

# METHADONE

*Methadone Mortality Working Group  
Drug Enforcement Administration  
Office of Diversion Control  
April 2007*

# Background

- In 2003, SAMHSA convened a multidisciplinary group for a national assessment of methadone-associated deaths.
- This meeting was prompted by
  - Increasing methadone-associated deaths
  - Negative press that regarded methadone as “widely abused and dangerous”
  - Uncertainty regarding the source of methadone (i.e. pain management or narcotic treatment)
  - Uncertainty regarding the cause of deaths
- The Methadone-Associated Mortality Assessment Report was published in 2004 (DHHS publication No. 04-3904).

# Methadone-Associated Mortality Assessment Findings

- Nearly all narcotics, including methadone, were increasingly associated with diversion, abuse and deaths.
- Both respiratory depressant effects and/or cardiovascular effects at high doses can be fatal.
- Methadone treatment for narcotic addiction has a proven safety record and actually reduces mortality in this population.

# Methadone-Associated Mortality Assessment Findings (cont)

Three primary scenarios were seen in methadone associated deaths:

- 1) Accumulation to toxic levels of methadone during the start of opioid treatment or pain management due to overestimation of tolerance and methadone's long, often variable, half-life.
- 2) Misuse of diverted methadone by individuals with little or no opioid tolerance.
- 3) Synergistic effects of methadone in combination with other CNS depressants (i.e., alcohol, benzodiazepines or other opioids).

# Methadone-Associated Mortality Assessment Findings (cont)

- Methadone is becoming more widely available due to increased use for pain management and a relaxation in regulations regarding take-home doses of methadone from narcotic treatment programs (NTPs).
- There is no comprehensive database of drug-related deaths in the U.S.
- Problems with uniform definition by Medical Examiners preclude uniformity in reporting “cause of death” on death certificates.
- It seemed more likely that the increased availability of methadone was the result of use in pain management as there was not a great increase in NTP patient population. In addition, the increased incidents of death started prior to a change in take-home regulations.

# Current Problem

- All available data indicate that methadone continues to be increasingly used, misused, diverted, and abused.
- Significant increases in methadone-related deaths are being reported. In some areas, deaths related to methadone are outpacing other narcotics.
- Federal agencies must address this public health crisis.

# FDA Health Advisory

On November 27, 2006, the Food and Drug Administration (FDA) put out a public health Advisory stating that **methadone use in pain control may result in death and life-threatening changes in breathing and heart beat.** Pain relief from a dose of methadone lasts about 4-8 hours but methadone stays in the body much longer, 8-59 hours after administration. As a result, patients may feel the need for more pain relief before methadone is cleared from the body. Methadone may build up in the body to a toxic level if it is taken too often, if the amount taken is too high, or if it is taken with certain other medicines or supplements. **FDA advised that methadone doses for pain should be carefully selected, slowly titrated to analgesic effect and closely monitored by their prescribing physician.** The black box warning in the approved labeling for Dolophine Hydrochloride (methadone-containing 5 and 10 mg tablets) has been altered to warn patients not to take a higher dose or take Dolophine more frequently than prescribed.

Note: This advisory has not resulted in any decrease in the numbers of prescriptions for methadone (IMS Health Prescription Audit).

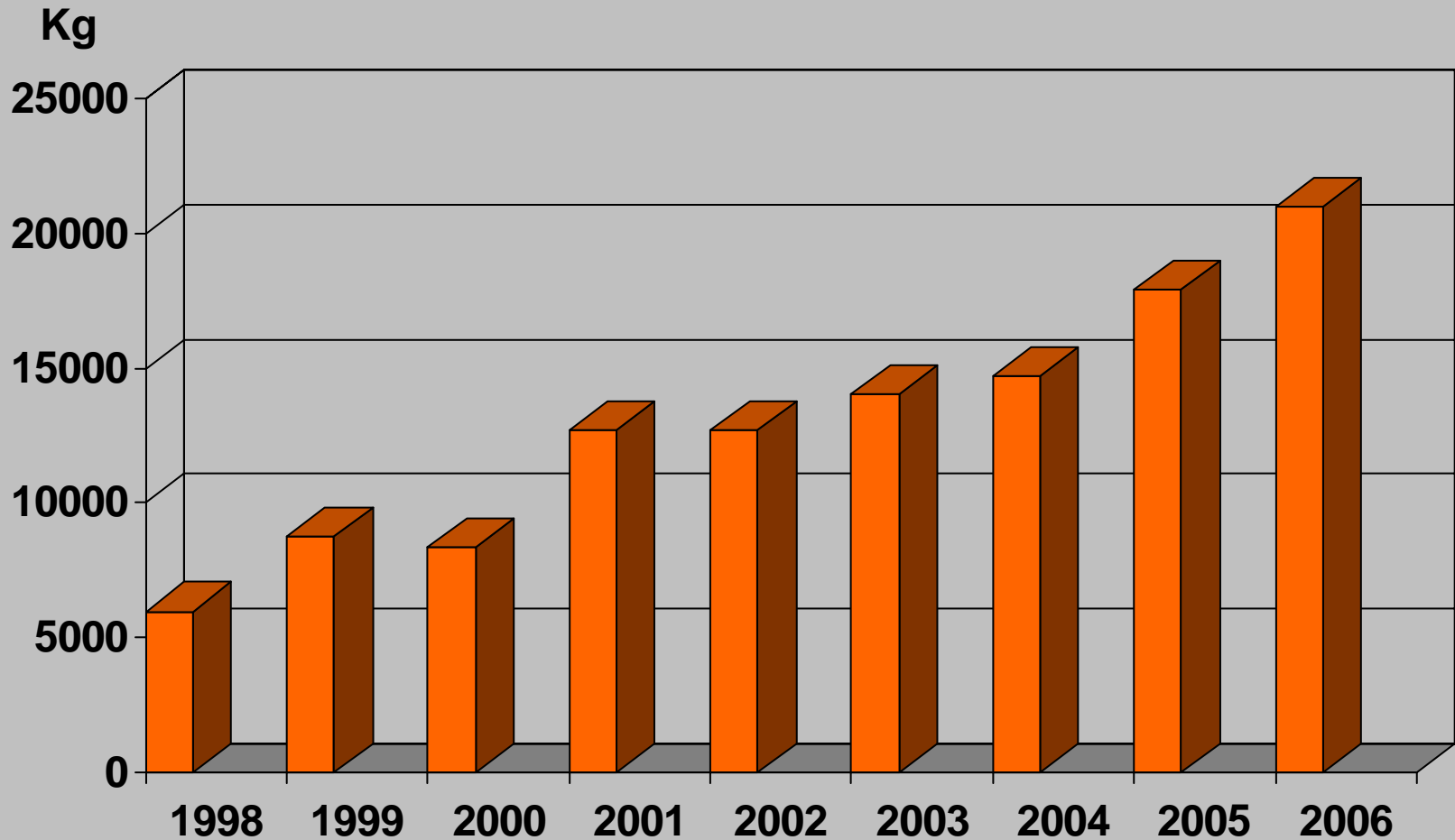
# Current Methadone Use

- As a schedule II substance, methadone manufacturers must obtain a quota from DEA. From 1998 thru 2006, the quota for methadone has increased by about 250%.
- Increased use is primarily associated with increased use for pain management not narcotic treatment.
- Prescriptions for methadone have increased by nearly 700% from 1998 thru 2006.



