

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.

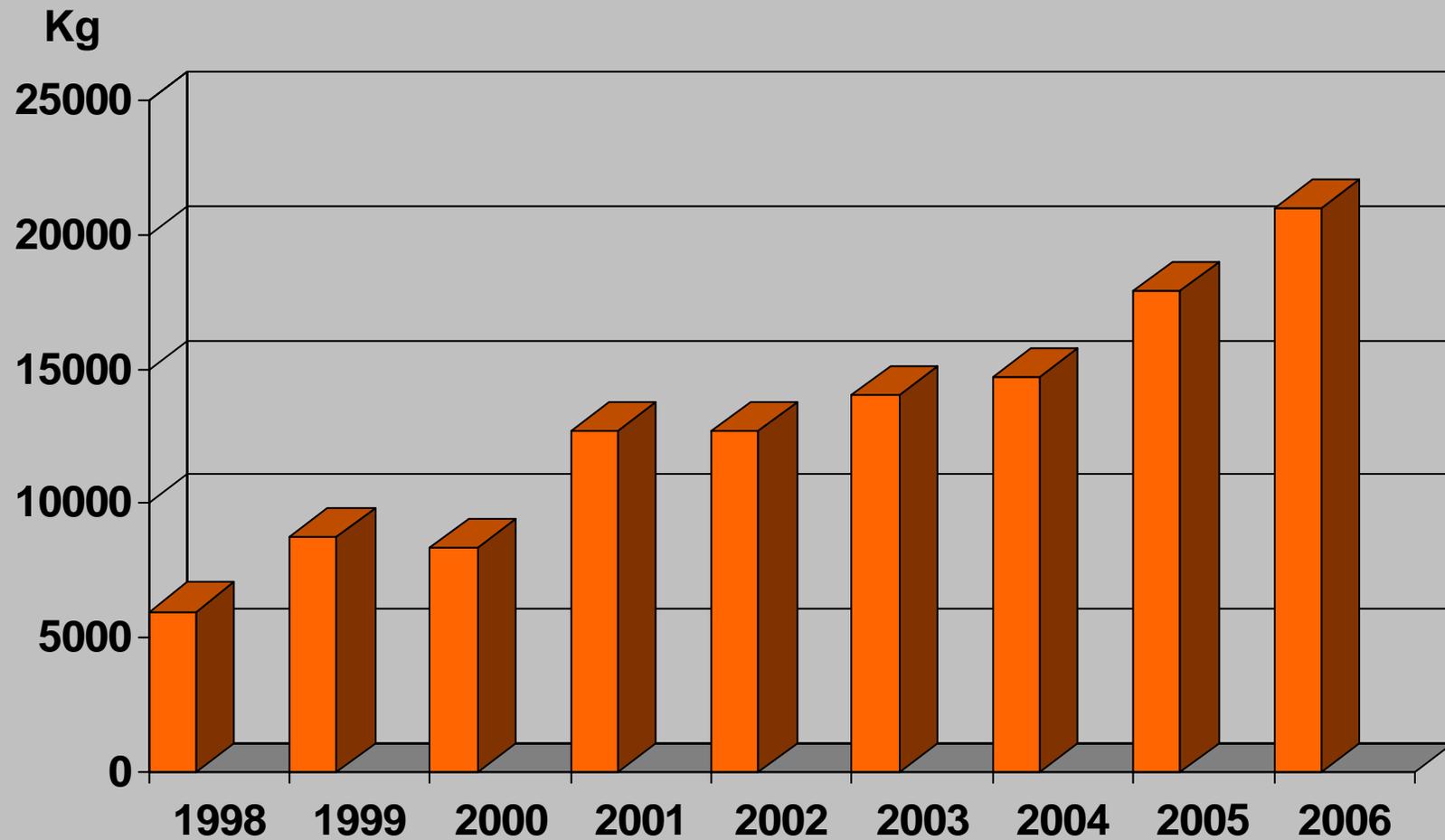
Note: This advisory has not resulted in any decrease in the numbers of prescriptions for methadone (IMS Health Prescription Audit).

