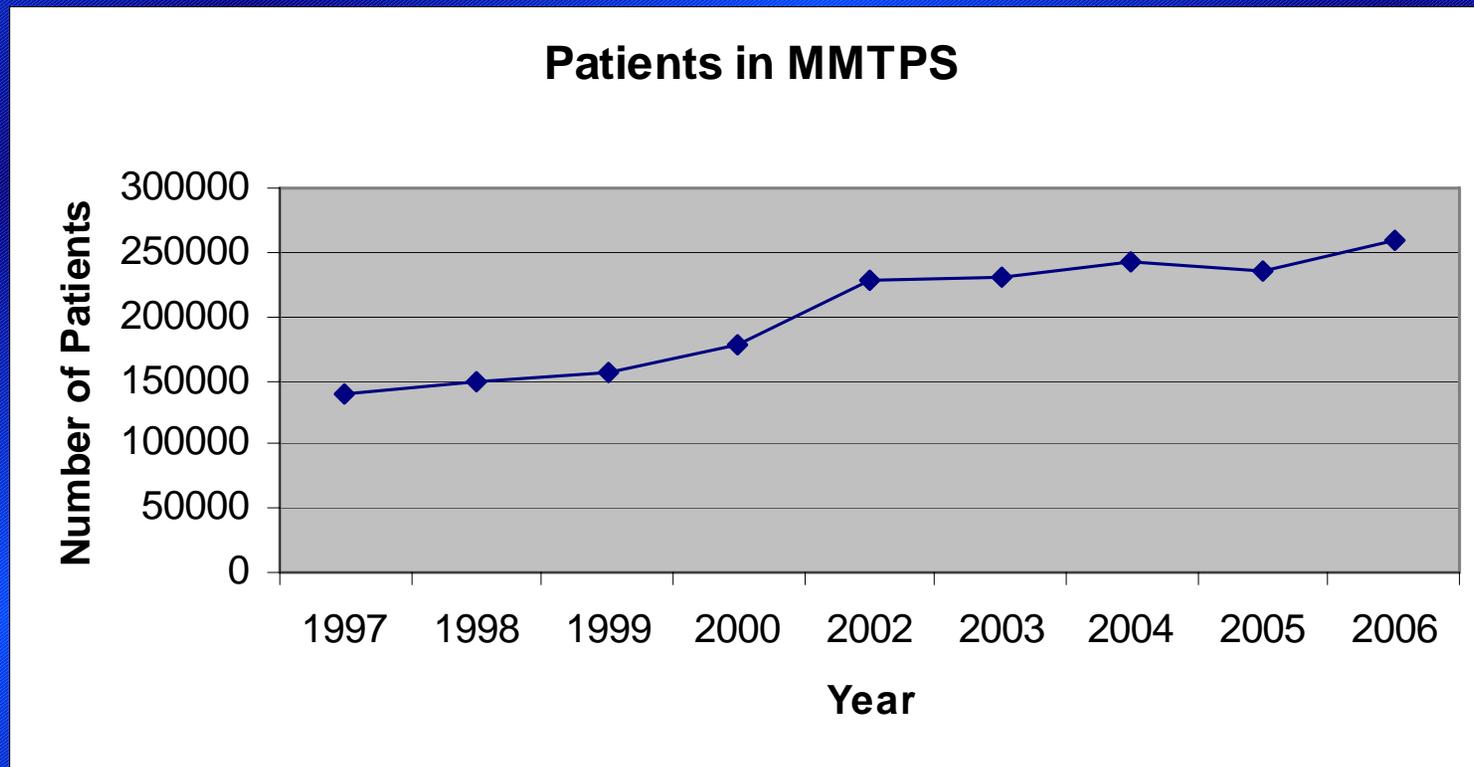
# Active Opioid Treatment Programs by State as of June 2008 (1,192)



## 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



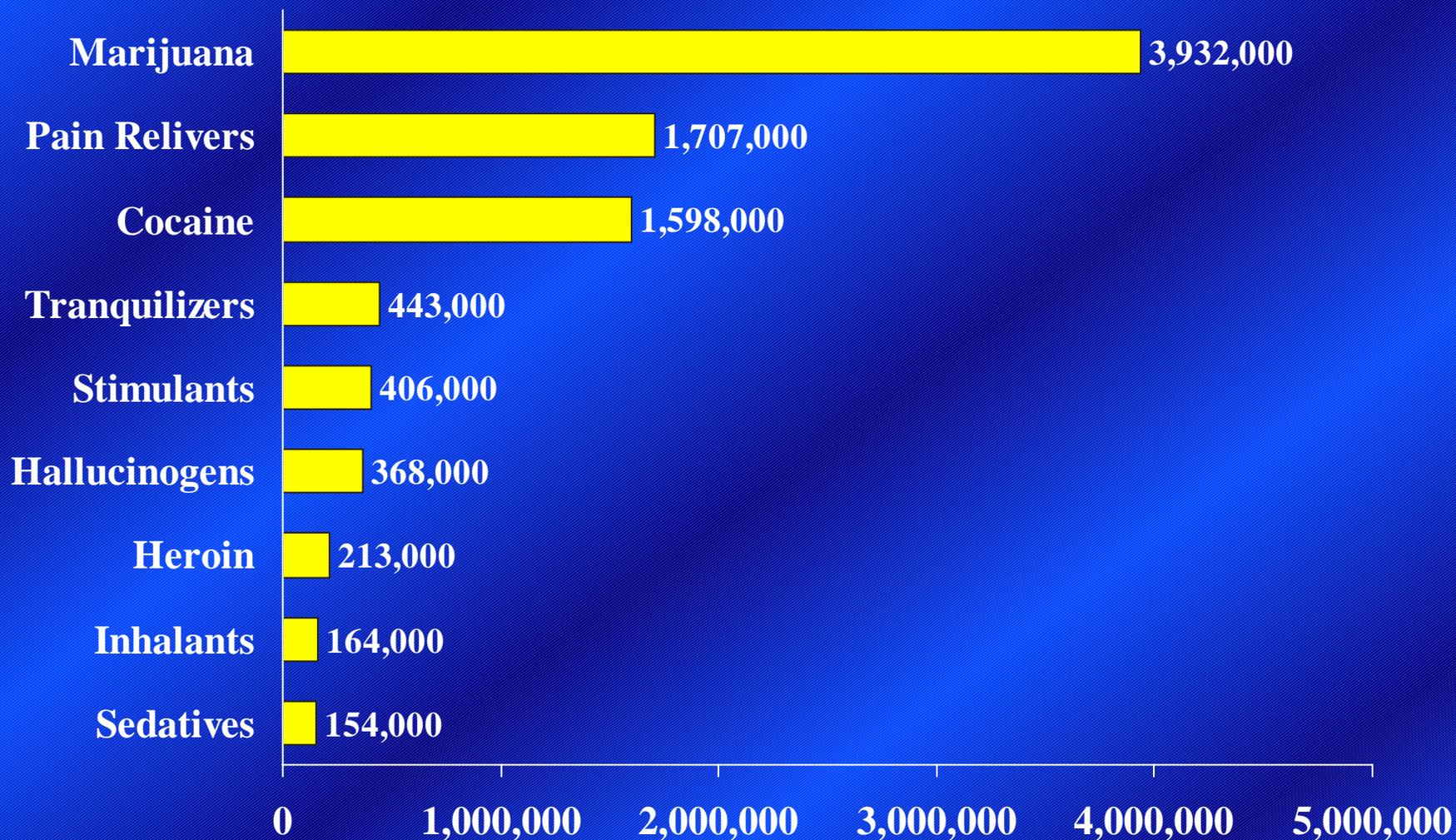
## Increase in Methadone Patients

- 2002 – 2006 (260,000)
- US – 2.3%
- TX – 27 %
- Oklahoma –114 %
- Louisiana –25 %
- Source National Survey on Substance Abuse Treatment Services, SAMHSA