# Methadone Quota History

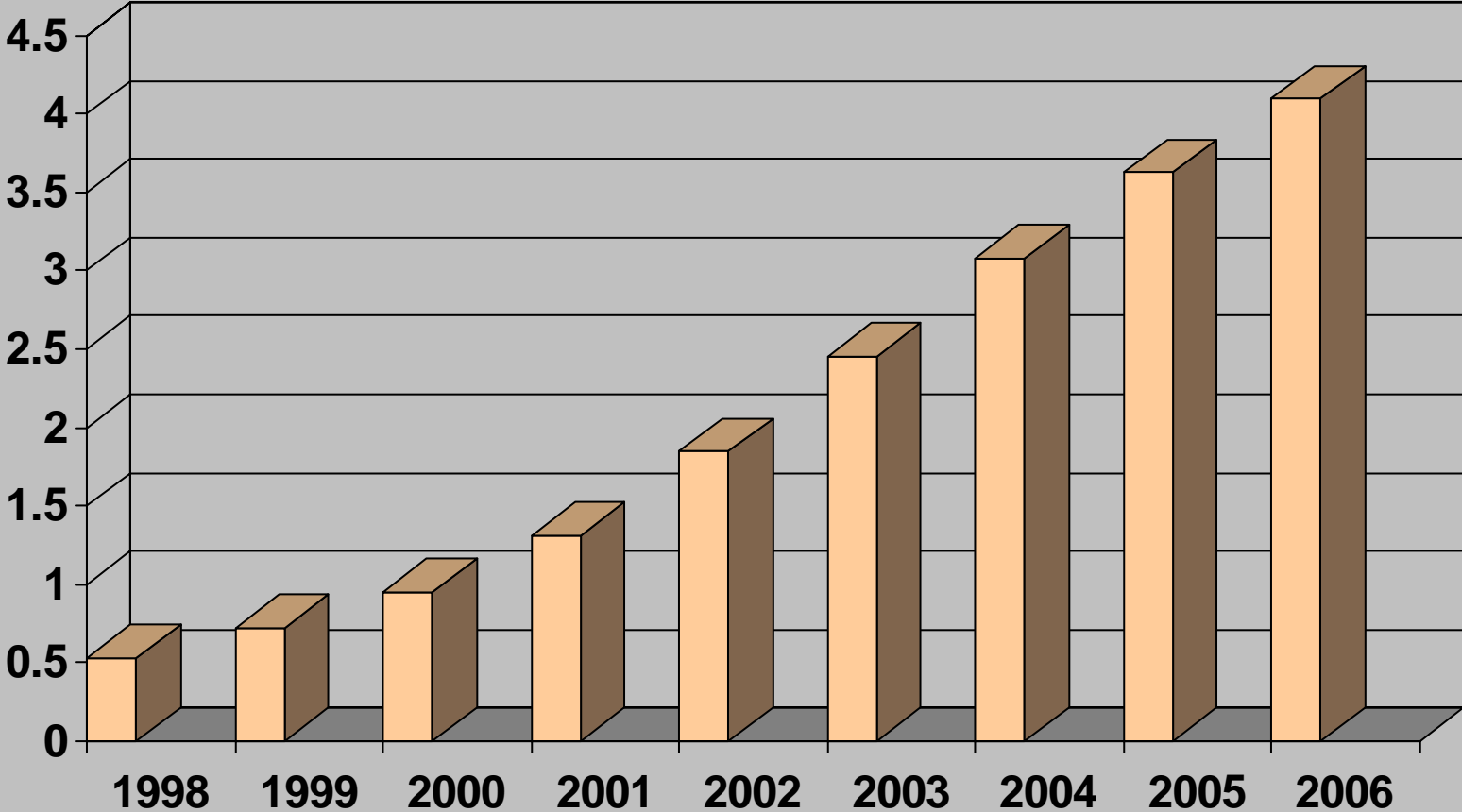
*Source: DEA*



# Methadone Prescriptions

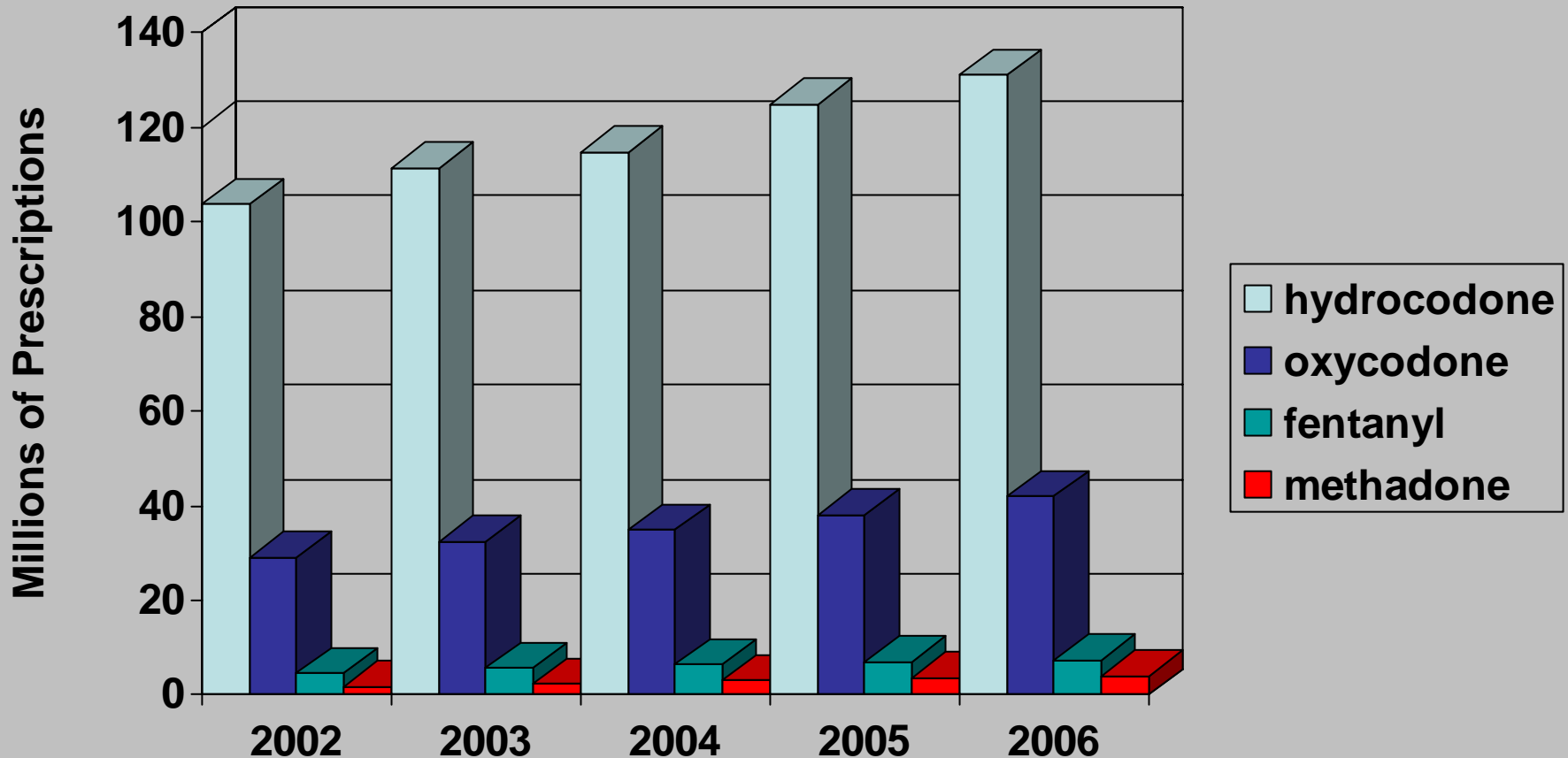
*Source: IMS Health Prescription Audit*

Millions



# Total Prescriptions Selected Narcotic Analgesics

Source: IMS Health Prescription Audit



**Note: In 2006, there were about 35-fold more hydrocodone prescriptions, 10-fold more oxycodone and 2-fold more fentanyl prescriptions compared to methadone prescriptions**

# Who is prescribing methadone?

## 5 and 10 mg tablets Rx

### **Top Prescribers:**

- Anesthesiologists
- Family Practitioners
- Internists
- Osteopaths
- Physical Med. & Rehab
- Neurologists
- Nurse Practitioners

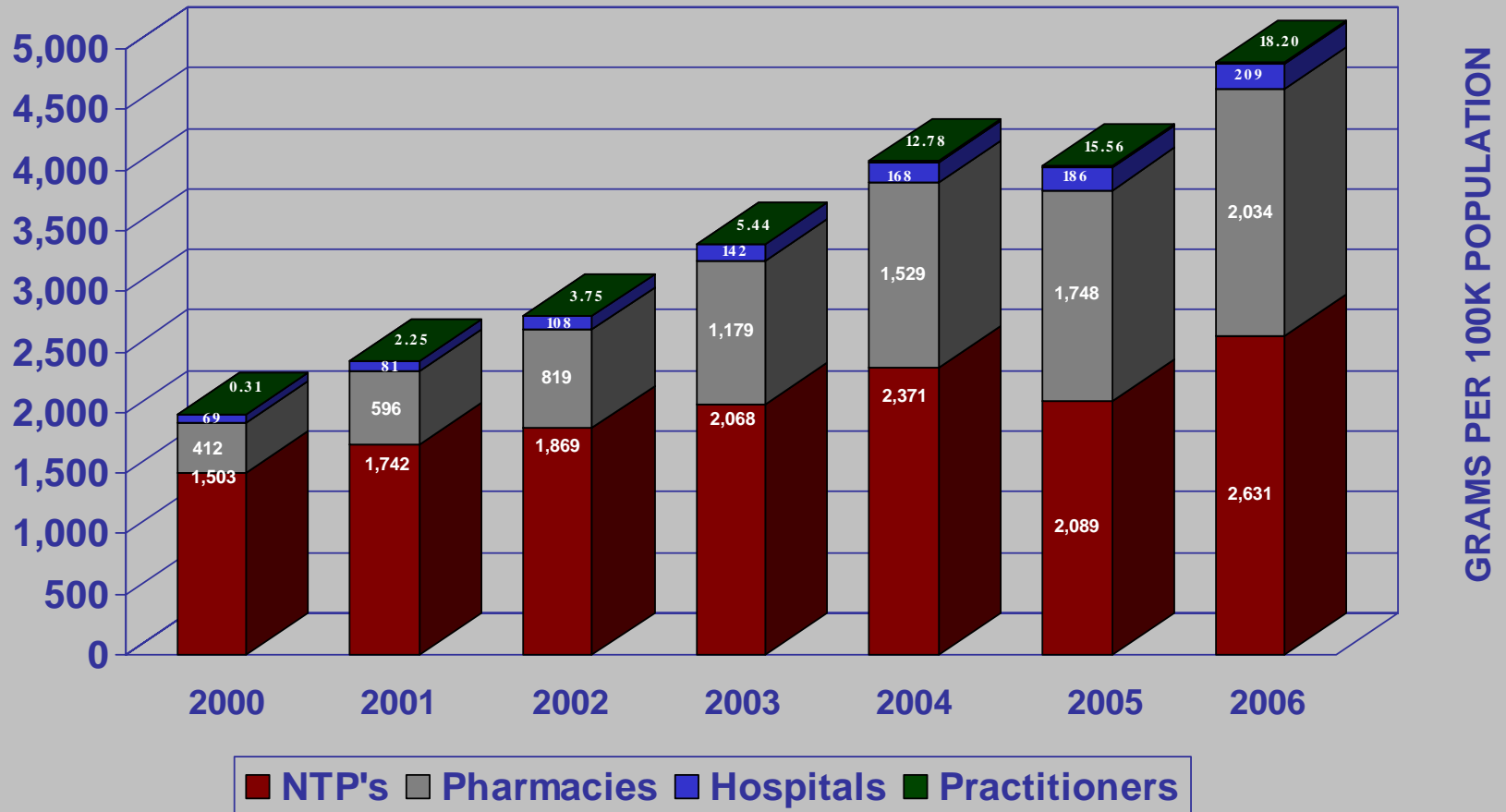
## 40 mg diskettes Rx

### **Top Prescribers:**

- Family Practitioners
- Anesthesiologists
- Internists
- Osteopaths
- Physical Med. & Rehab
- Nurse Practitioners
- General Practitioners

***Source: IMS Health, National Prescription Audit, November 2006***

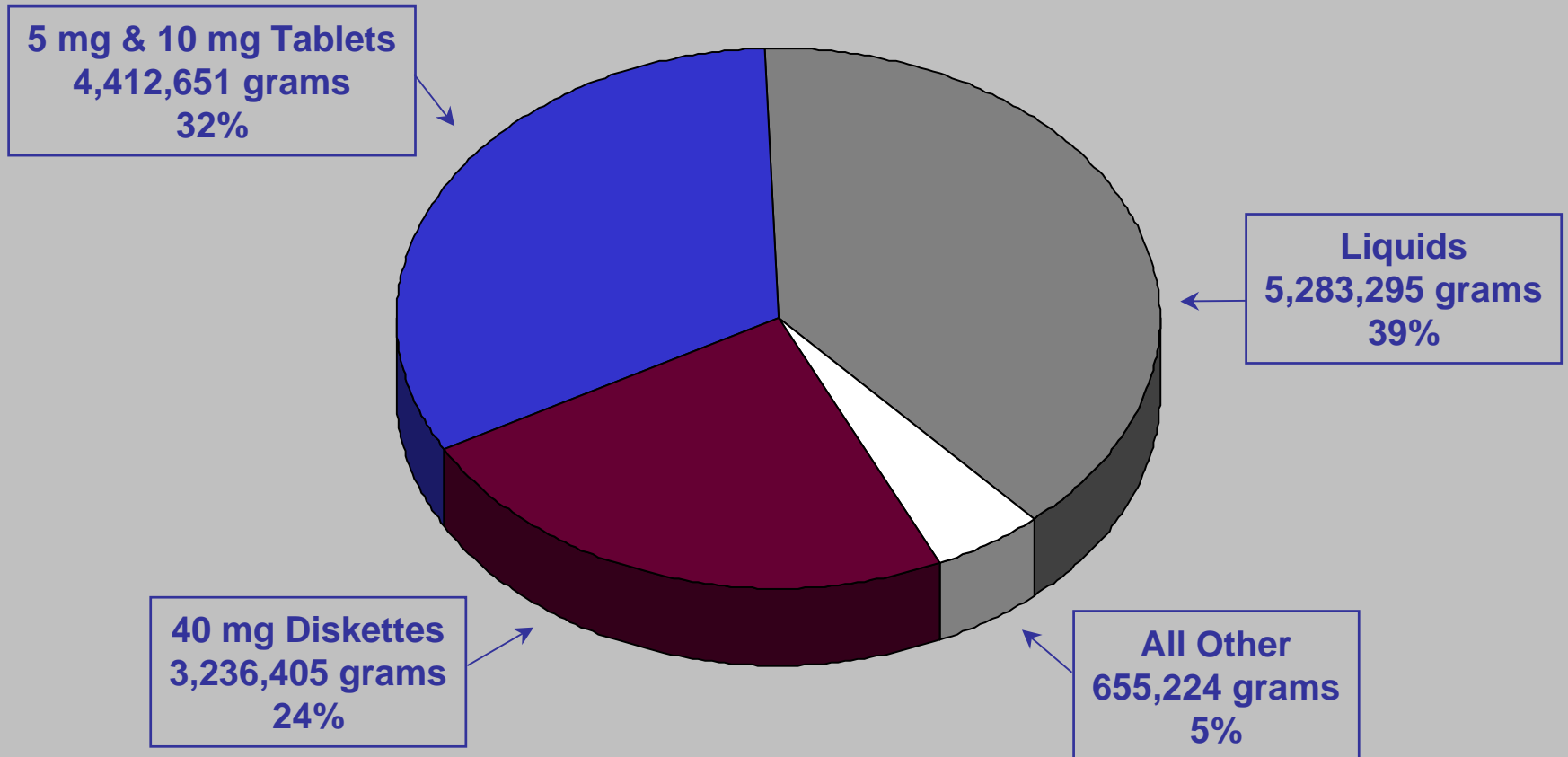
# 2000 - 2006 Methadone Distribution Business Activity Comparison