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

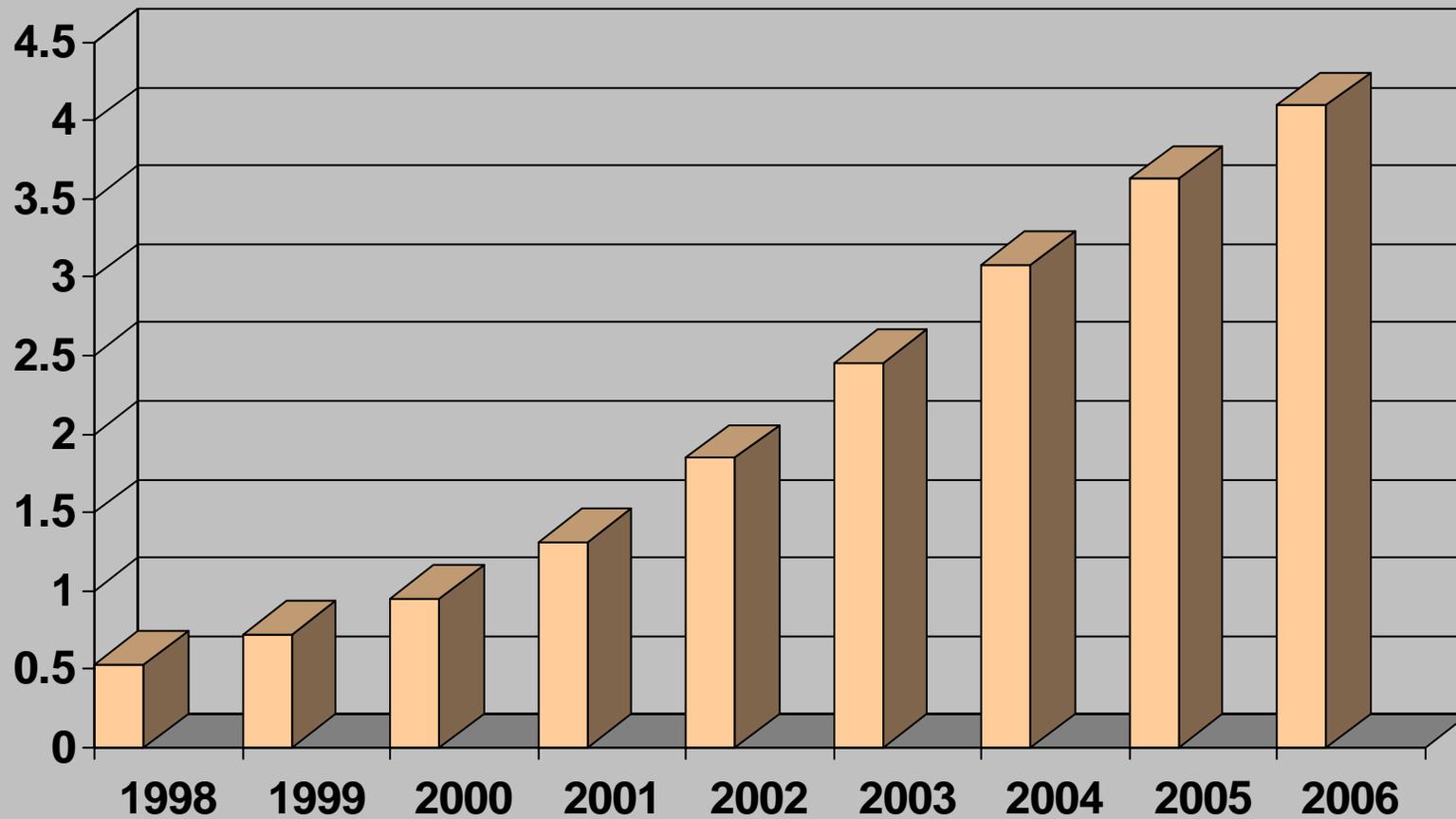
Source: DEA



Methadone Prescriptions

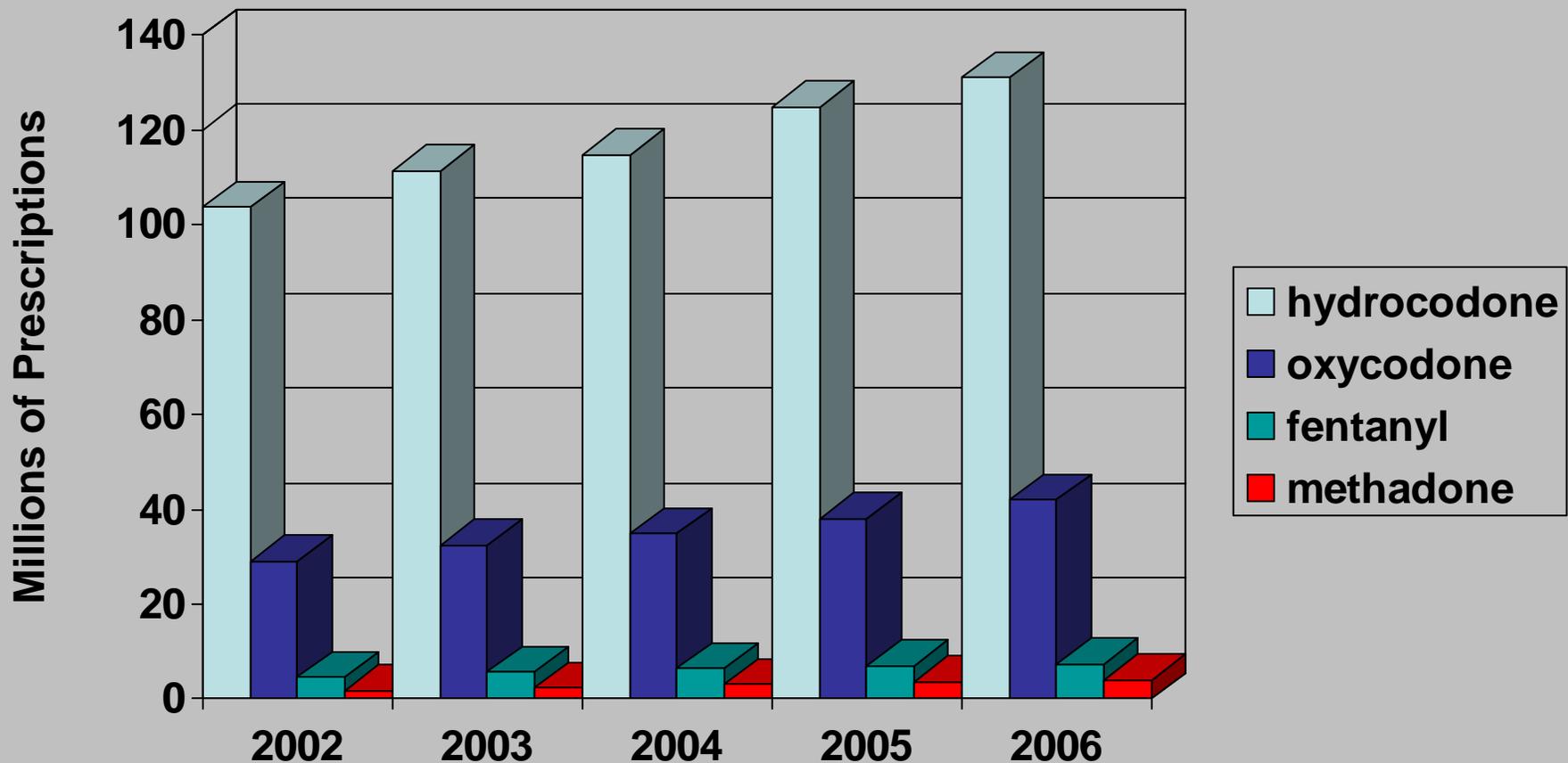
Source: IMS Health Prescription Audit

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