Fig  
7.2

SAMHSA

# Dependence on or Abuse of Specific Illicit Drugs in the Past Year among Persons Aged 12 or Older: 2007



Numbers of Persons with Drug Use Disorder

Center for Substance Abuse Treatment

# 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?

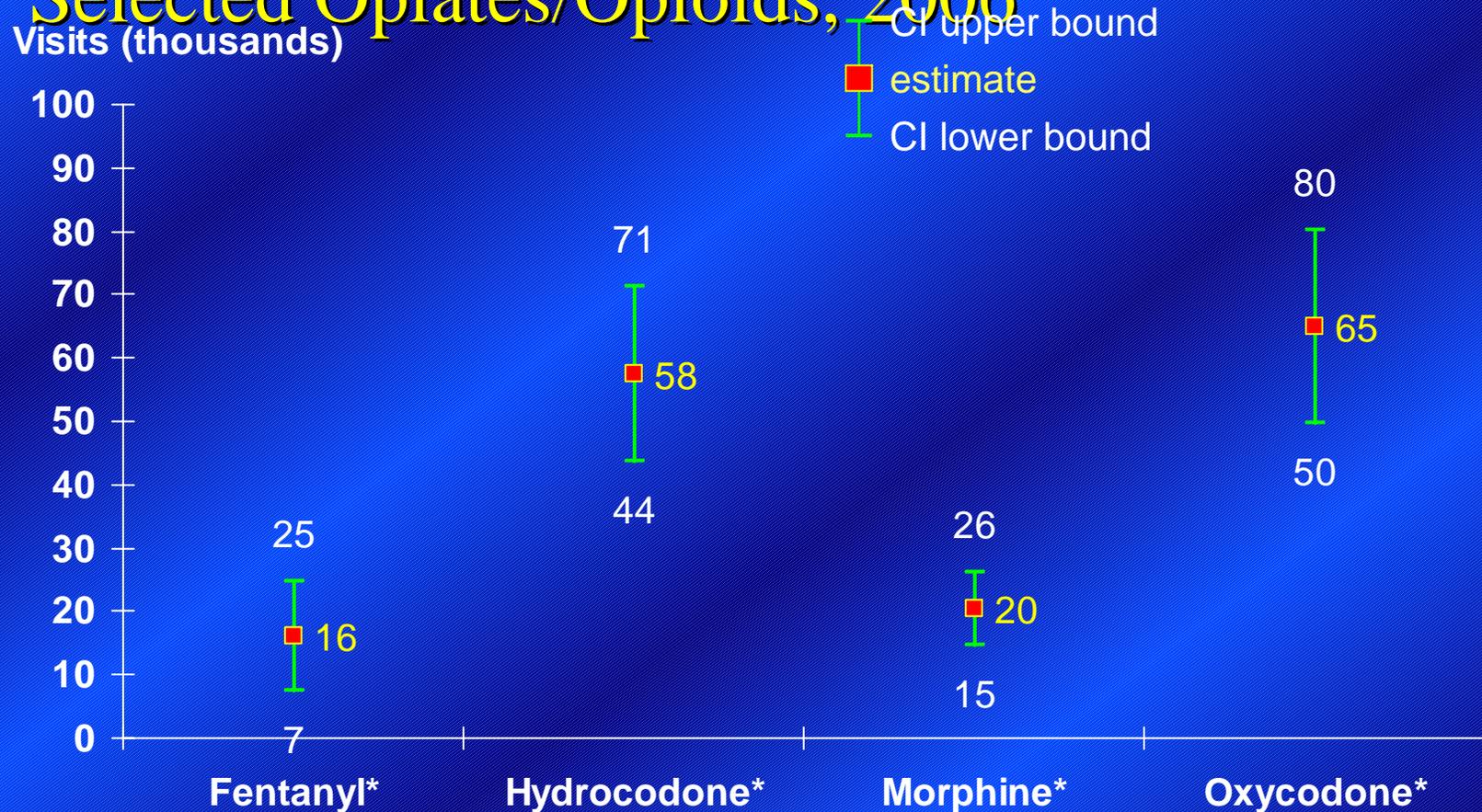
- Methadone maintenance treatment is safe and effective when used appropriately, when treatment is individualized to each patient, and when provided with counseling and other services.
- Has saved thousands of lives from overdose, HIV-AIDS
- NIH concluded most effective for opiate addiction.

# 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?

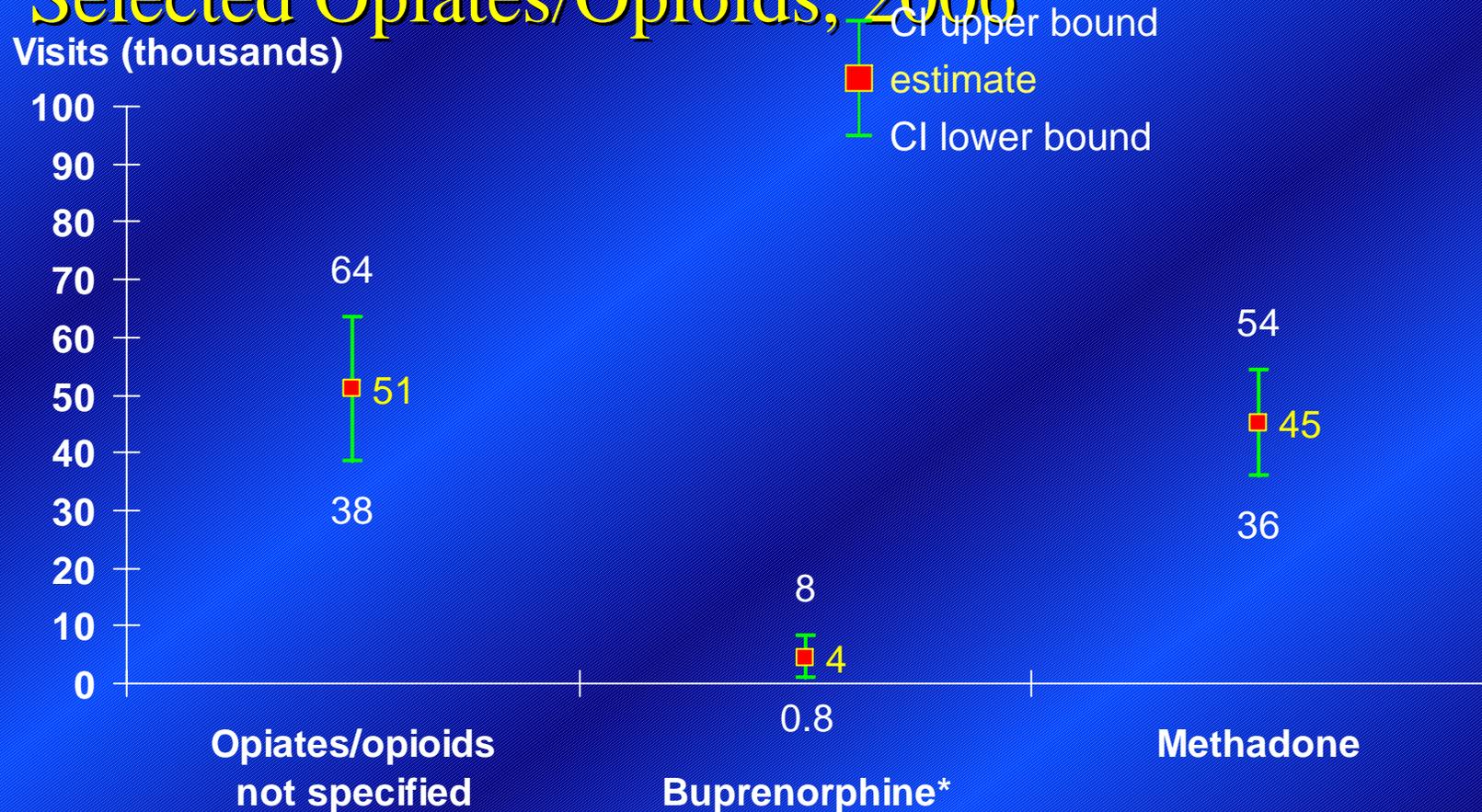
# Nonmedical Use of Pharmaceuticals, Selected Opiates/Opioids, 2006