Source: DEA ARCOS 04/2007

# 2006 Distribution\* of Methadone

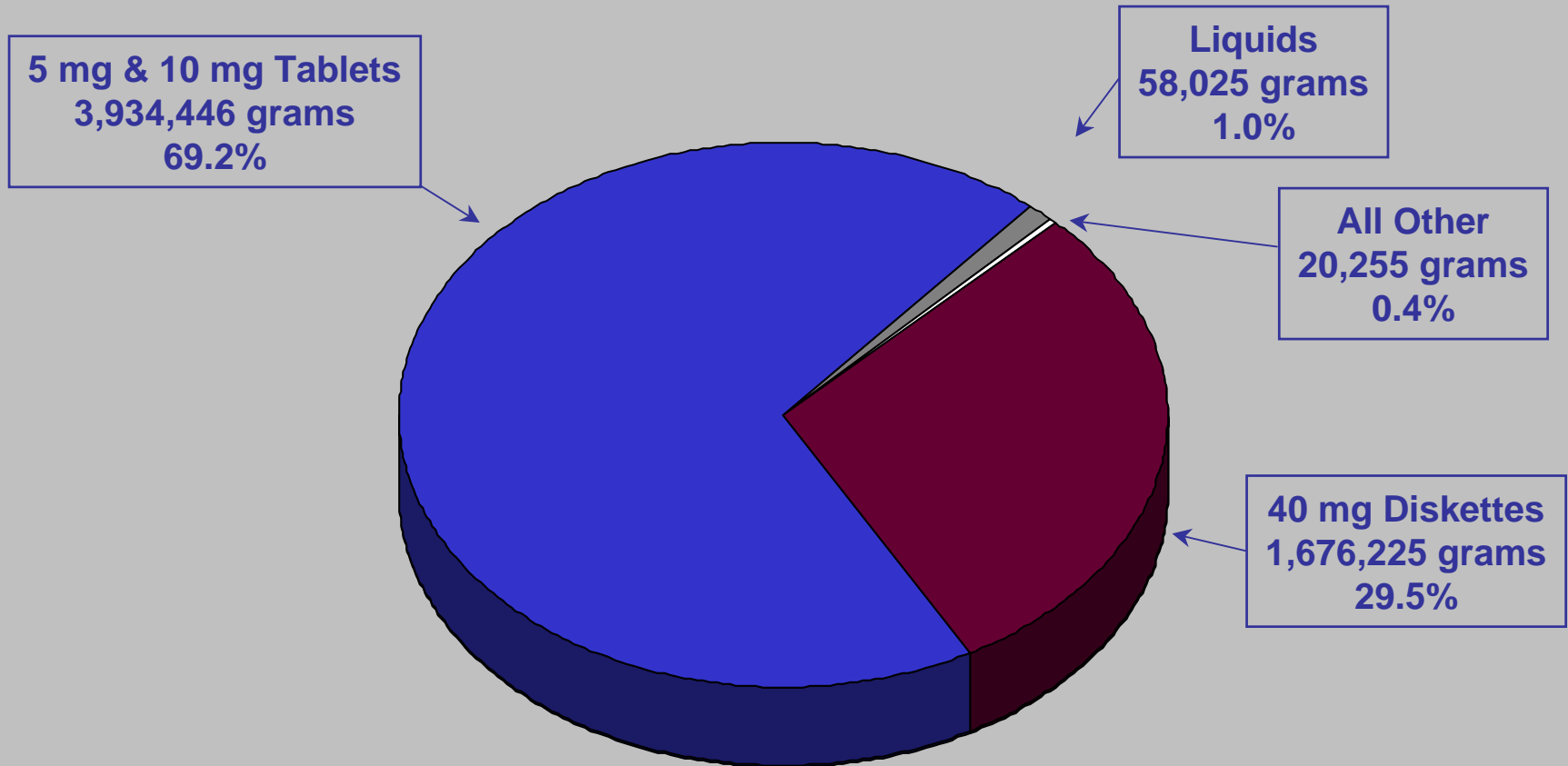
Source: DEA ARCOS 04/2007



\* Based on total gram amount  
Includes NTP's

# 2006 Distribution\* of Methadone to Pharmacies

Source: DEA ARCOS 04/2007



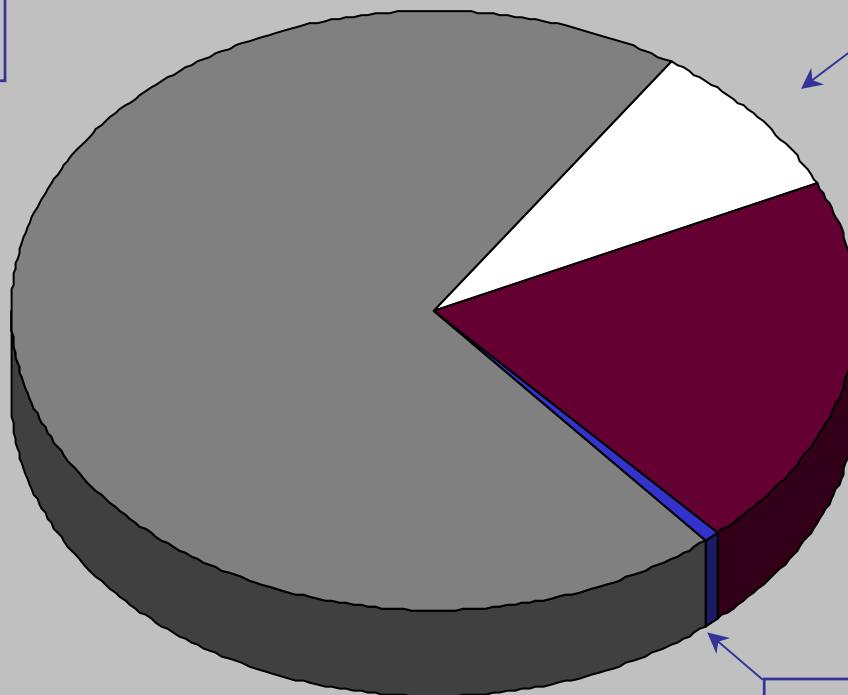
\* Based on total gram amount

# 2006 Distribution\* of Methadone to NTP's

Source: DEA ARCOS 04/2007

Liquids  
5,192,096 grams  
70.7%

All Other  
632,878 grams  
8.6%



40 mg Diskettes  
1,481,873 grams  
20.2%

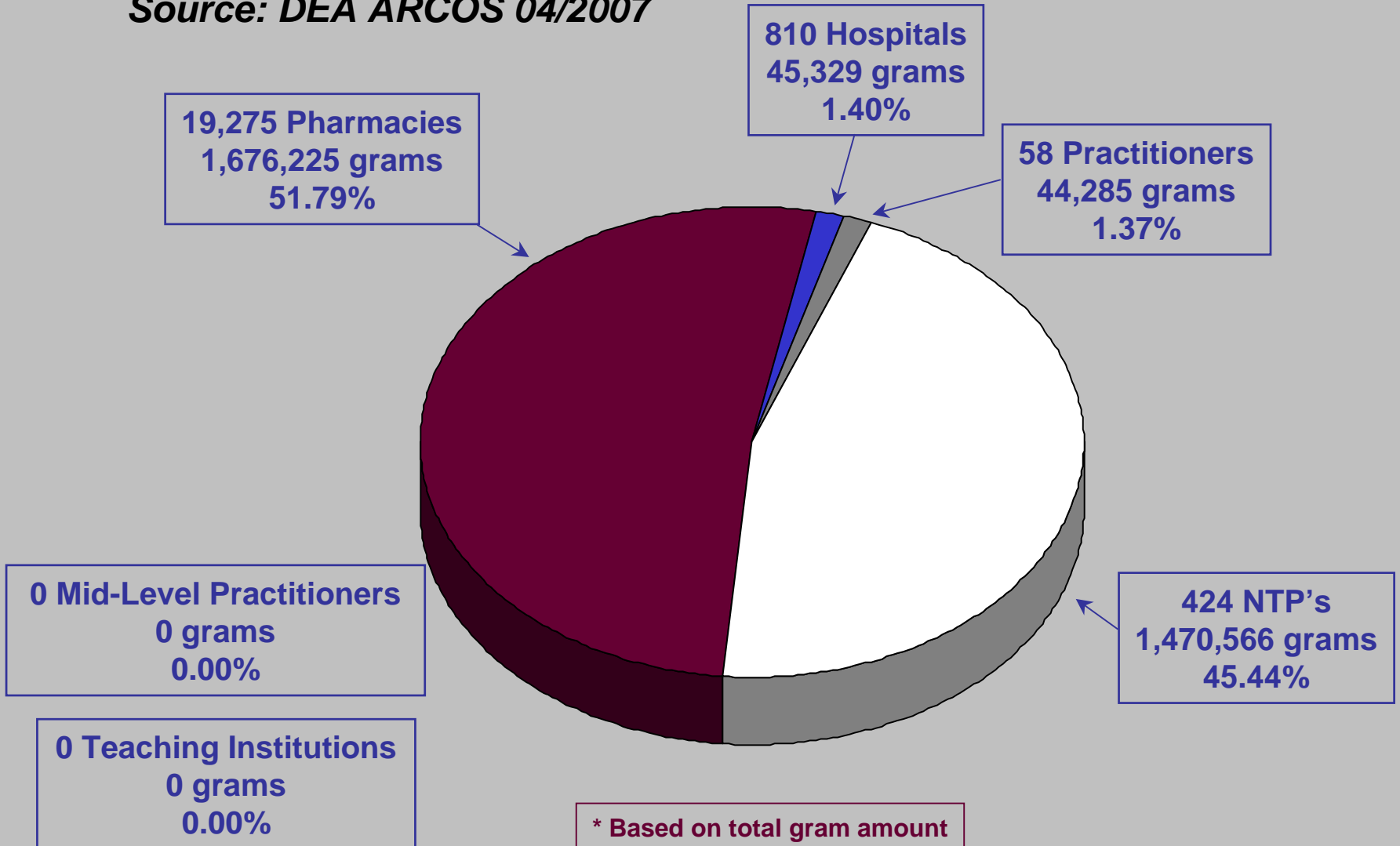
5 mg & 10 mg Tablets  
41,103 grams  
0.6%

\* Based on total gram amount



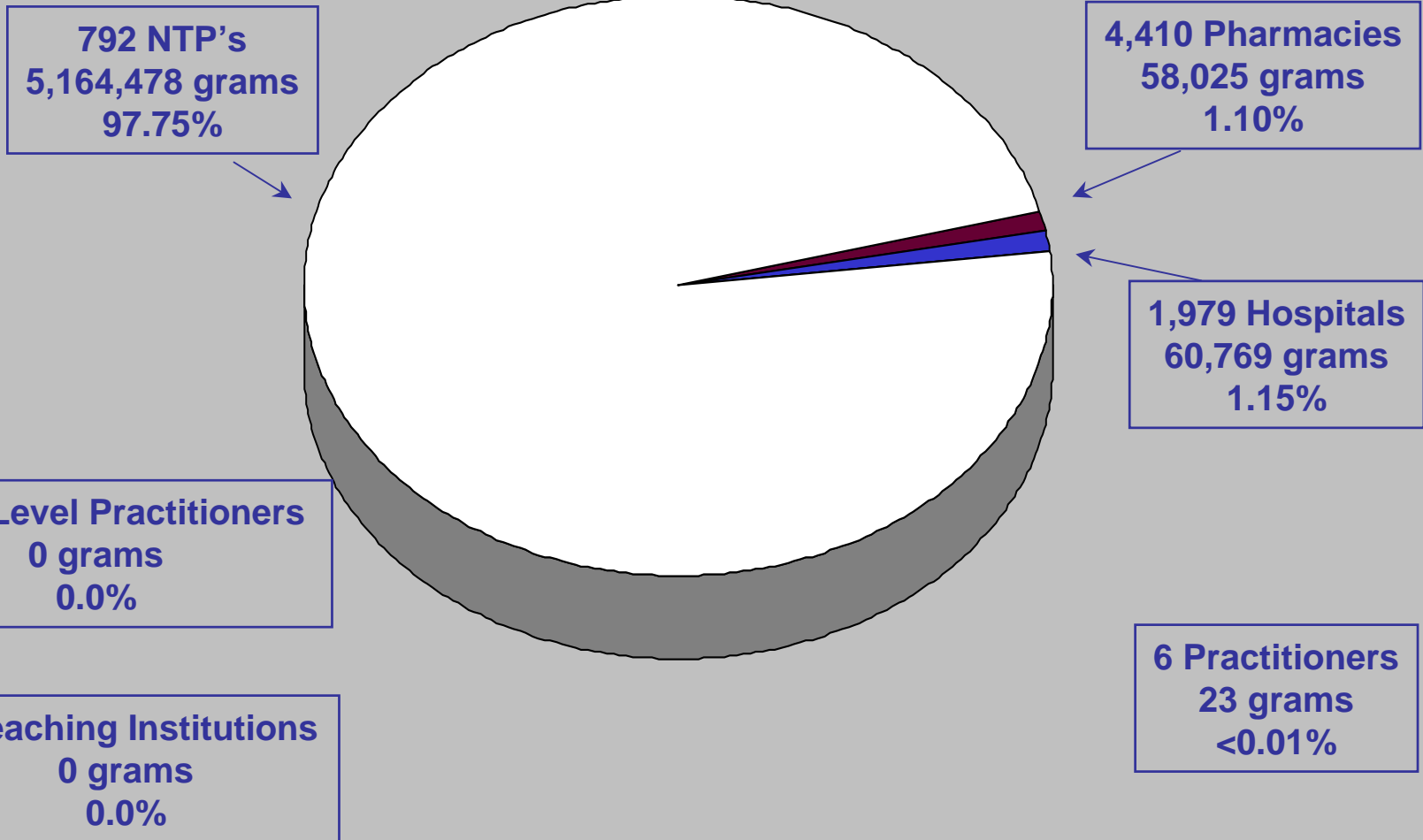
# 2006 Purchases\* of Methadone 40 mg Diskettes by Business Activity