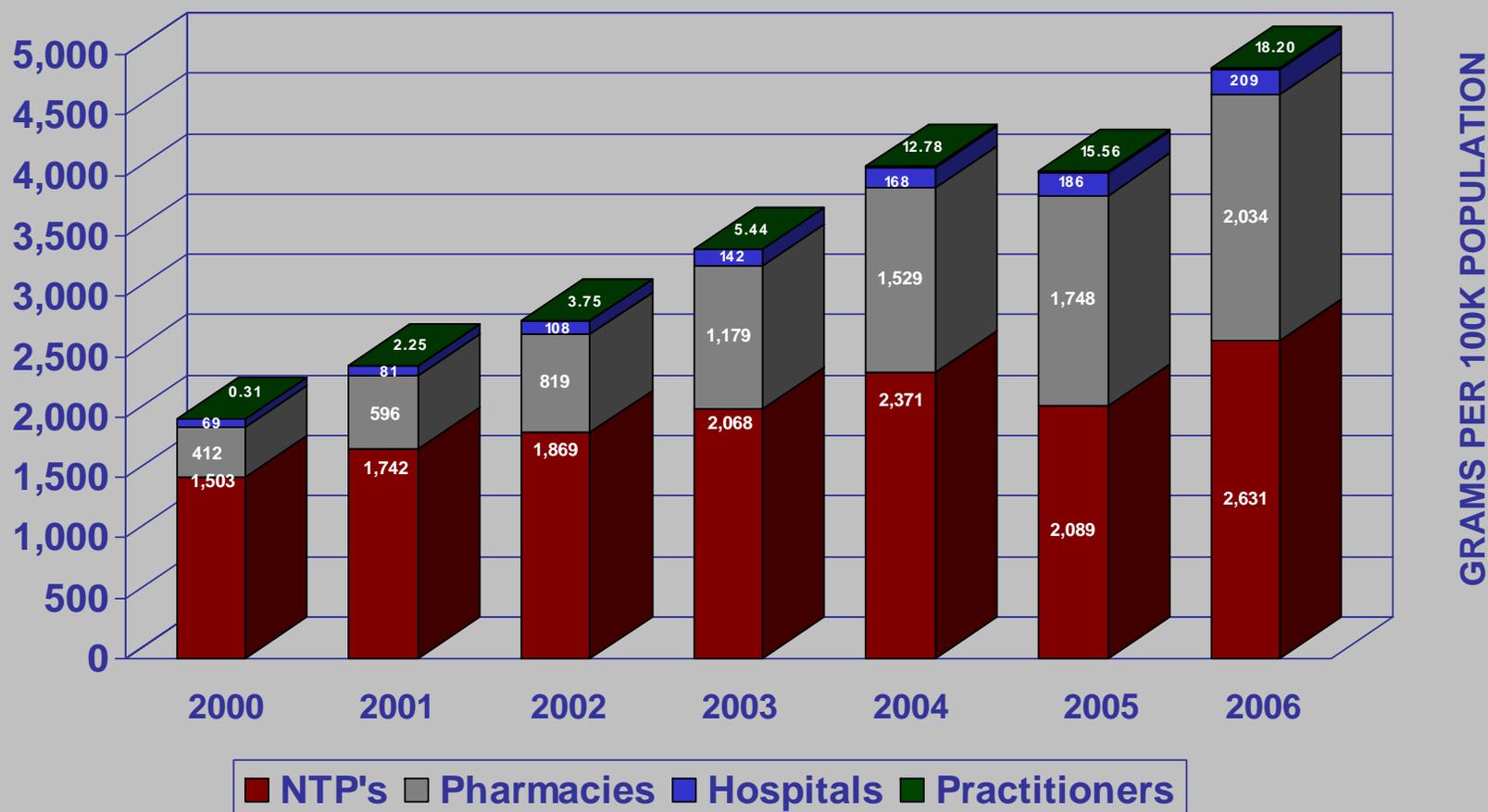
40 mg diskettes Rx

Top Prescribers:

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

Source: IMS Health, National Prescription Audit, November 2006

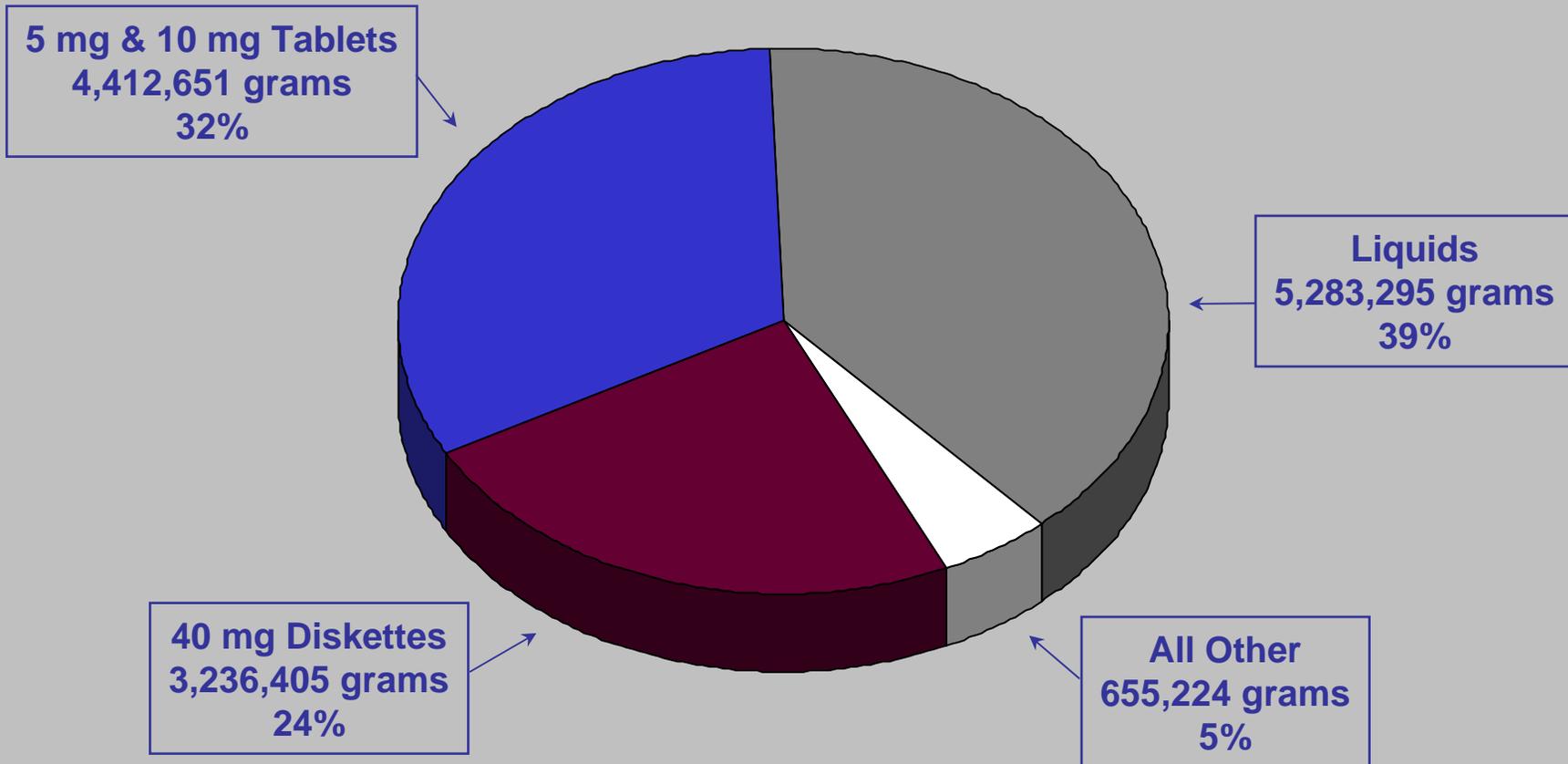
2000 - 2006 Methadone Distribution Business Activity Comparison