\* Single- & multi-ingredient formulations

Source: National estimates from DAWN, 2006  
 Center for Substance Abuse Treatment

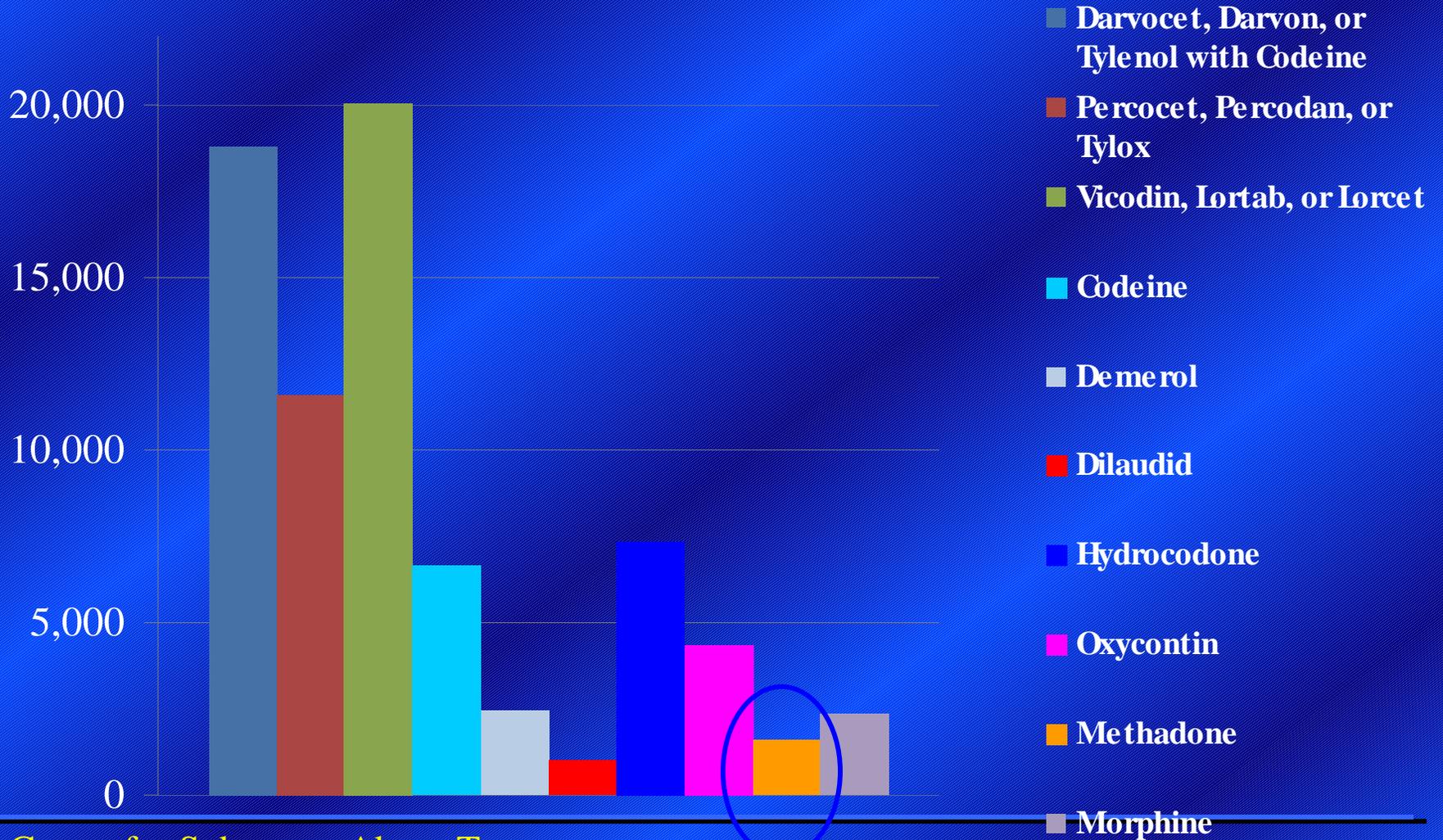
# Nonmedical Use of Pharmaceuticals, Selected Opiates/Opioids, 2006



\* Single- & multi-ingredient formulations

Source: National estimates from DAWN, 2006  
 Center for Substance Abuse Treatment