Source: DEA ARCOS 04/2007



# 2006 Purchases\* of Methadone Liquids by Business Activity

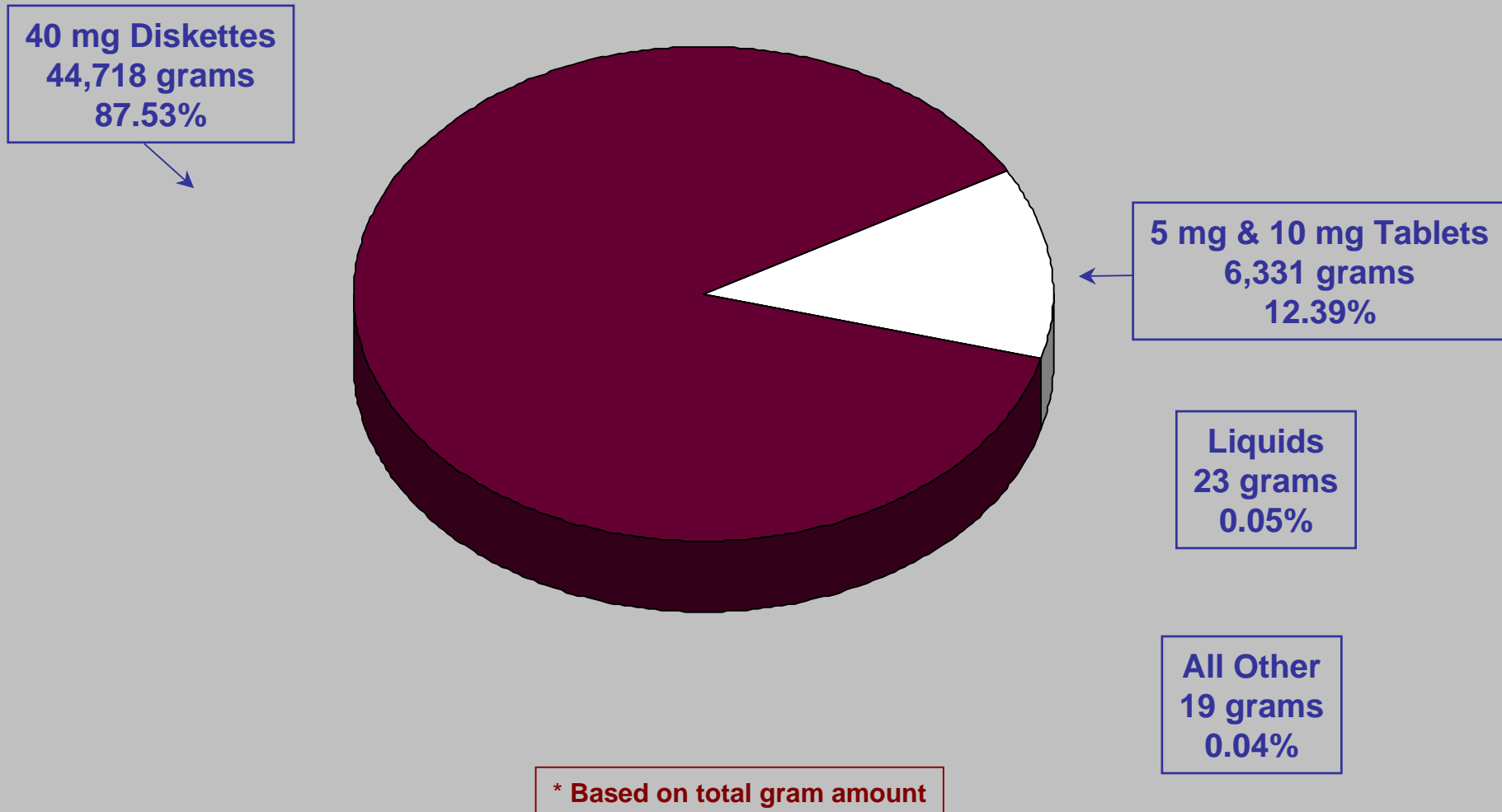
Source: DEA ARCOS 04/2007



\* Based on total gram amount

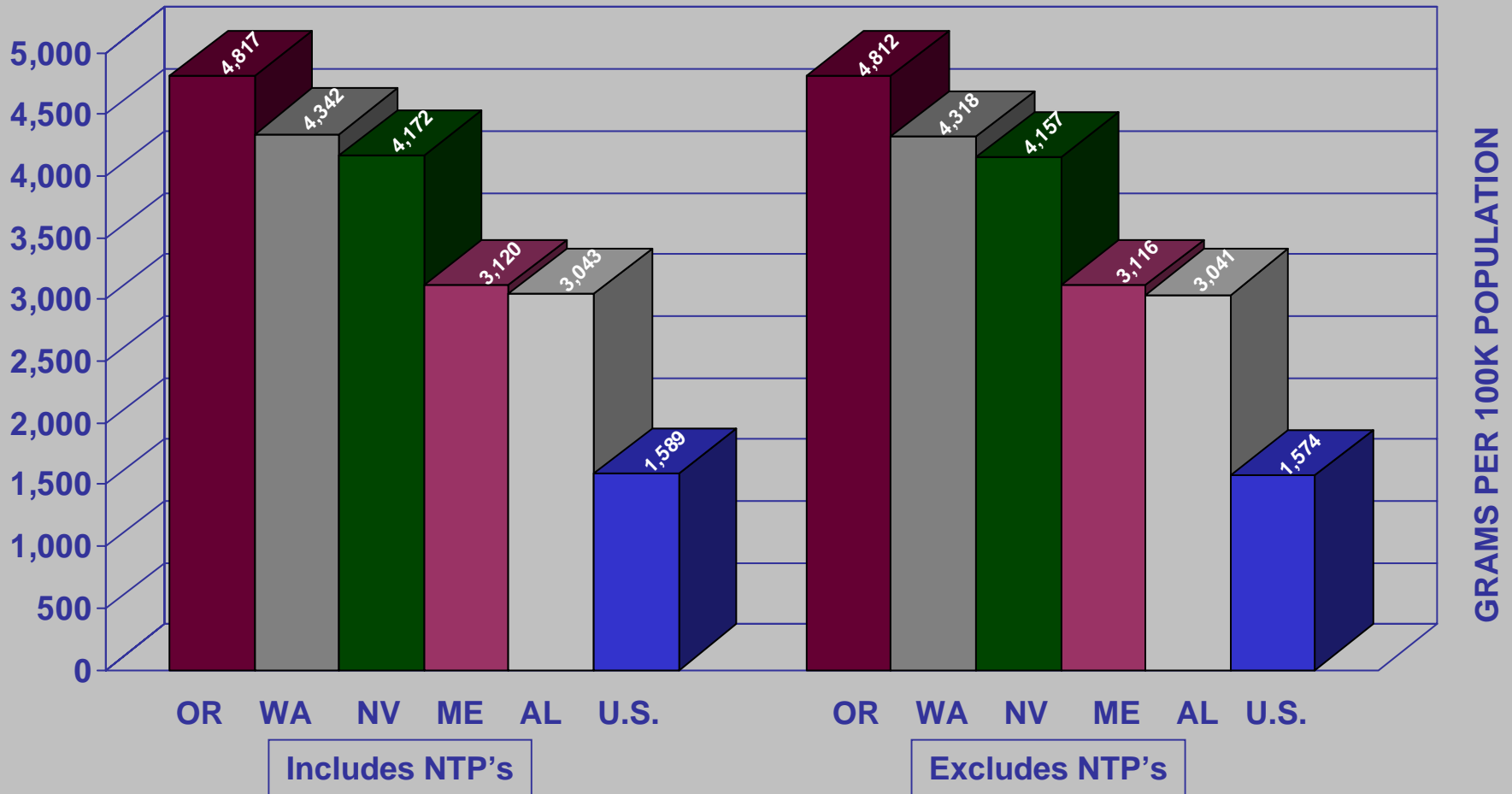
# 2006 Distribution\* of Methadone to Practitioners