Source: DEA ARCOS 04/2007

2006 Distribution* of Methadone

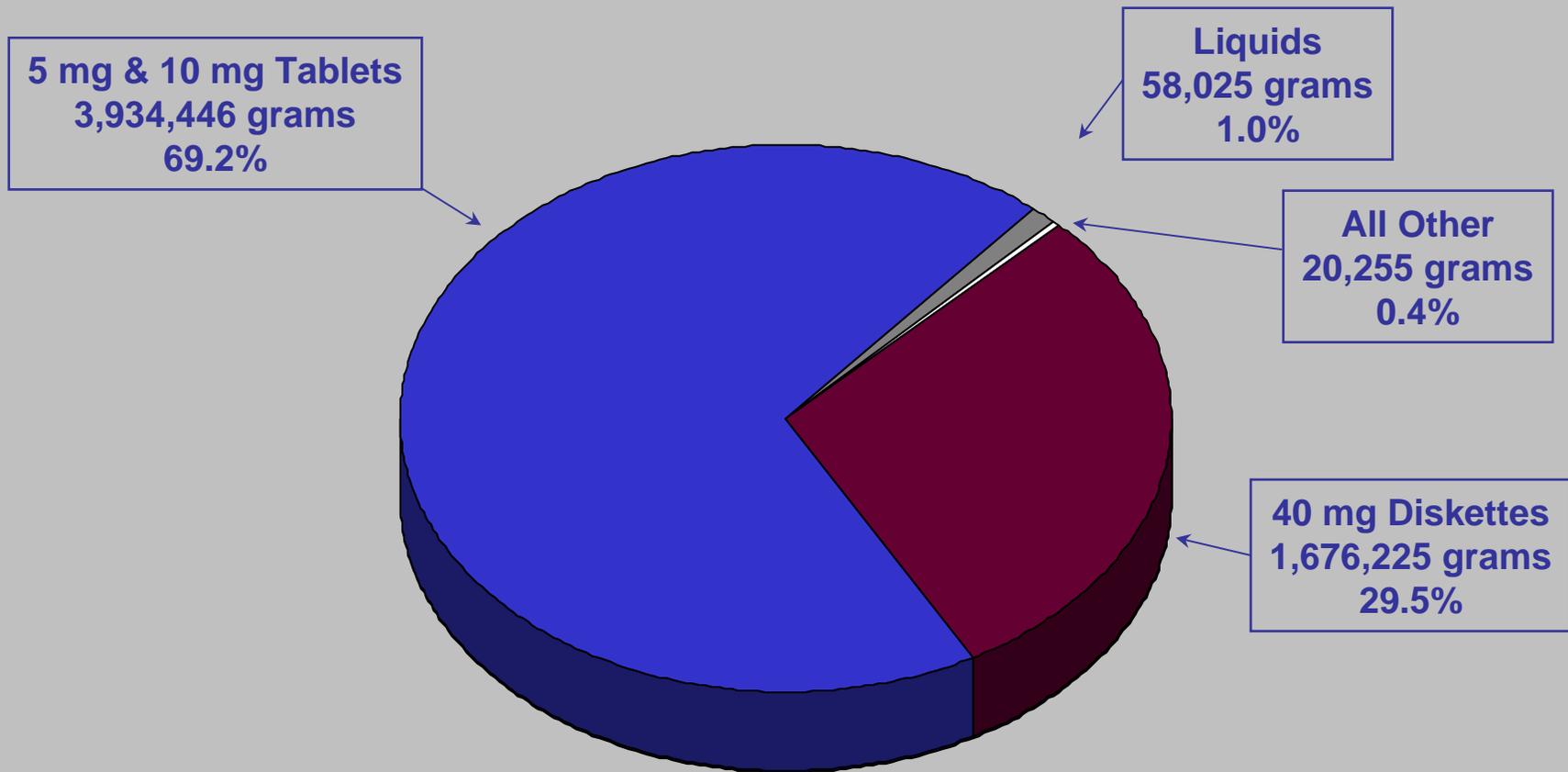
Source: DEA ARCOS 04/2007



* Based on total gram amount
Includes NTP's

2006 Distribution* of Methadone to Pharmacies

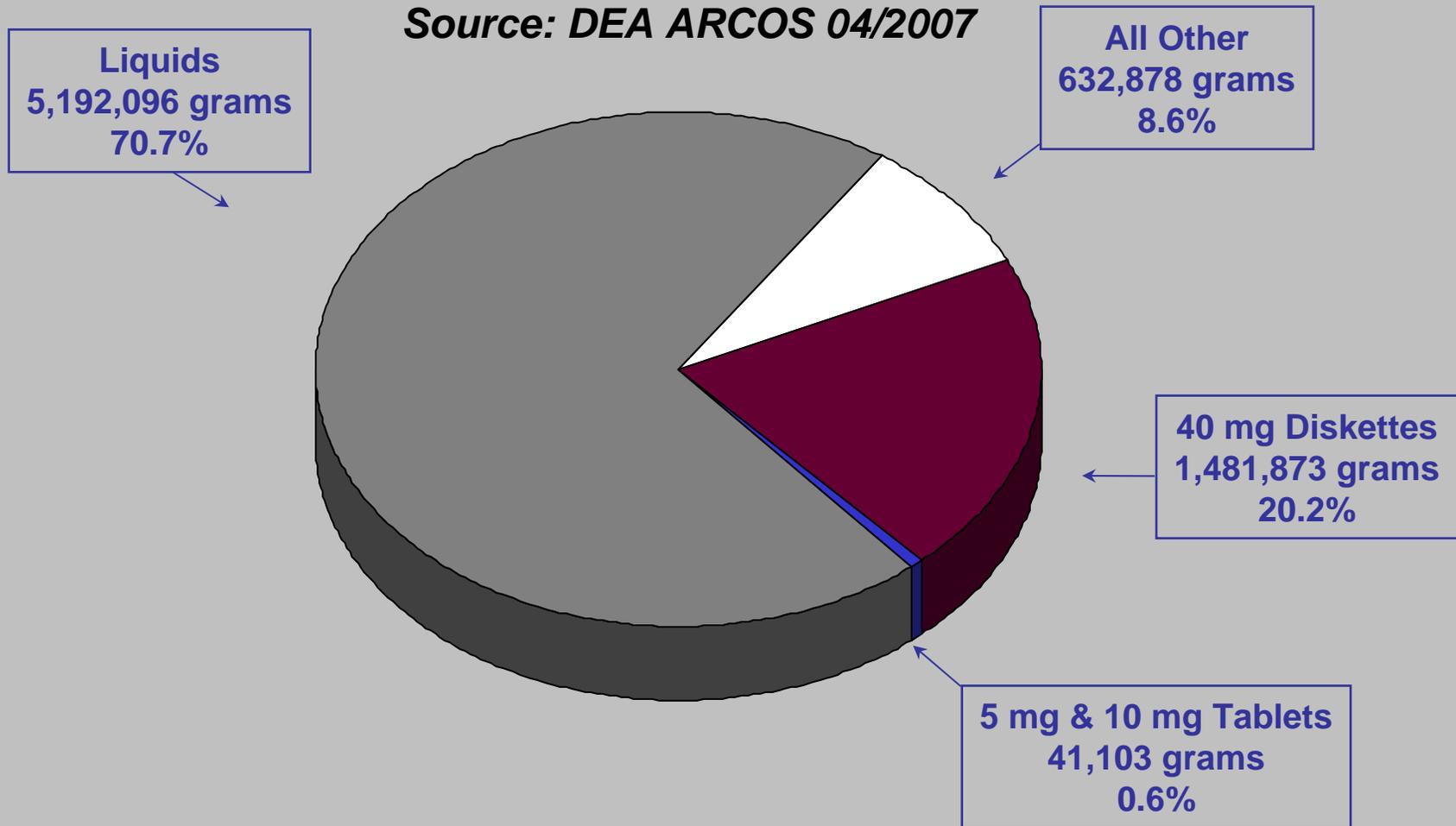
Source: DEA ARCOS 04/2007