# Nonmedical Use of Specific Pain Relievers in Lifetime, Numbers in Thousands, 2007

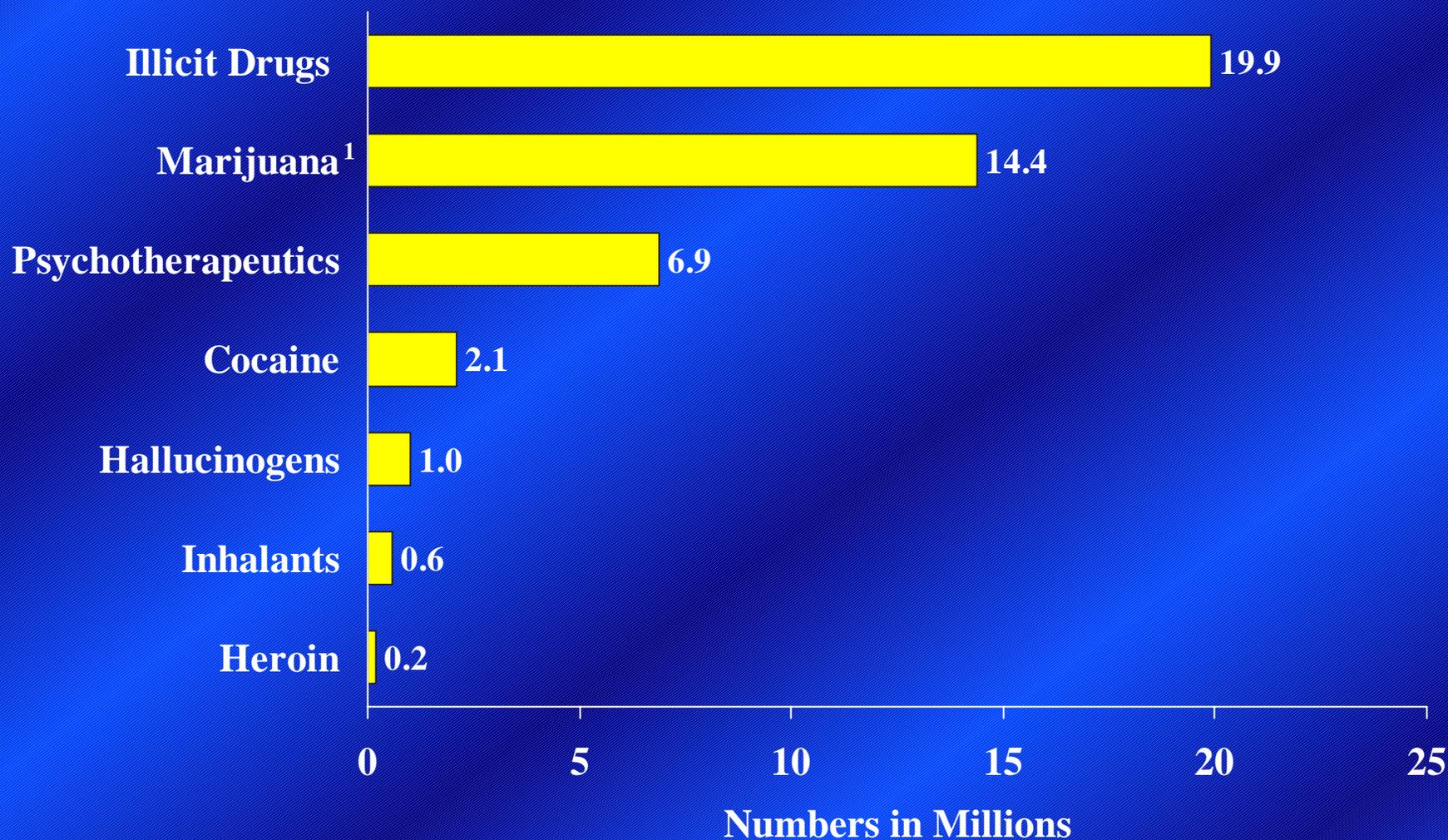


Center for Substance Abuse Treatment

Fig  
2.1

SAMHSA

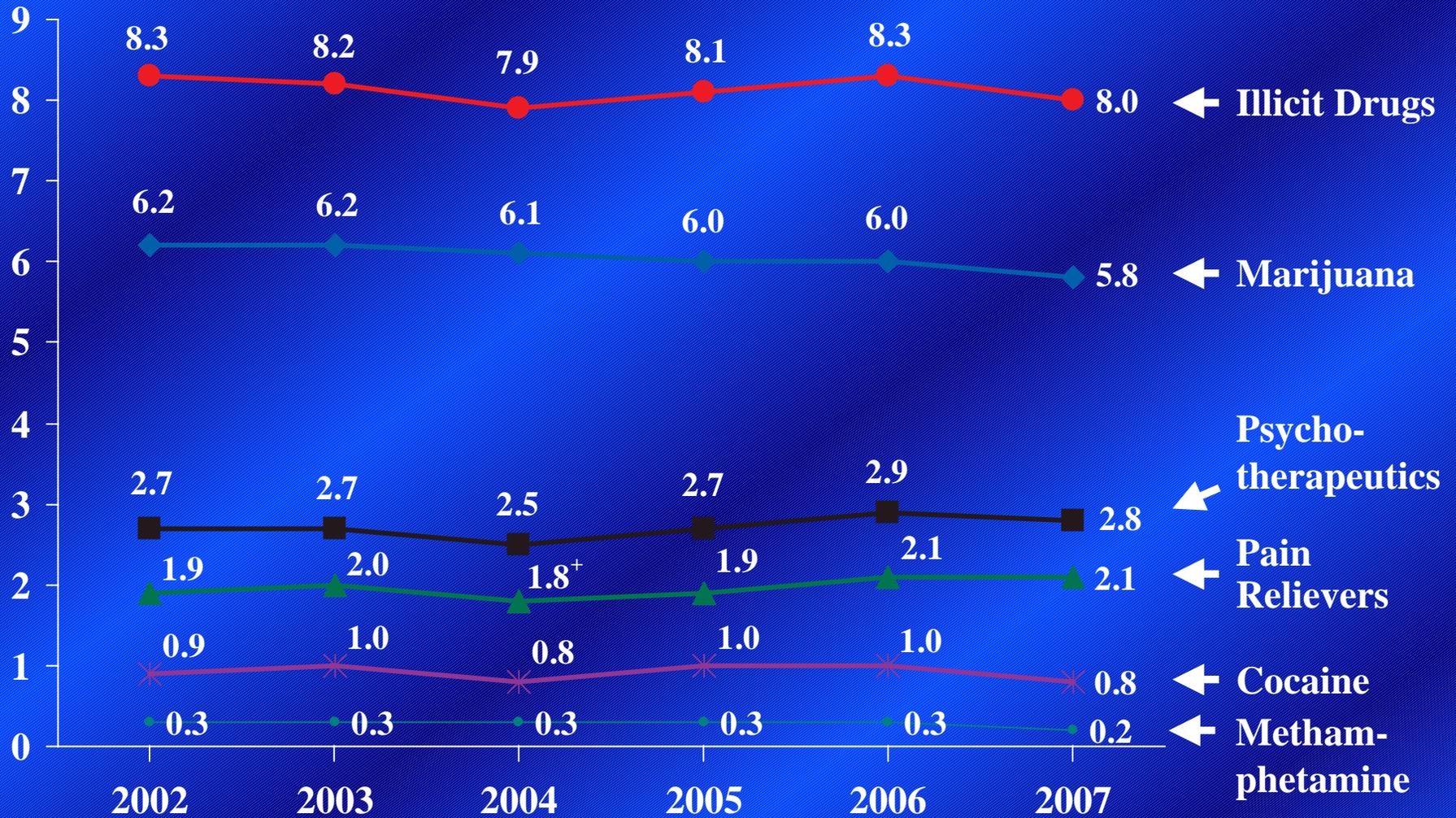
# Past Month Illicit Drug Use among Persons Aged 12 or Older: 2007



<sup>1</sup> Illicit Drugs include marijuana/hashish, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription-type psychotherapeutics used nonmedically.

Fig 2.2 **SAMHSA** Past Month Use of Selected Illicit Drugs among Persons Aged 12 or Older: 2002-2007