Source: DEA ARCOS 04/2007



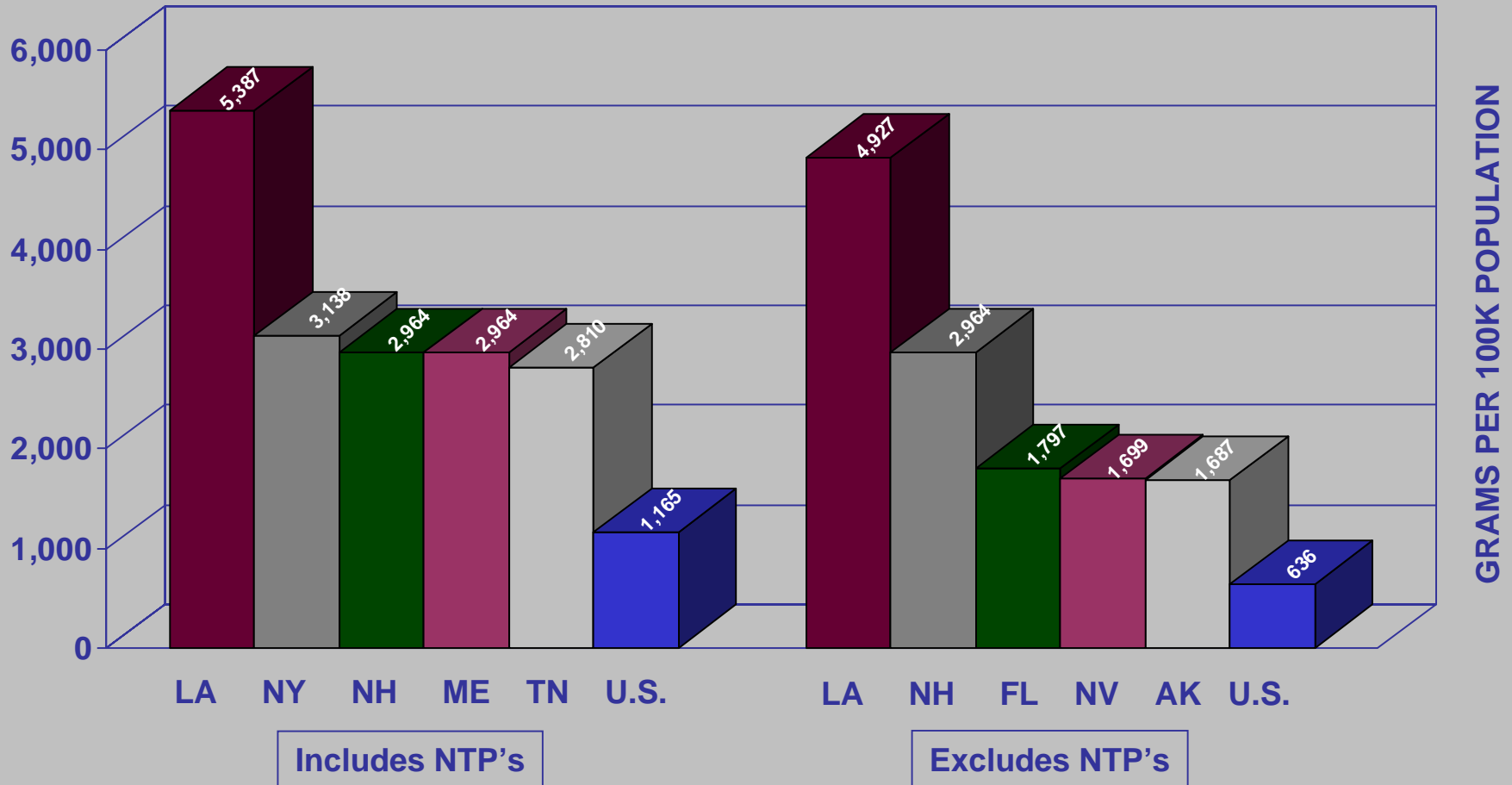
# DRUG DISTRIBUTION

TOP 5 STATES, January - December, 2006  
Methadone 5 mg and 10 mg Tablets



# DRUG DISTRIBUTION

TOP 5 STATES, January - December, 2006  
Methadone 40 mg Diskettes

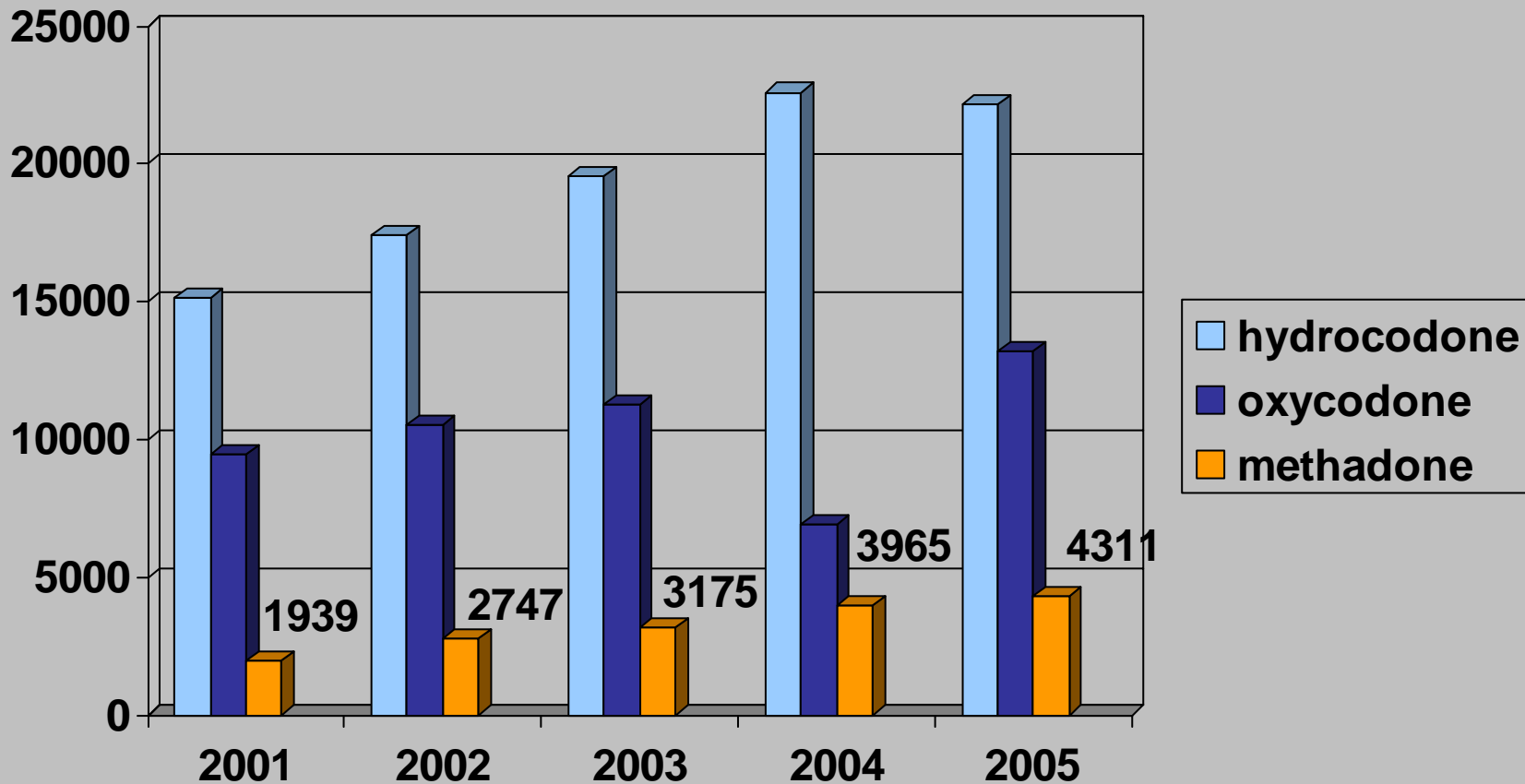


Source: DEA ARCOS 04/2007

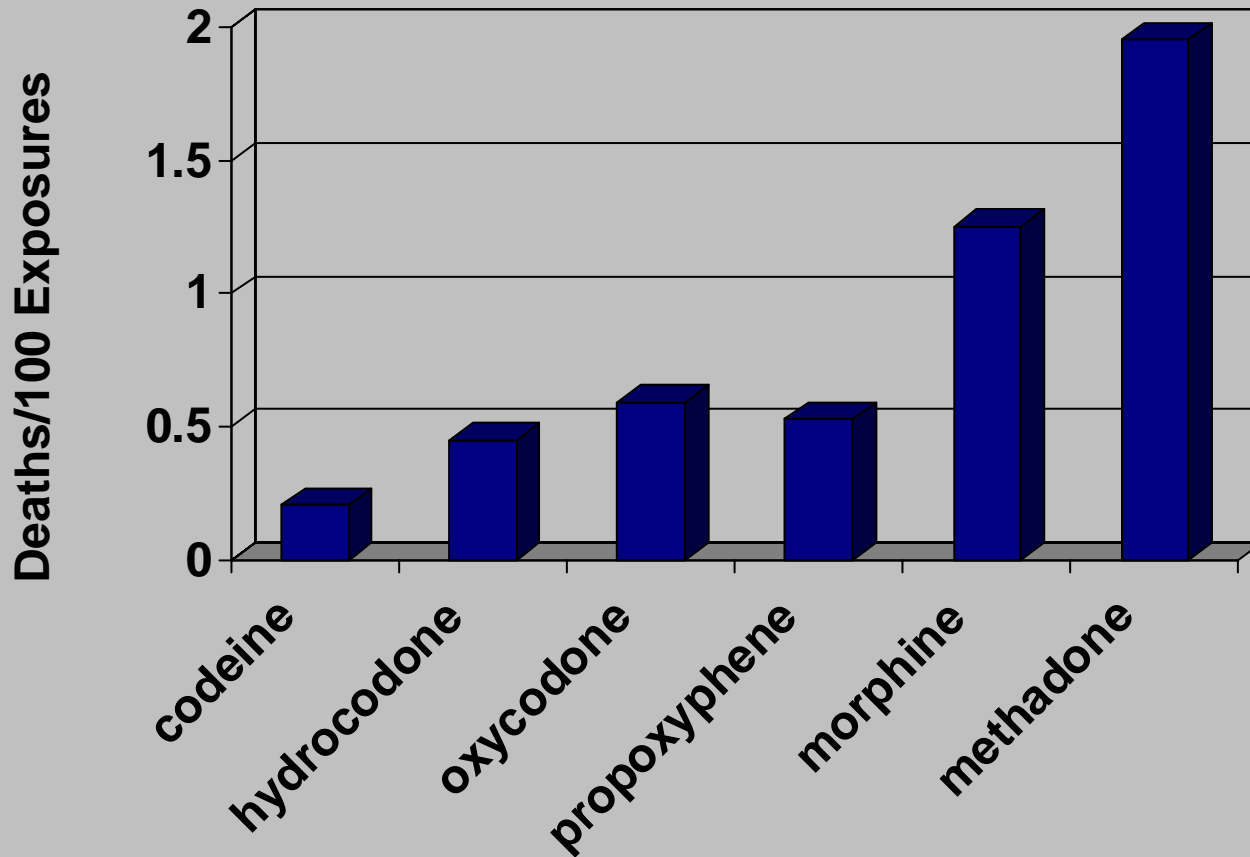
What problems are associated  
with methadone products?

# Poison Control Data Drug Exposures

Source: National Association of Poison Control Centers (AAPCC)