* Based on total gram amount

2006 Distribution* of Methadone to NTP's

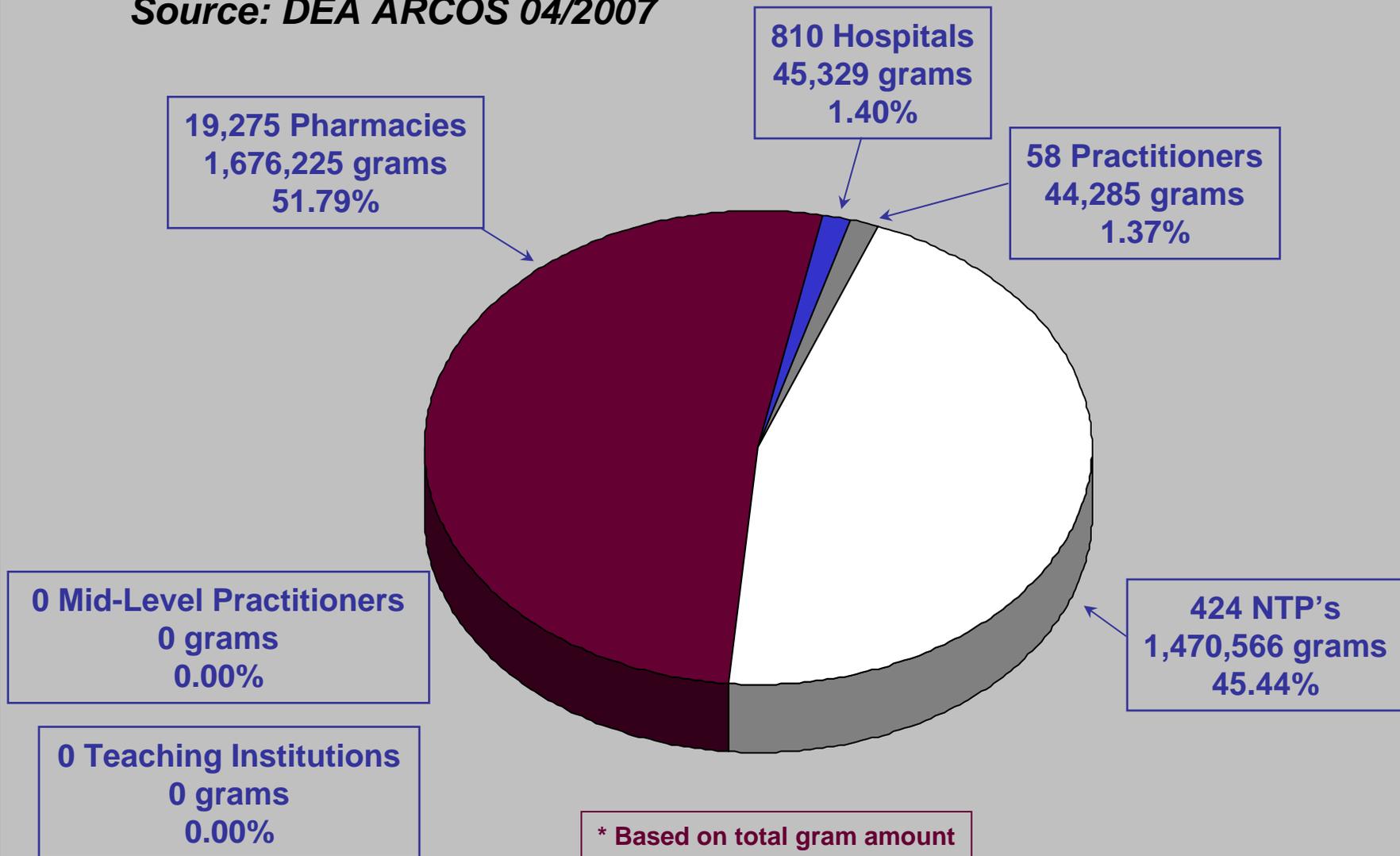
Source: DEA ARCOS 04/2007



* Based on total gram amount

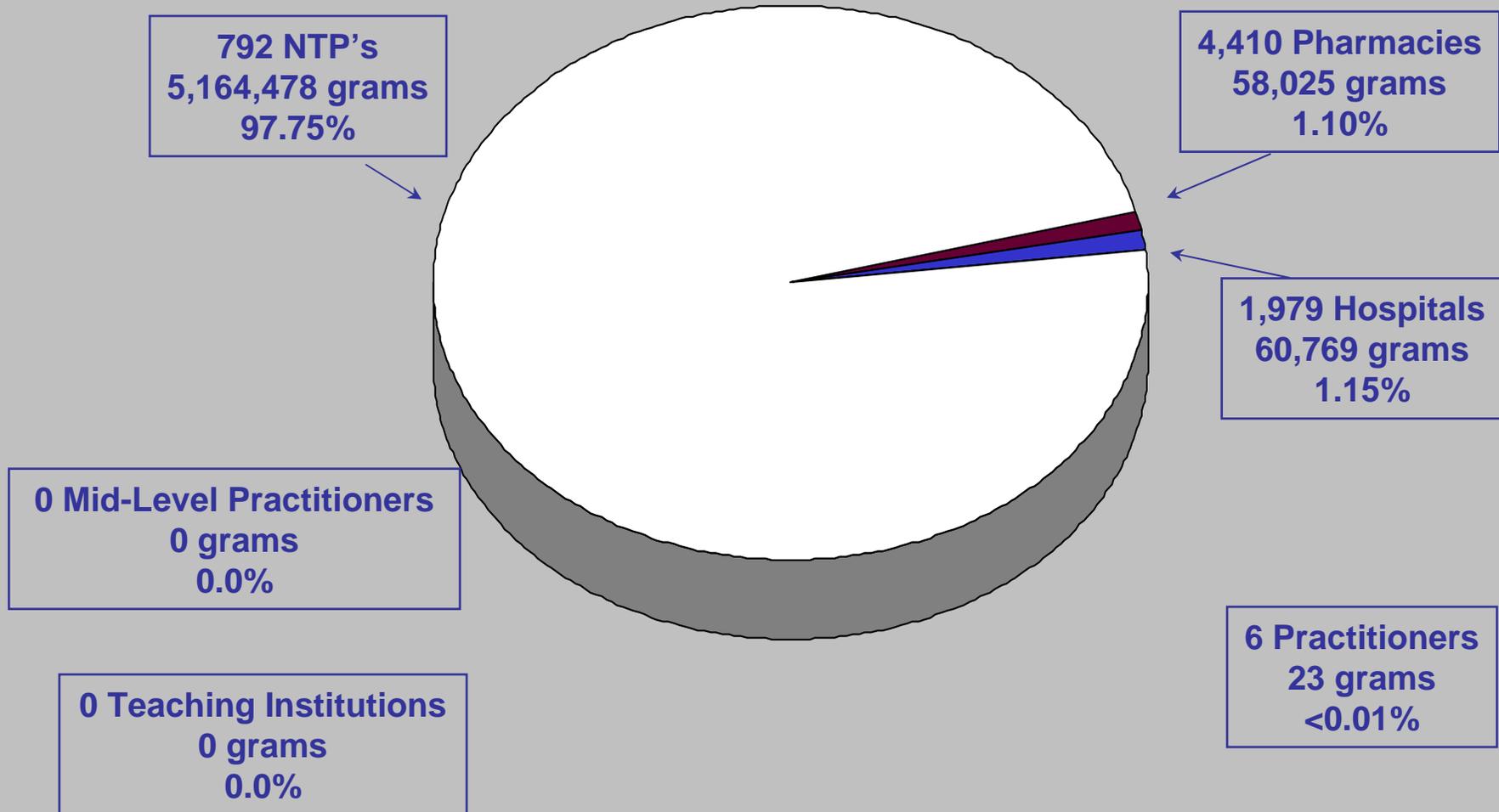
2006 Purchases* of Methadone 40 mg Diskettes by Business Activity