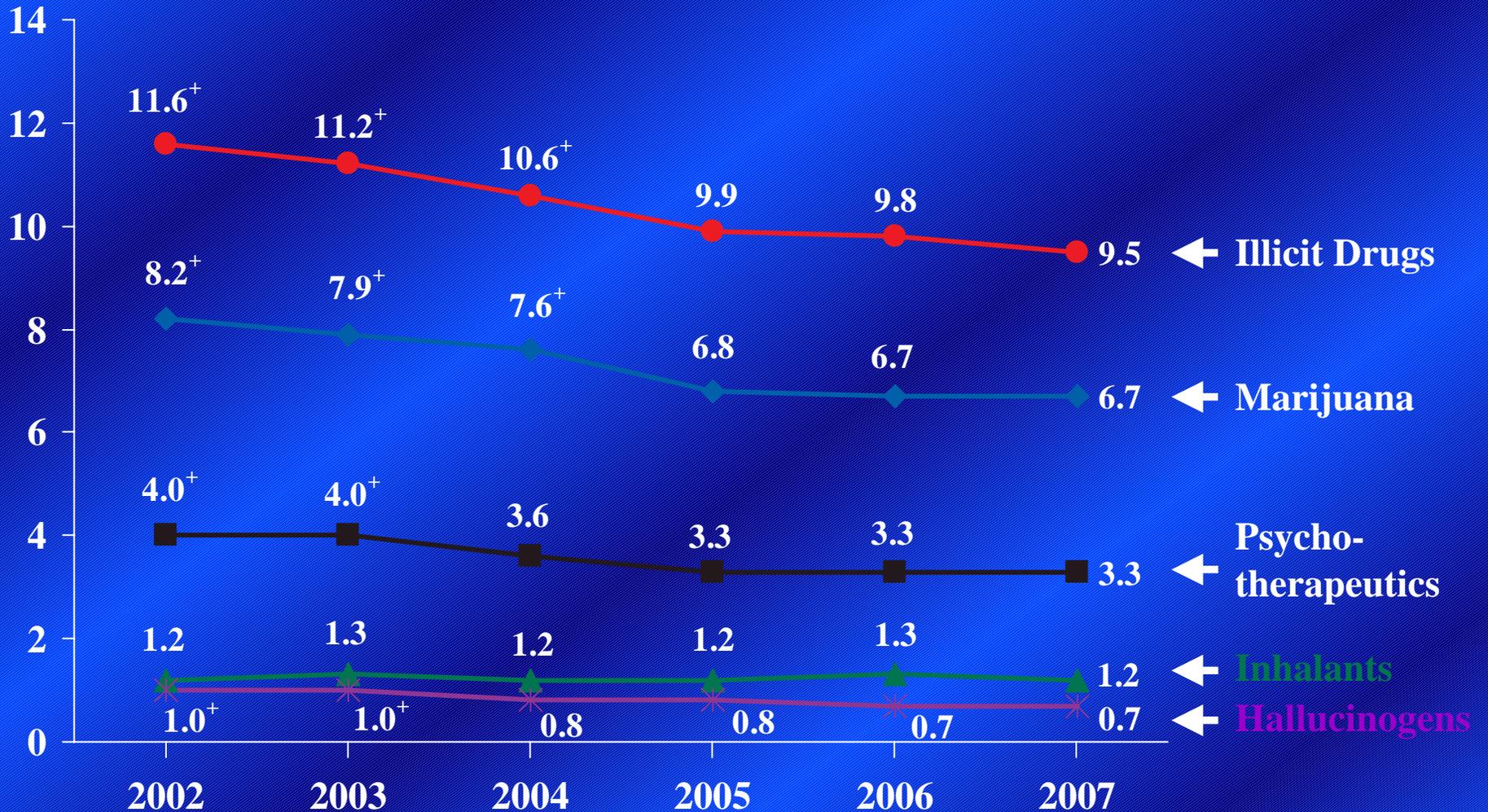
Percent Using in Past Month



<sup>+</sup> Difference between this estimate and the 2004 estimate is statistically significant at the .05 level.

Fig 2.5 **SAMHSA** Past Month Use of Selected Illicit Drugs among Youths Aged 12 to 17: 2002-2007

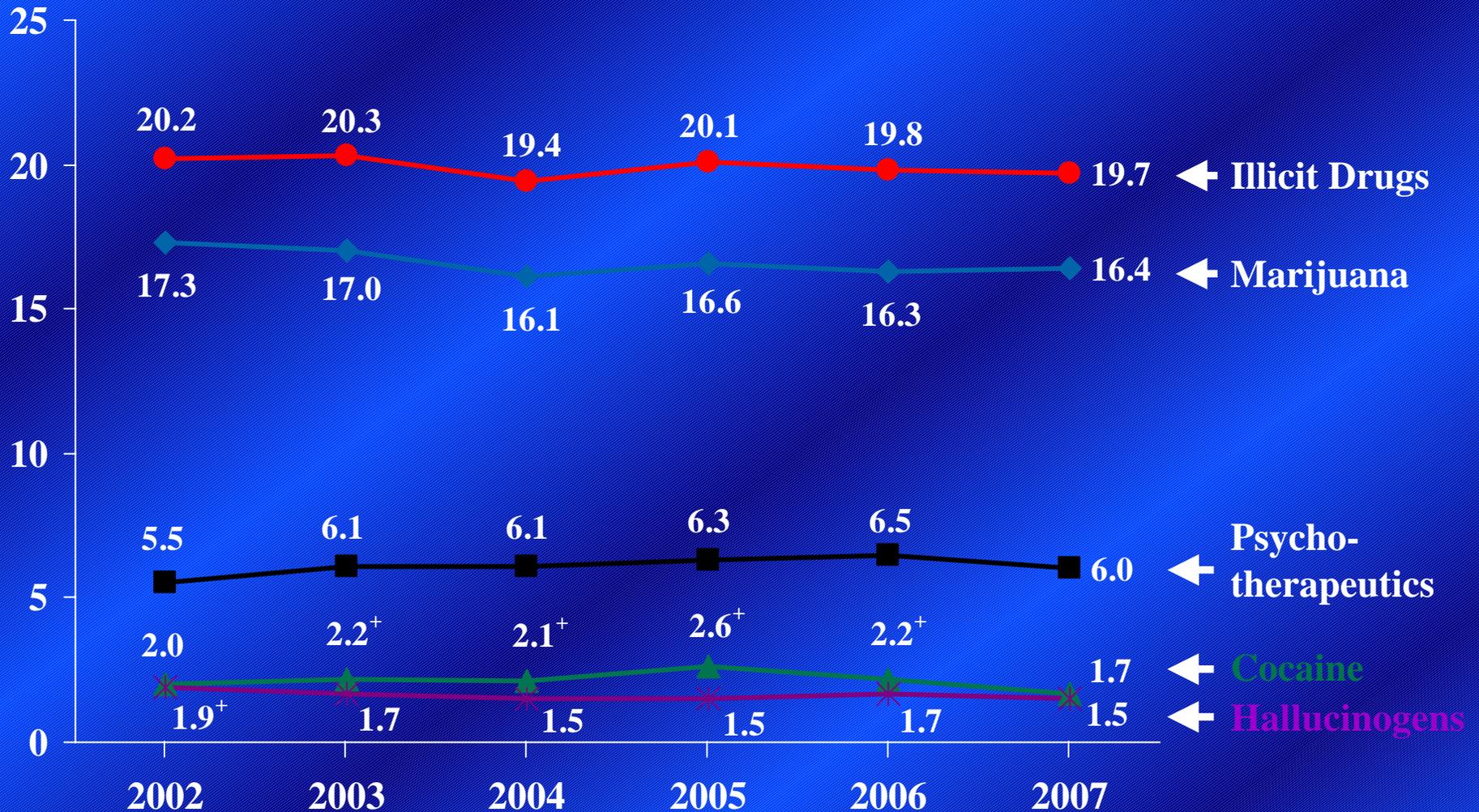
Percent Using in Past Month



<sup>+</sup> Difference between this estimate and the 2007 estimate is statistically significant at the .05 level.

Fig 2.6 **Past Month Use of Selected Illicit Drugs among Young Adults Aged 18 to 25: 2002-2007**

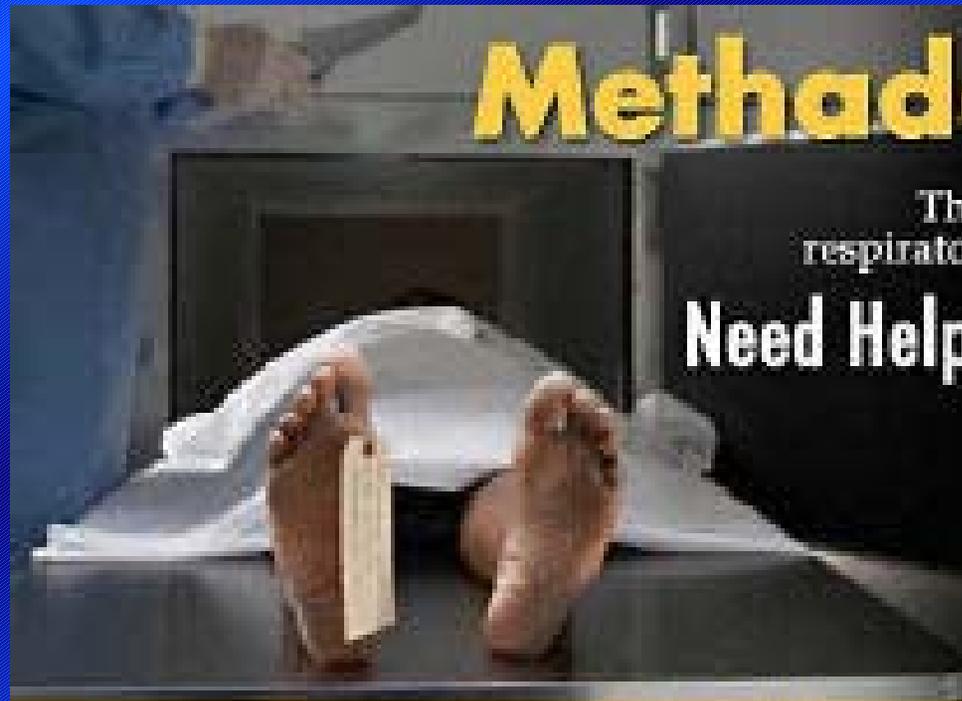
Percent Using in Past Month



<sup>+</sup> 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 Newcastle 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