# 2005 AAPCC Deaths/100 Exposures

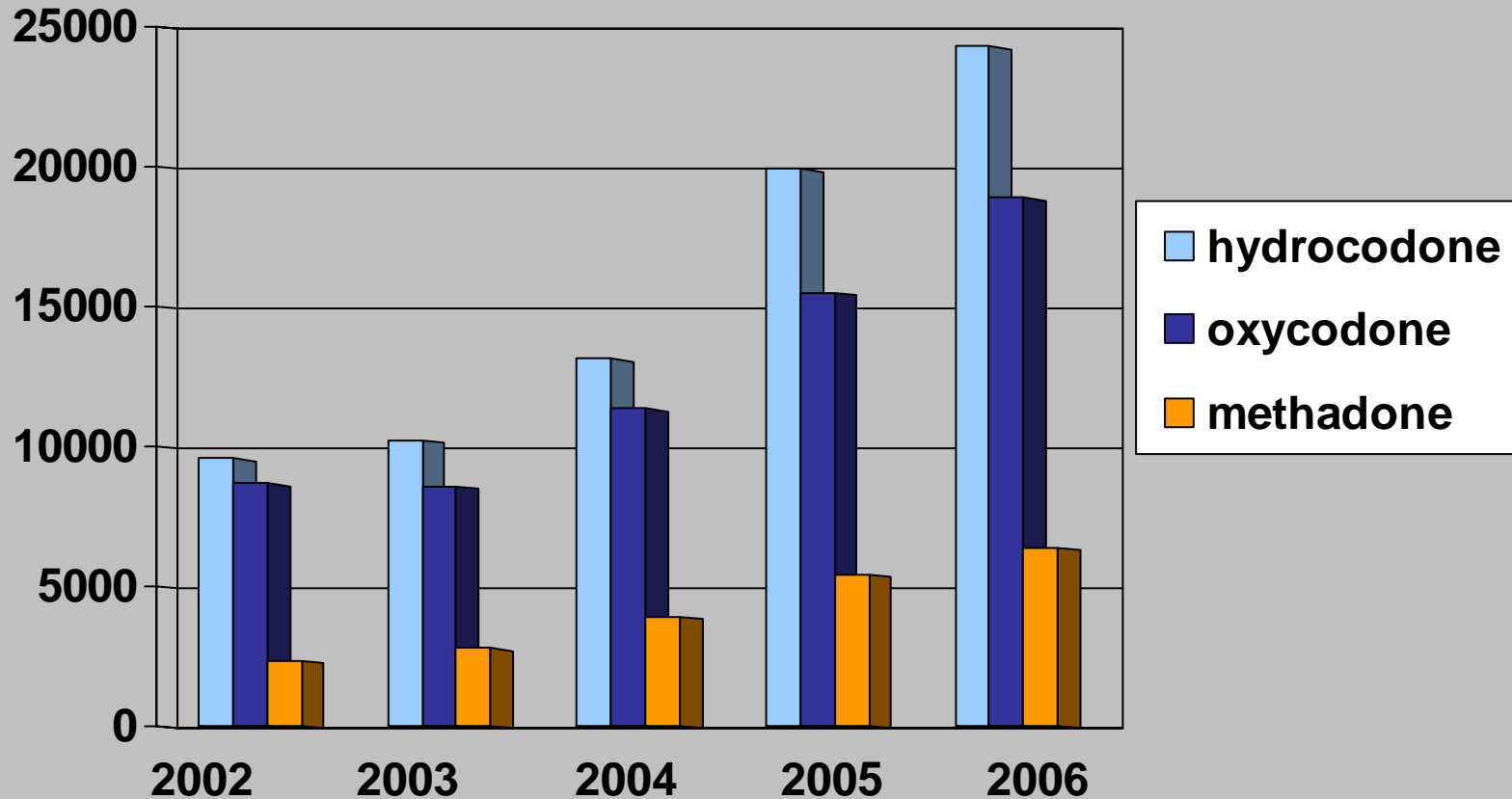


**Source: National Association of Poison Control Centers (AAPCC)**



# NFLIS Exhibits

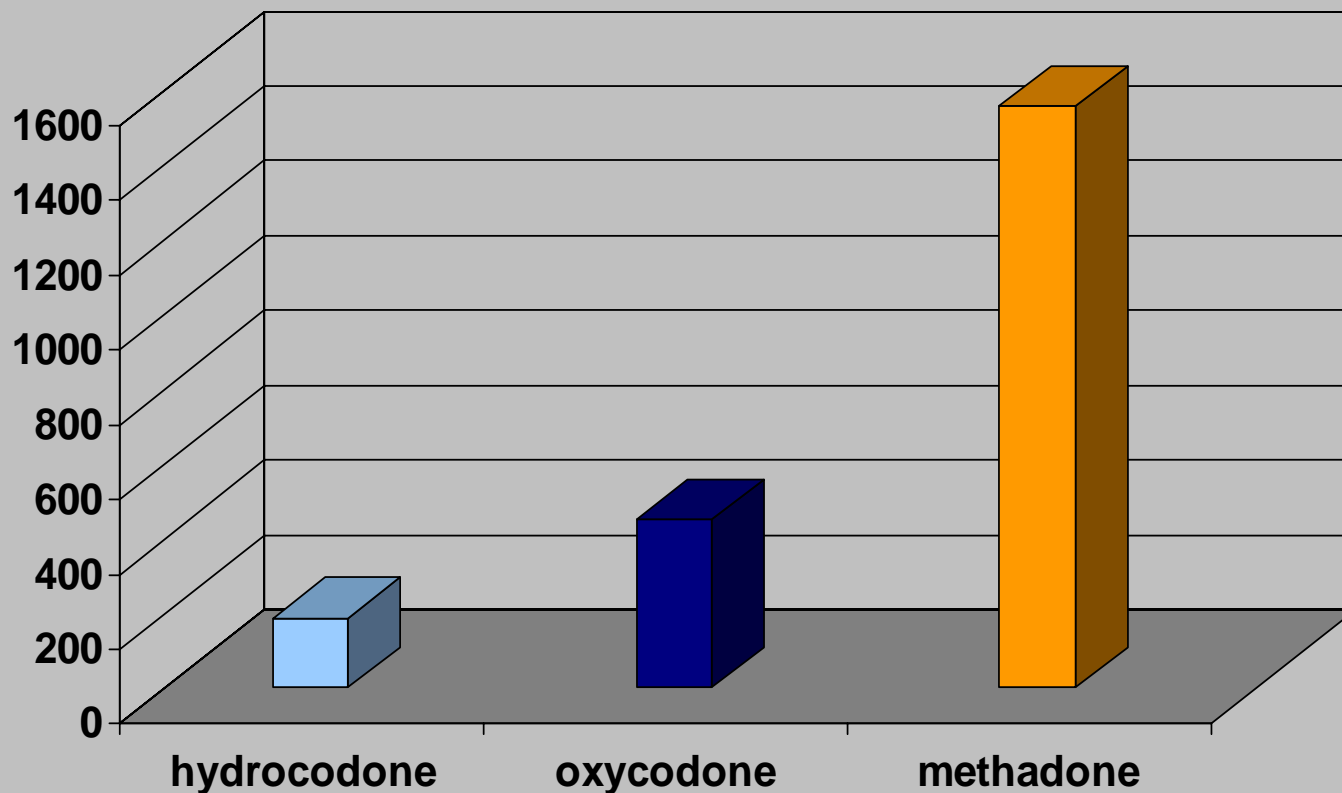
*Source: DEA National Forensic Laboratory Information System*



**There was a 170% increase in methadone exhibits from 2002 to 2006**

# 2006 NFLIS Exhibits/Million Prescriptions

*Source: DEA National Forensic Laboratory Information System*



**This data suggests that on a per prescription basis, methadone is more likely to be involved in illicit activities (diverted and abused) than either hydrocodone or oxycodone.**

# Methadone Formulations Analyzed in Forensic Laboratories

(Source: 2006 NFLIS and STRIDE)

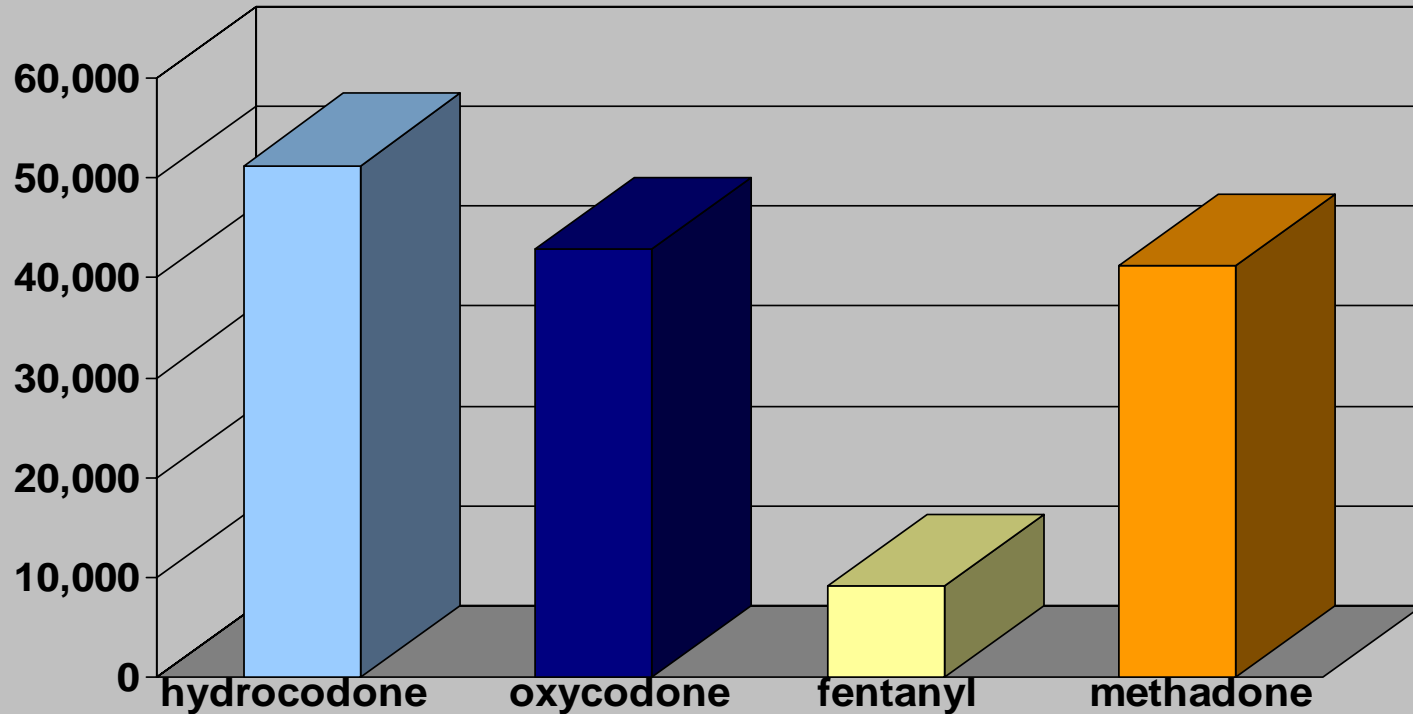
Data regarding the types of methadone formulations submitted to forensic laboratories show:

- Most laboratories are not reporting the physical form of the exhibits for methadone (59% are unknown/unspecified).
- 41% of the methadone exhibits were associated with a report of drug form. Of those exhibits, 94% were tablets and 6% were liquids.
- The diskettes, if reported, would be reported as tablets as there is no “field” for diskettes.

## 2005 DAWN

### Nonmedical Emergency Department Visits

*Source: Drug Abuse Warning Network, Substance Abuse and Mental Health Services Administration (SAMHSA)*



**Methadone ranked 3<sup>rd</sup> among all opioid analgesics, 4<sup>th</sup> among all controlled pharmaceuticals, and 8<sup>th</sup> among all controlled substances.**

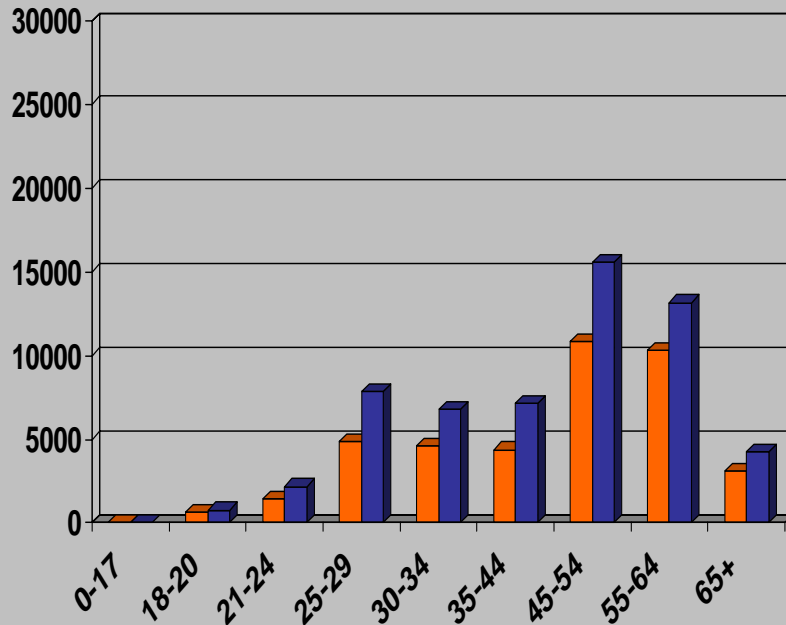
# 2005 DAWN ED Estimates by Age

Source: Office of Applied Science, SAMHSA, DAWN

## Methadone

**Total ED visits – 60,135**  
55% males

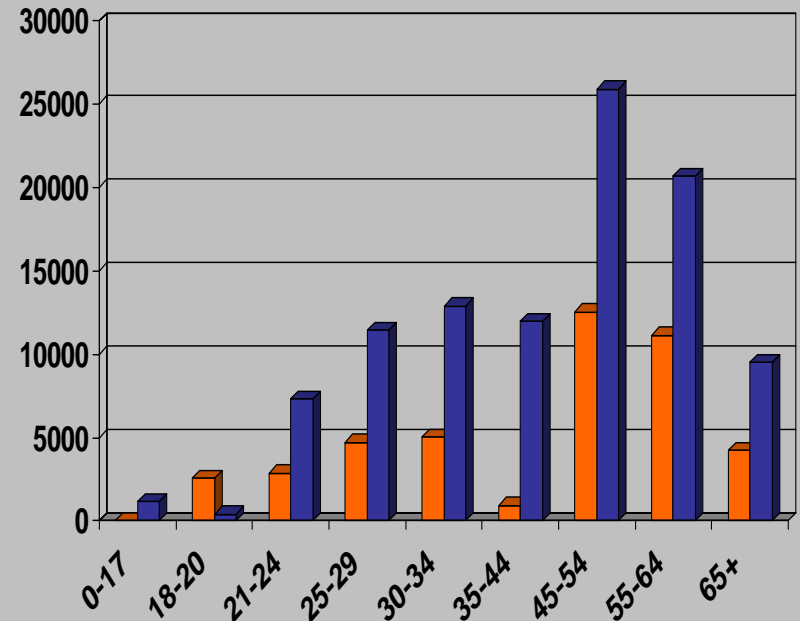
**Nonmedical ED Visits – 41,216**  
55% males