Source: DEA ARCOS 04/2007



2006 Purchases* of Methadone Liquids by Business Activity

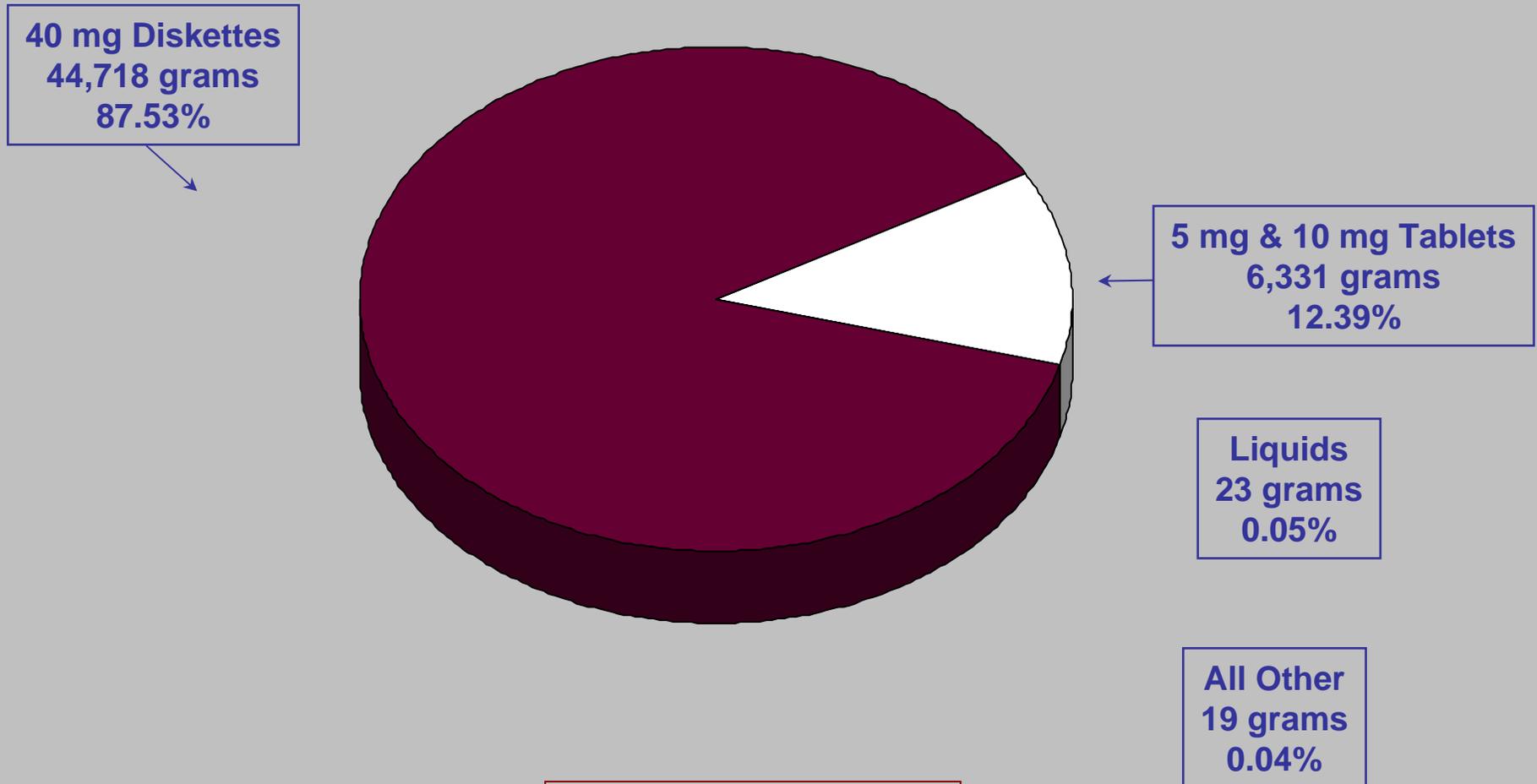
Source: DEA ARCOS 04/2007



* Based on total gram amount

2006 Distribution* of Methadone to Practitioners