# CDC MMWR Data - 2007

- 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
- West Virginia Unintentional Poisoning Deaths Increased 550% between 1999-2004
- 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)

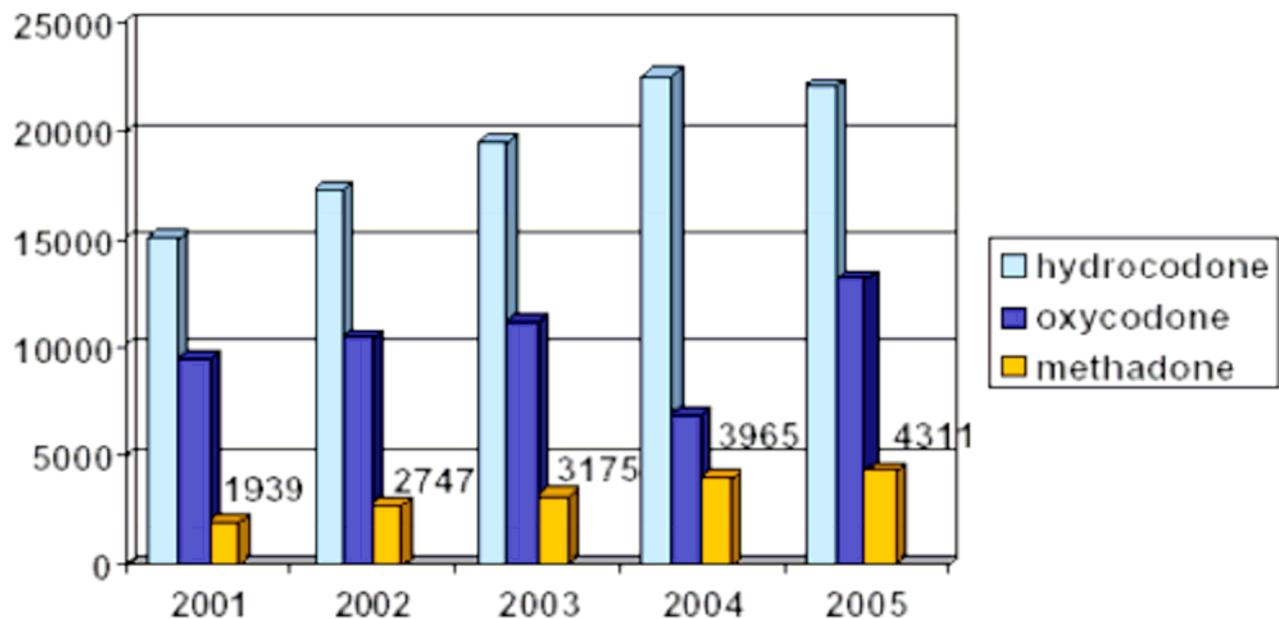
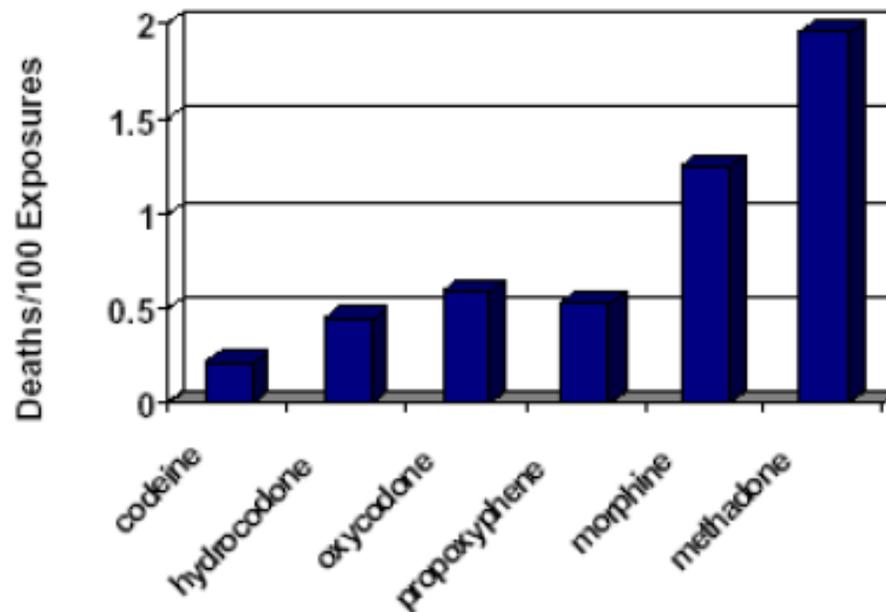


Figure 3.

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



Source: American Association of Poison Control Centers (AAPCC)

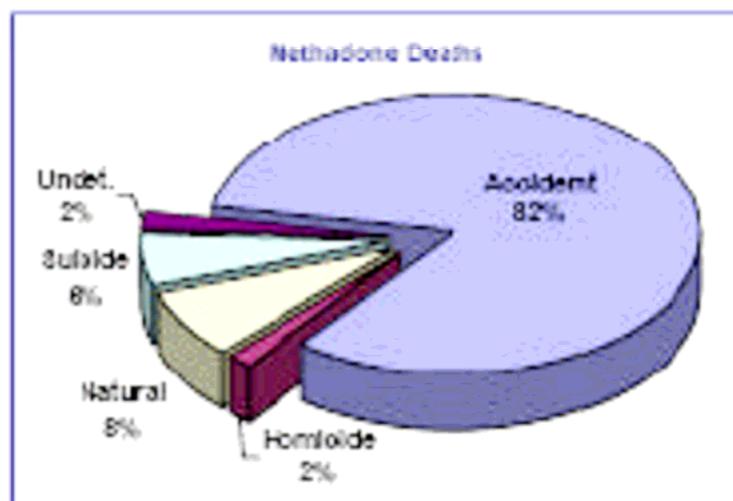
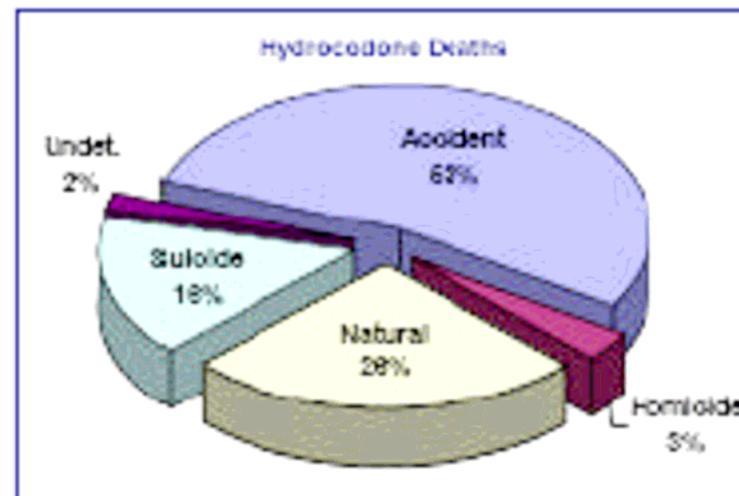
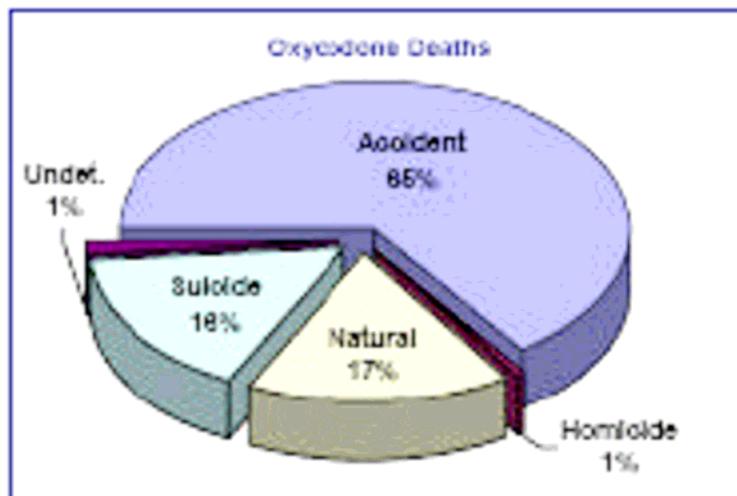
Table 2.