## Hydrocodone

**Total ED visits – 119,138**  
40% males

**Nonmedical ED visits – 51,225**  
43% males



# Methadone-related Deaths (1999-2004)

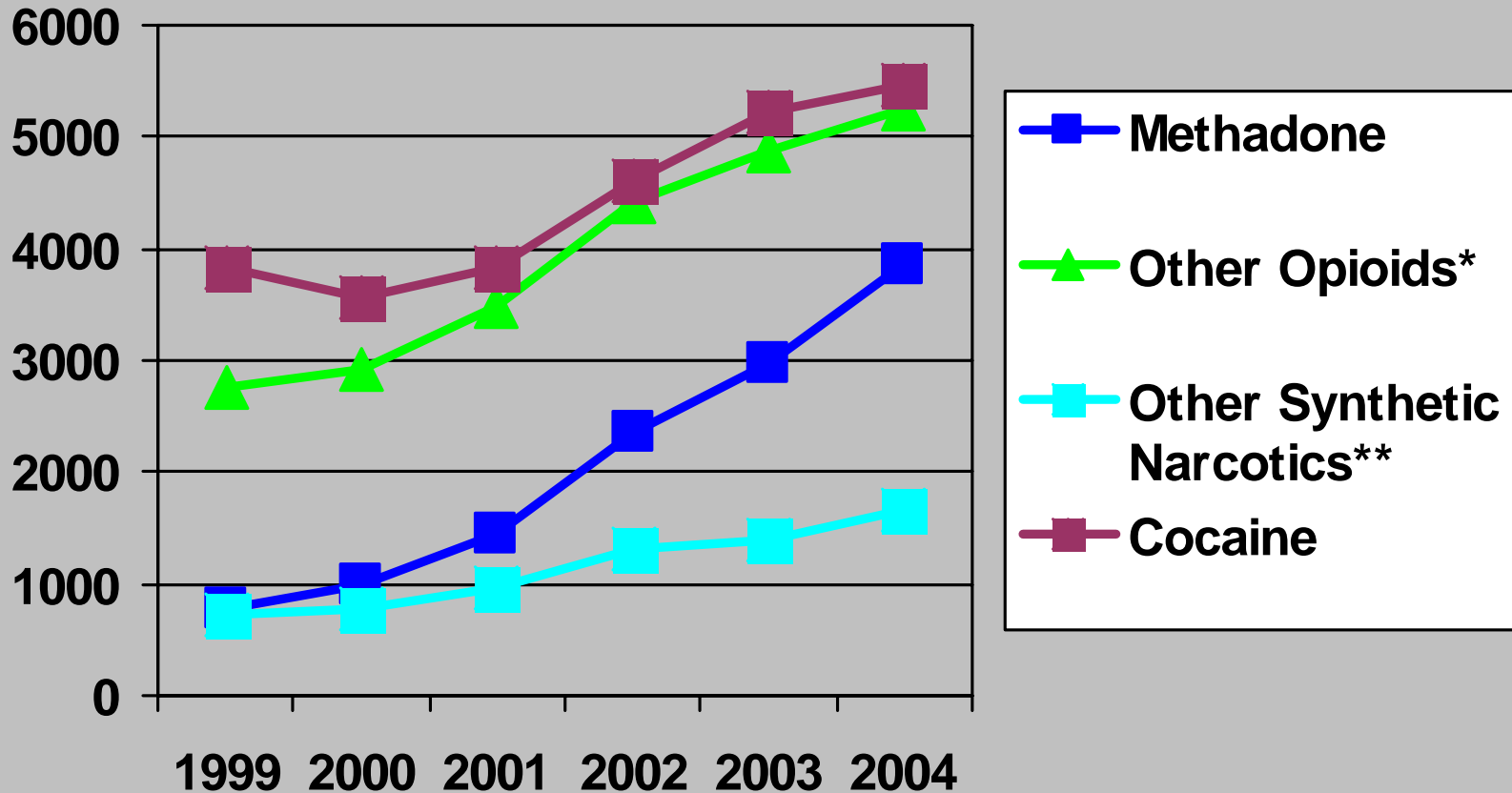
*Source: Center for Disease Control (CDC)*

- Nationally, all poisoning deaths by all drugs increased by 54%.
- The number of methadone-related deaths increased by 390%: 786 in 1999 to 3,849 in 2004.
- Other opioid (e.g. hydrocodone and oxycodone) deaths increased by 90%.
- Most methadone deaths (73 to 79% depending on the year) were classified as unintentional.
- The rate of methadone deaths in younger individuals (15-24) increased 11-fold.
- The age-specific rates of methadone death are higher for persons age 35 to 44 and 45 to 54 than for other age groups.

# Poisoning Deaths in the U.S.

Source: Center for Disease Control (CDC)

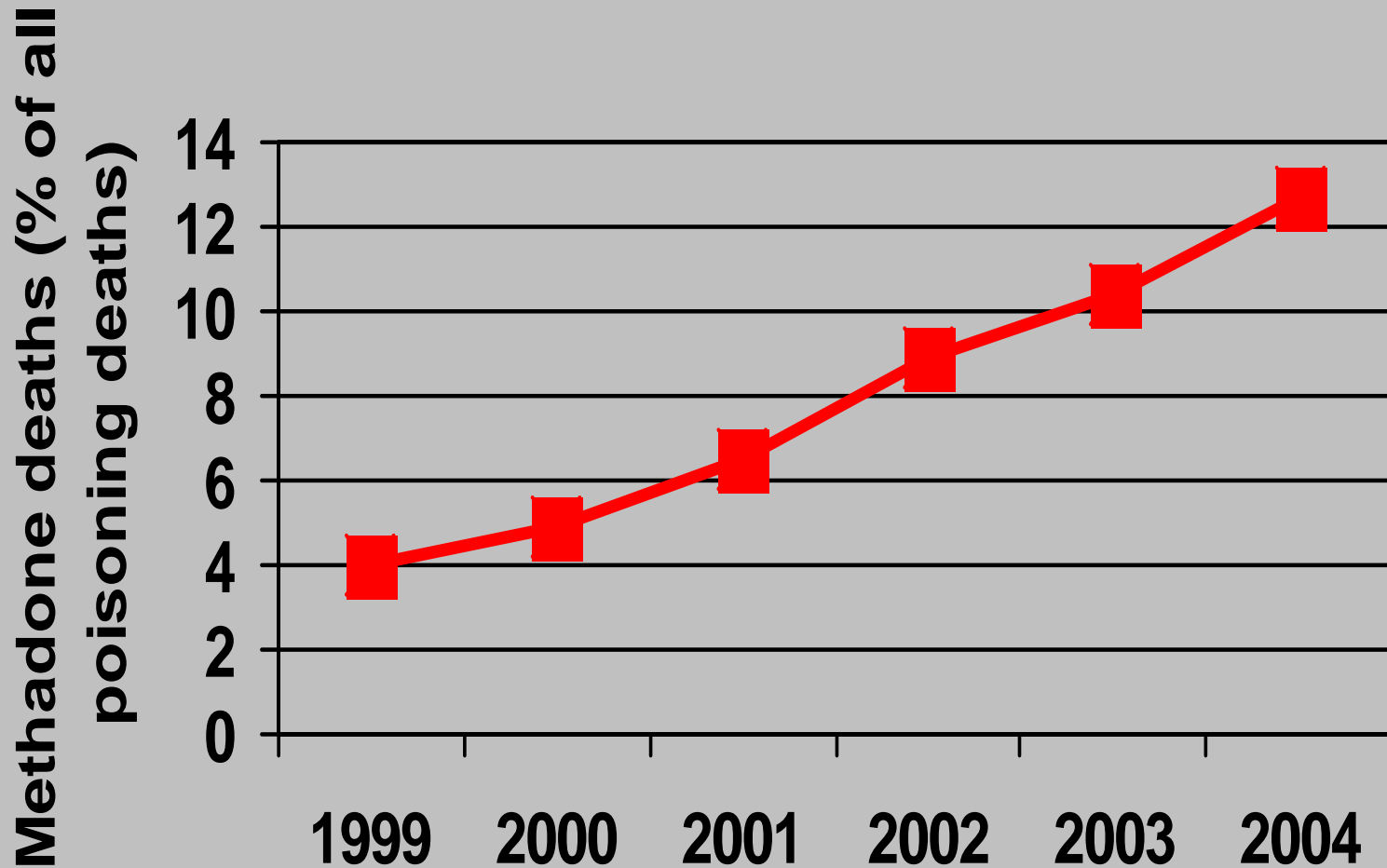
Deaths



\*Other Opioids include drugs like morphine, oxycodone, hydrocodone, hydromorphone

\*\*Other Synthetic Narcotics include drugs like propoxyphene, fentanyl, meperidine

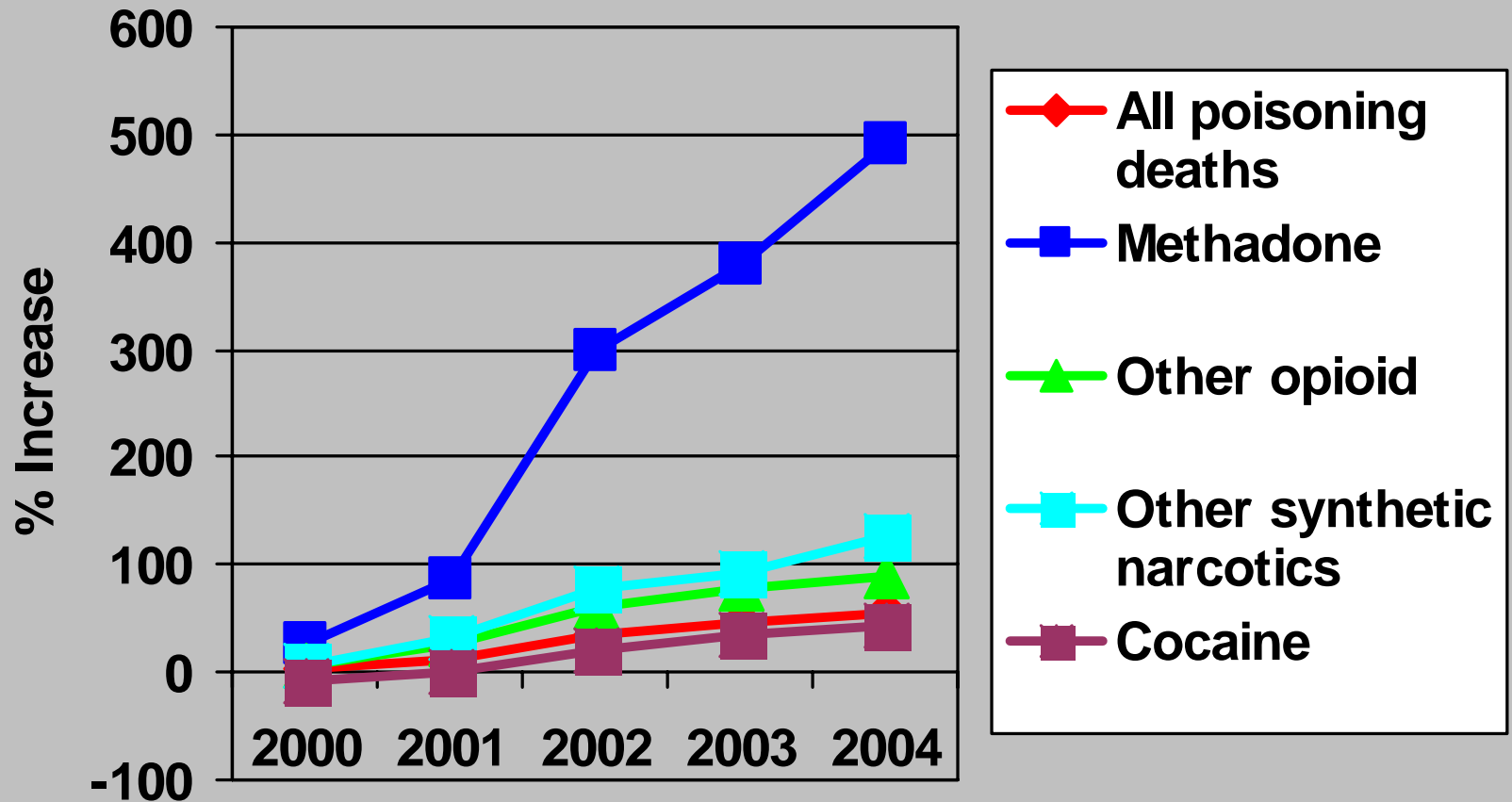
# Methadone deaths expressed as percent of all poisoning deaths





# Percent Increase in Poisoning Deaths

Source: Center for Disease Control (CDC)



# States With Highest Number of Methadone Deaths in 2004

*Source: Center of Disease Control (CDC)*

<b>Ranking</b>	<b>State</b>	<b>Deaths</b>
1	Florida	400
2	North Carolina	245
3	Washington	228
4	Texas	138
5	Ohio	122
6	Kentucky	121
7	Oklahoma	120
8	Virginia	104
9	Tennessee	99
10	West Virginia	99

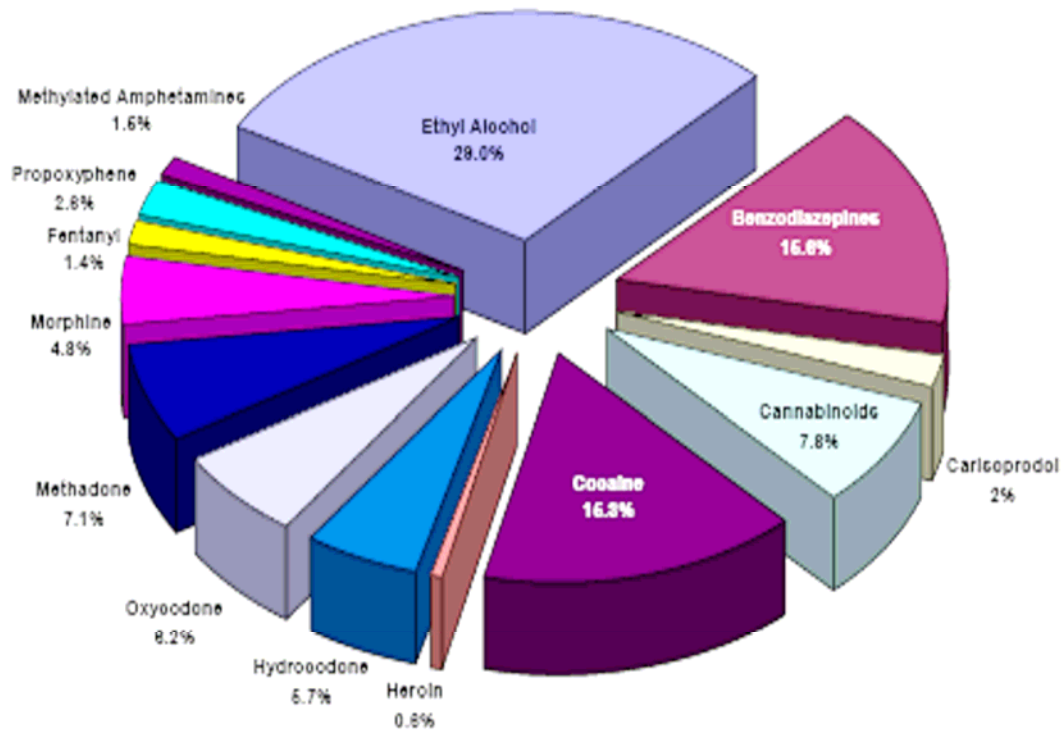
# States With the Largest Rate of Increase in Methadone Deaths 1999 to 2004