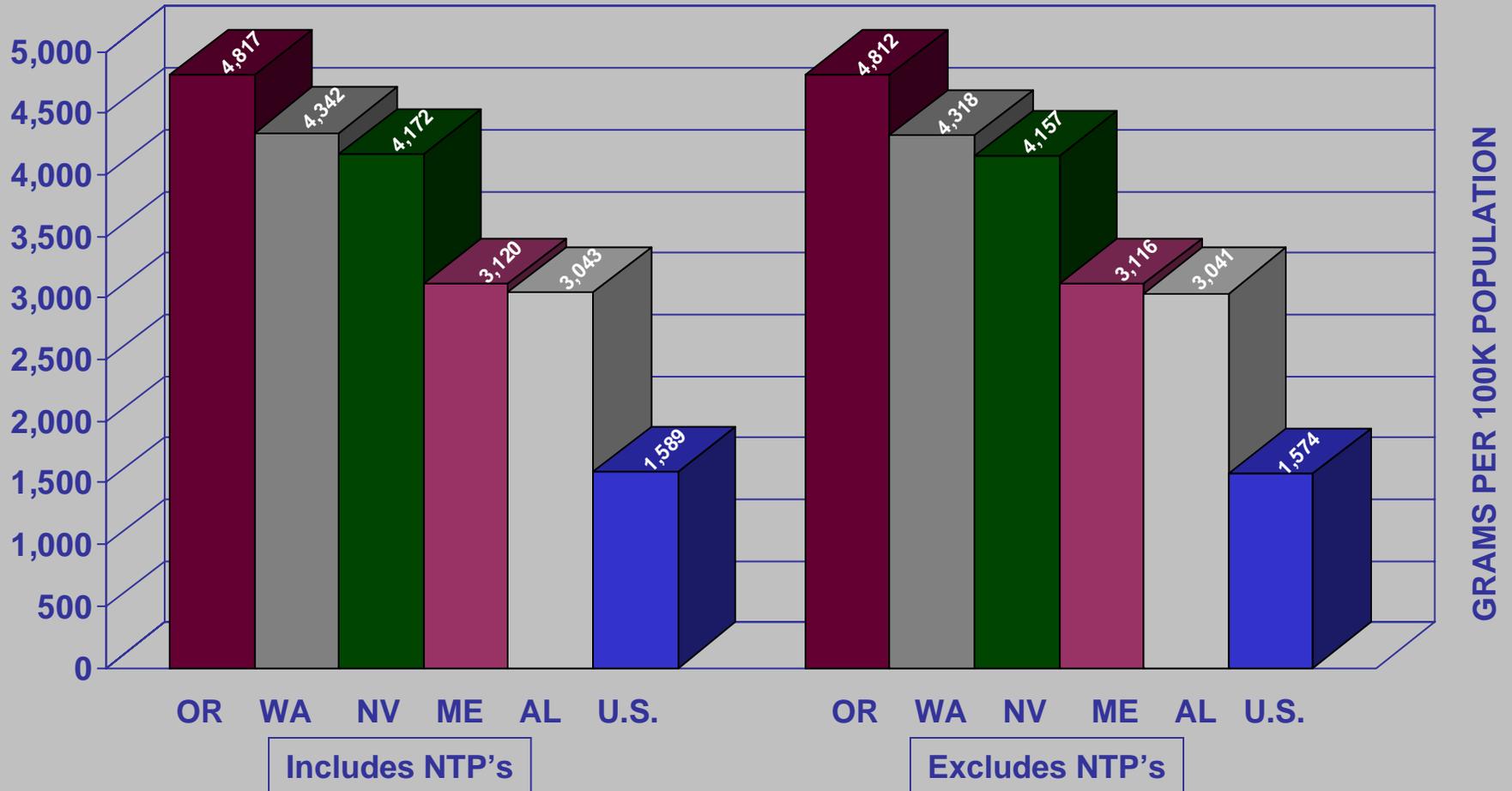
Source: DEA ARCOS 04/2007



* Based on total gram amount

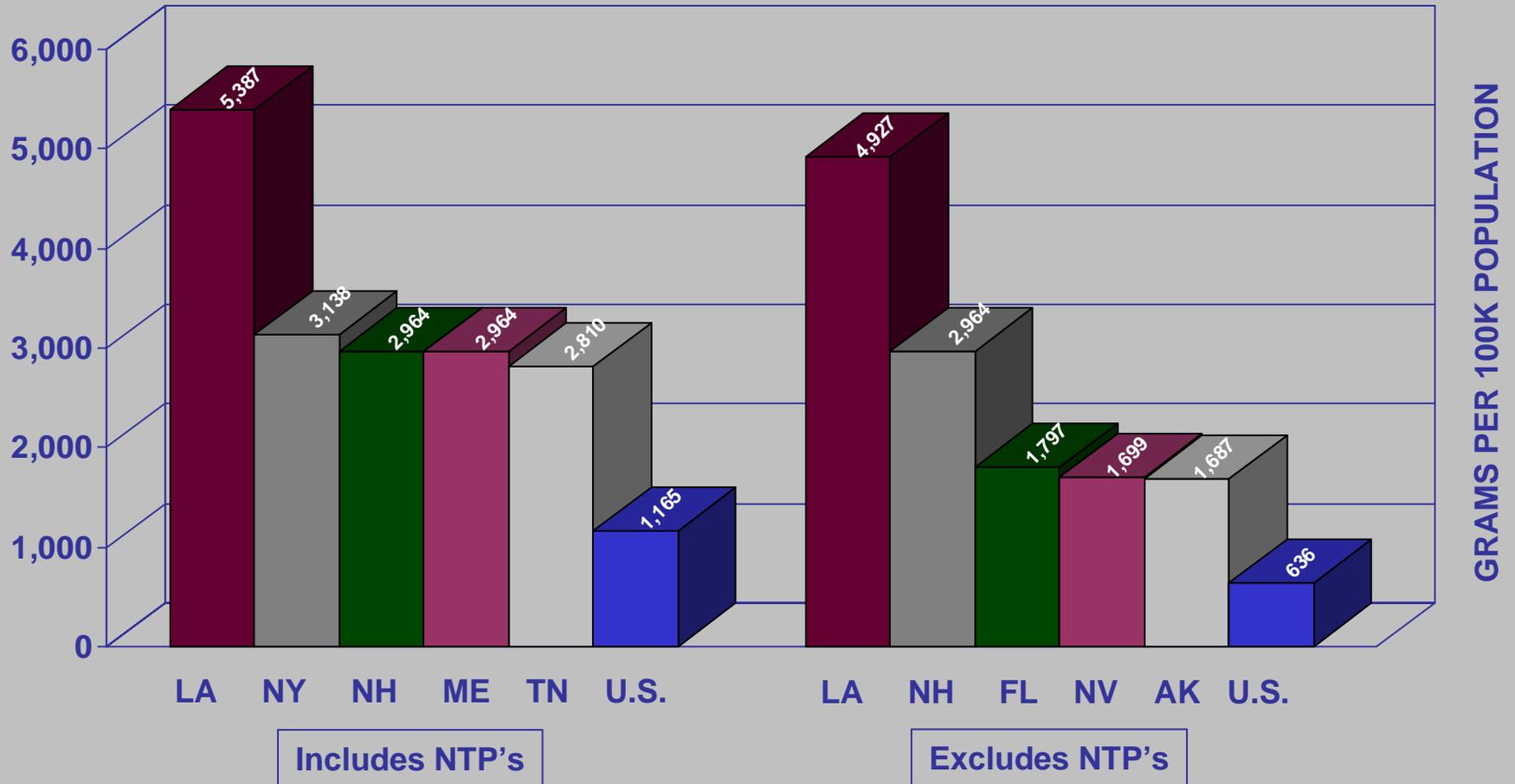
DRUG DISTRIBUTION

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

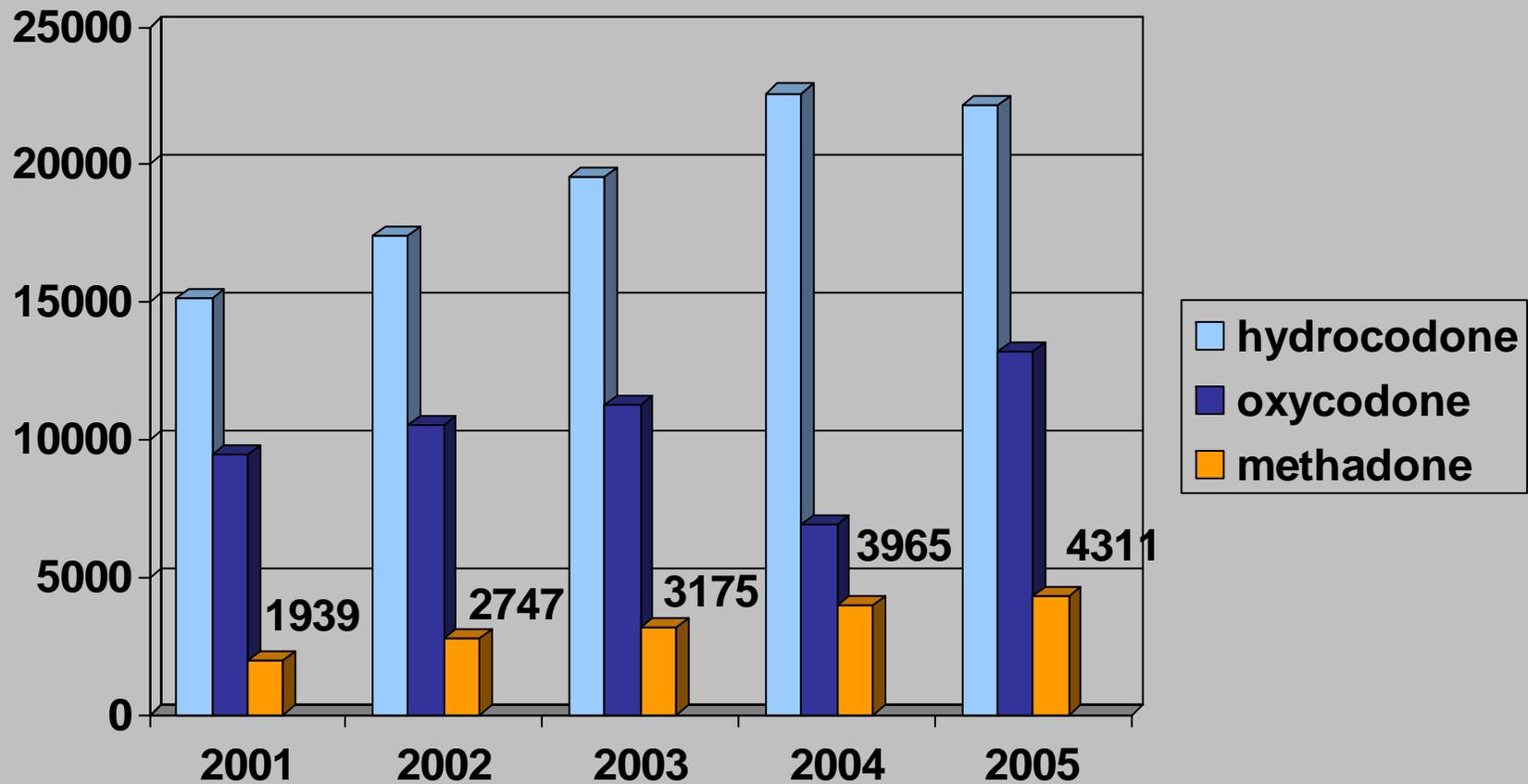