**States With the Largest Rate of Increase  
in Methadone Deaths, 1999 to 2004**

*Source: Centers for Disease Control and Prevention (CDC)*

	1999 Deaths	2004 Deaths	Death Ratios 2004 Deaths/1999 Deaths
Total US	623	3,202	5.1
West Virginia	4	99	24.8
Ohio	7	122	17.4
Louisiana	4	64	16
Kentucky	8	121	15.1
New Hampshire	2	29	14.5
Florida	29	400	13.8
Oregon	5	68	13.6
Pennsylvania	7	88	12.6
Tennessee	8	99	12.4
Wisconsin	6	63	10.5
Maine	5	52	10

**Manners of Death for Cases Reported**  
 (Accidental, Homicide, Natural, Suicide or Undetermined)



# Reasons for methadone toxicity

# Pharmacology

- Slow onset
- Long duration of action
  - Half life 24-36 hours
  - Steady state 4-5 days
  - Half of each days dose remains to be added to next days 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?

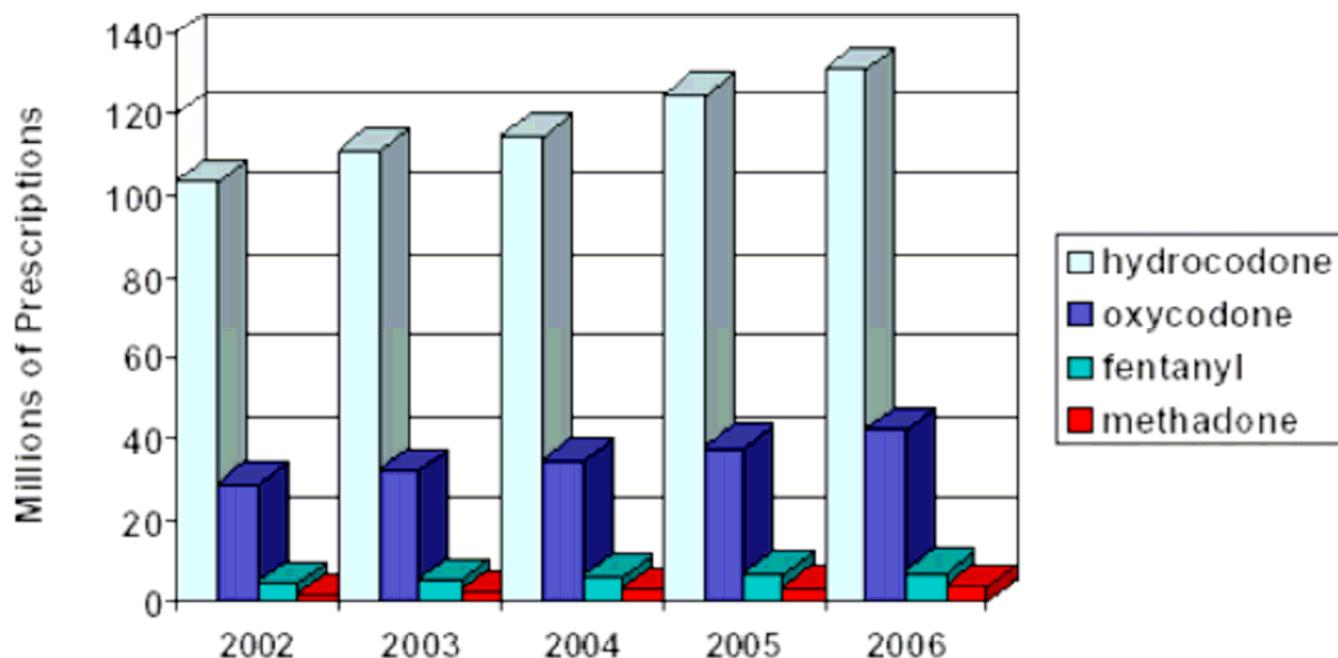
# Methadone Prescriptions

- 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

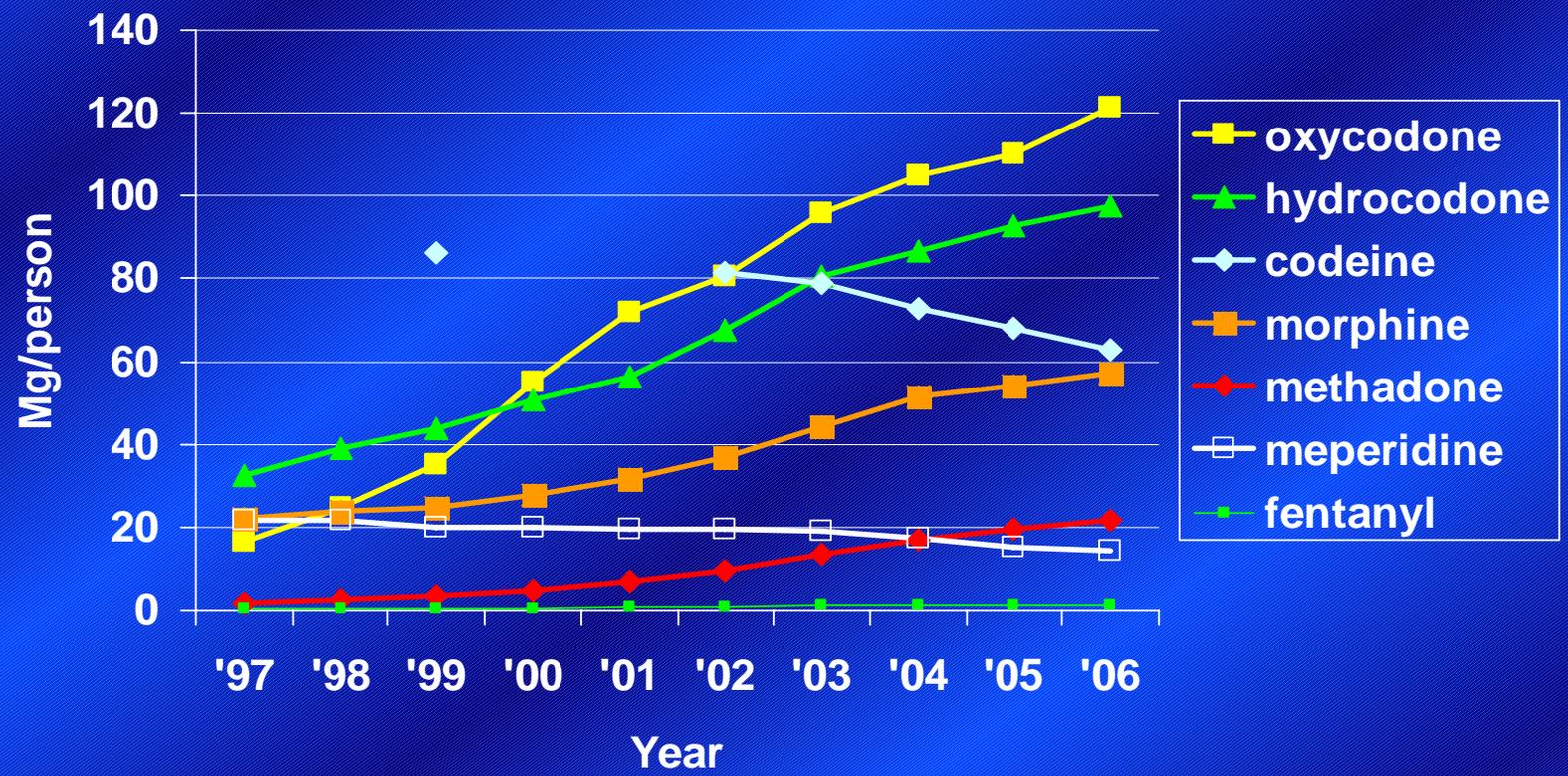


Note: In 2006, there were about 35 times more prescriptions dispensed for hydrocodone, 10 times more prescriptions for oxycodone, and twice as many prescriptions for fentanyl as for methadone