*Source: Center for Disease Control (CDC)*

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

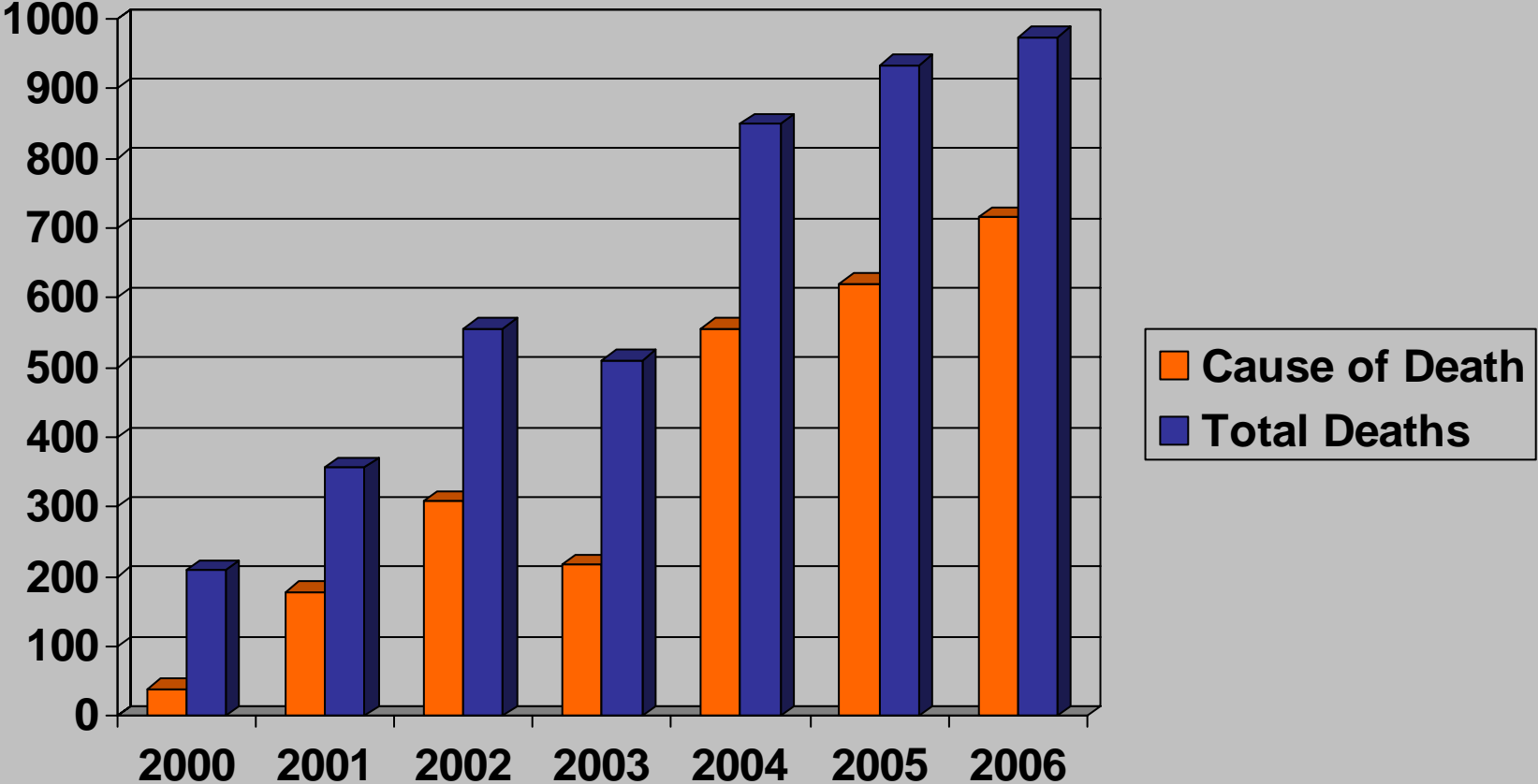
# Florida Medical Examiner Data Drug-Deaths

Frequency of Occurrence of Drugs in Decedents  
January - June 2006



**Source: Florida Department of Law Enforcement 2006  
Interim Drug Report by Medical Examiners**

# FDLE ME Reports of Methadone Deaths



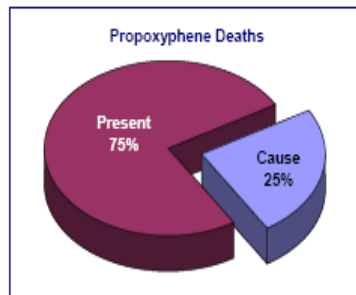
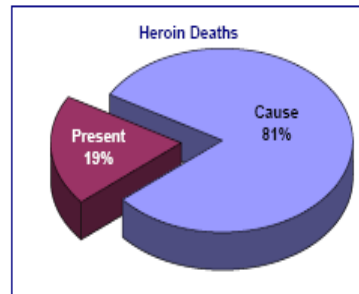
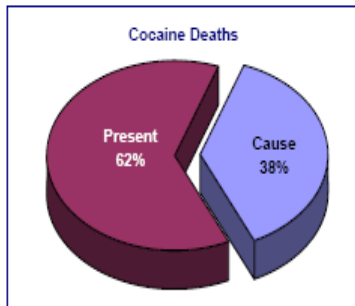
# Florida Medical Examiners Report January – June 2006

*Source: Florida Department of Law Enforcement 2006 Interim  
Drug Report by Medical Examiners*

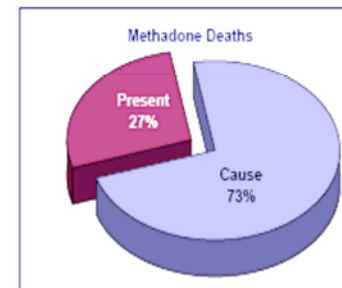
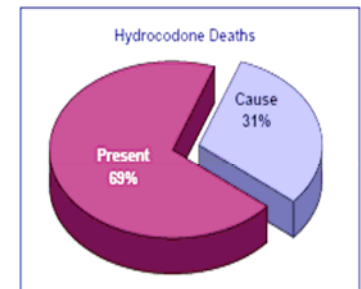
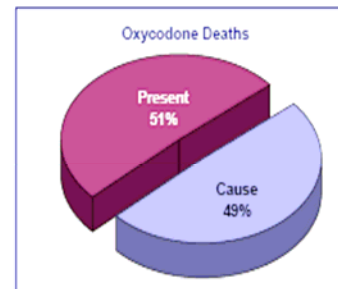
<b>Drug Found in Body</b>	<b>Total Occurrences</b>	<b>Cause of Death</b>
<b>Heroin</b>	36	29
<b>Fentanyl</b>	85	51
<b>Hydrocodone</b>	346	106
<b>Hydromorphone</b>	63	13
<b>Meperidine</b>	25	3
<b>Methadone</b>	428+(546)=974	312+(400)=712
<b>Morphine</b>	289	106
<b>Oxycodone</b>	377	185
<b>Propoxyphene</b>	155	38
<b>Tramadol</b>	59	18

# Florida Medical Examiners Data January-June 2006

Drug Detected at Death: Lethal vs. Non-Lethal



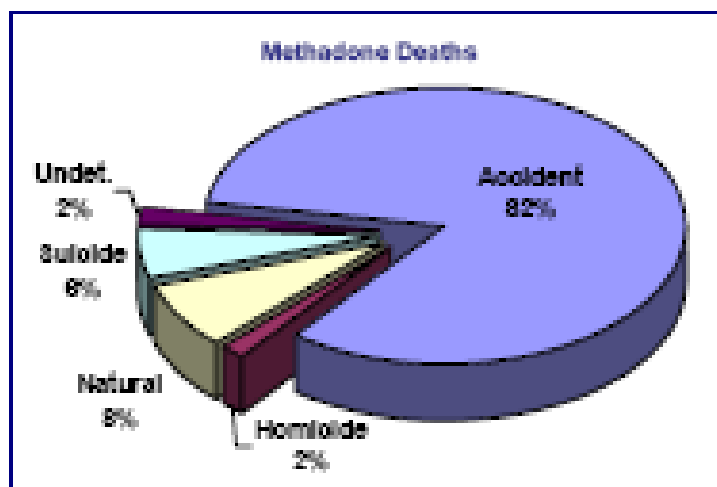
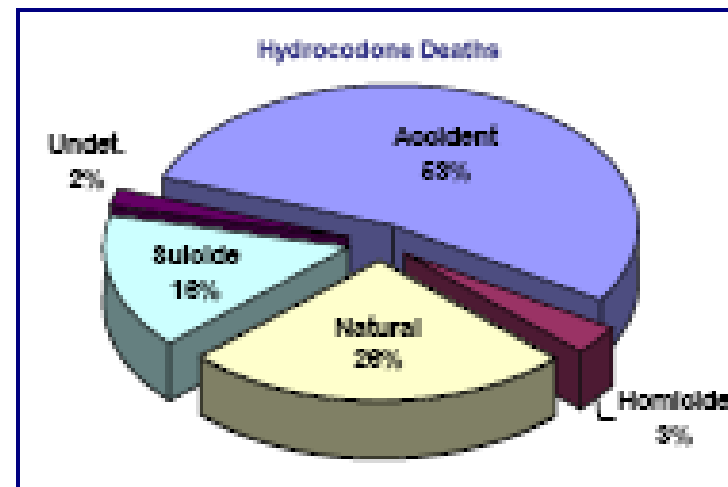
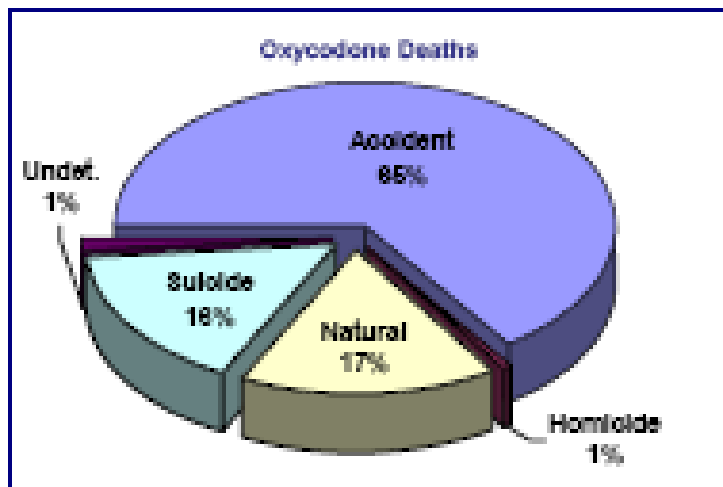
Drug Detected at Death: Lethal vs. Non-Lethal



**When detected at autopsy, methadone is more likely to be the cause of death (like heroin) than either hydrocodone or oxycodone.**

# Florida ME Data January-June 2006

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





# Summary

- Methadone-related deaths continue to escalate.
- The Methadone-Associated Mortality Assessment Report stated that methadone tablets and/or diskettes distributed through channels other than NTPs are most likely the central factor in methadone-associated mortality.
- Current data suggest that medication from pain management is likely the source of methadone for illicit use. However, DEA cannot discount diversion from NTPs.
- Several of the top prescribers of methadone are practitioners with specialties not generally associated with extensive training in pain management.
- DEA is not aware of any methadone-specific CME courses available to physicians or specific guidelines for initiating pain management with methadone.
- More than half of all 40 mg diskettes are distributed to pharmacies.