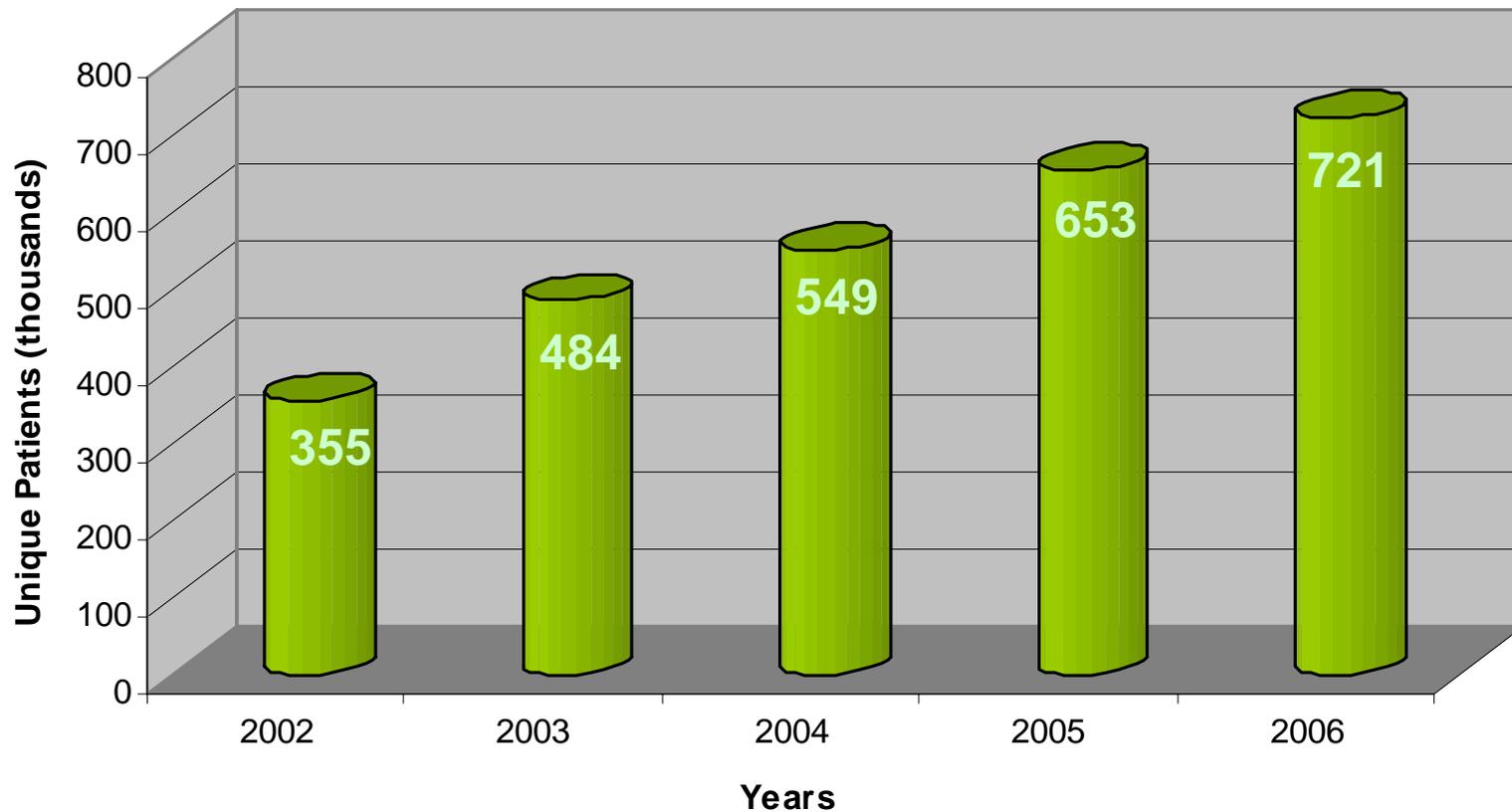
## Methadone Rx Increases - 2006

- 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 3<sup>rd</sup> 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

• Agent	Dosage	Cost*
• Methadone	90 pills	\$ 8.00
• SR morphine	60 pills	101.50
• MS Contin	60 pills	113.50
• Oxycontin	60 pills	176.50
• Duragesic	10 patches	154.00*

-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

# Maxwell – NTP Patient Deaths – Texas – 1994-2002 - 1

- 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 1<sup>st</sup> 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

# FDA Advisory - 1

- 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,"**

# 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

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
<b>Dose Schedule A</b>	<b>30</b>	<b>30</b>	<b>30</b>	<b>30</b>	<b>30</b>	<b>30</b>
50%		15	22.5	26.25	28.125	29.0625
<b>Effect</b>		<b>45</b>	<b>52.5</b>	<b>56.25</b>	<b>58.125</b>	<b>59.0625</b>
<b>Dose Schedule B</b>	<b>30</b>	<b>30</b>	<b>40</b>	<b>40</b>	<b>40</b>	<b>40</b>
50%		15	22.5	31.25	35.625	37.8125
<b>Effect</b>		<b>45</b>	<b>62.5</b>	<b>71.25</b>	<b>75.625</b>	<b>77.8125</b>
<b>Dose Schedule C</b>	<b>30</b>	<b>40</b>	<b>50</b>	<b>60</b>	<b>60</b>	<b>60</b>
50%		15	27.5	38.75	49.375	54.6875
<b>Effect</b>		<b>55</b>	<b>77.5</b>	<b>98.75</b>	<b>109.375</b>	<b>114.688</b>
<b>Dose Schedule D</b>	<b>30</b>	<b>50</b>	<b>70</b>	<b>70</b>	<b>70</b>	<b>70</b>
50%		15	32	51	60.5	65.25
<b>Effect</b>		<b>65</b>	<b>102</b>	<b>121</b>	<b>130.5</b>	<b>135.25</b>
<b>Dose Schedule L</b>	<b>Day 1</b>	<b>Day 2</b>	<b>Day 3</b>	<b>Day 4</b>	<b>Day 5</b>	<b>Day 6</b>
	<b>30</b>	<b>40</b>	<b>50</b>	<b>60</b>	<b>70</b>	<b>80</b>
		15	27.5	38.75	49.375	59.6875
		<b>55</b>	<b>77.5</b>	<b>98.75</b>	<b>119.375</b>	<b>139.688</b>

Opioid Maintenance Pharmacotherapy - A Course for Clinicians

## 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 3yrs, varying amounts, based upon how much money available; denied cocaine
- UDS + opiates
- +HCV, HBV

# George B

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
	1/12/07	1/13/07	1/14/07	1/15/07	1/16/07	1/17/07	1/22/07
Dose Schedule	<b>30</b>	<b>40</b>	<b>50</b>	<b>60</b>	<b>70</b>	<b>80</b>	
	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-wv

- 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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