Source: DEA ARCOS 04/2007

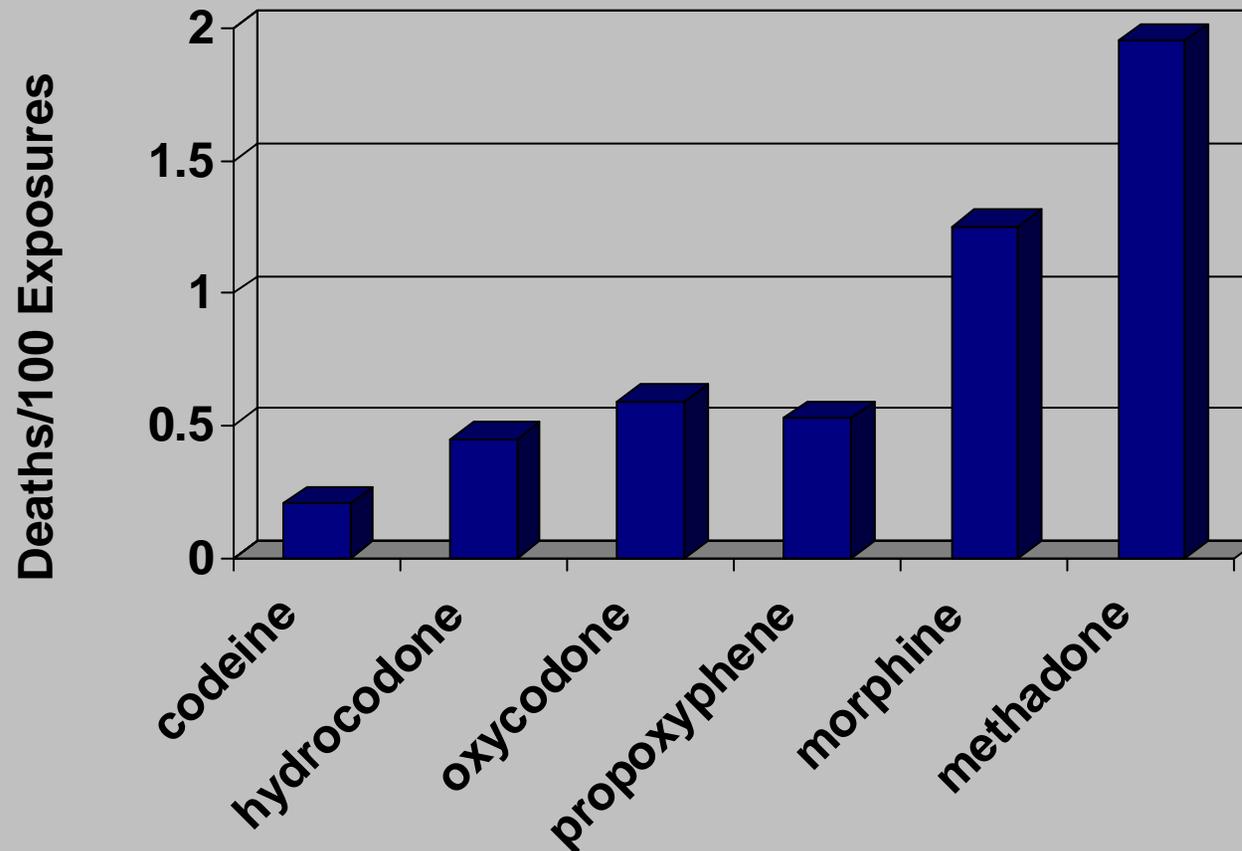
What problems are associated
with methadone products?

Poison Control Data Drug Exposures

Source: National Association of Poison Control Centers (AAPCC)



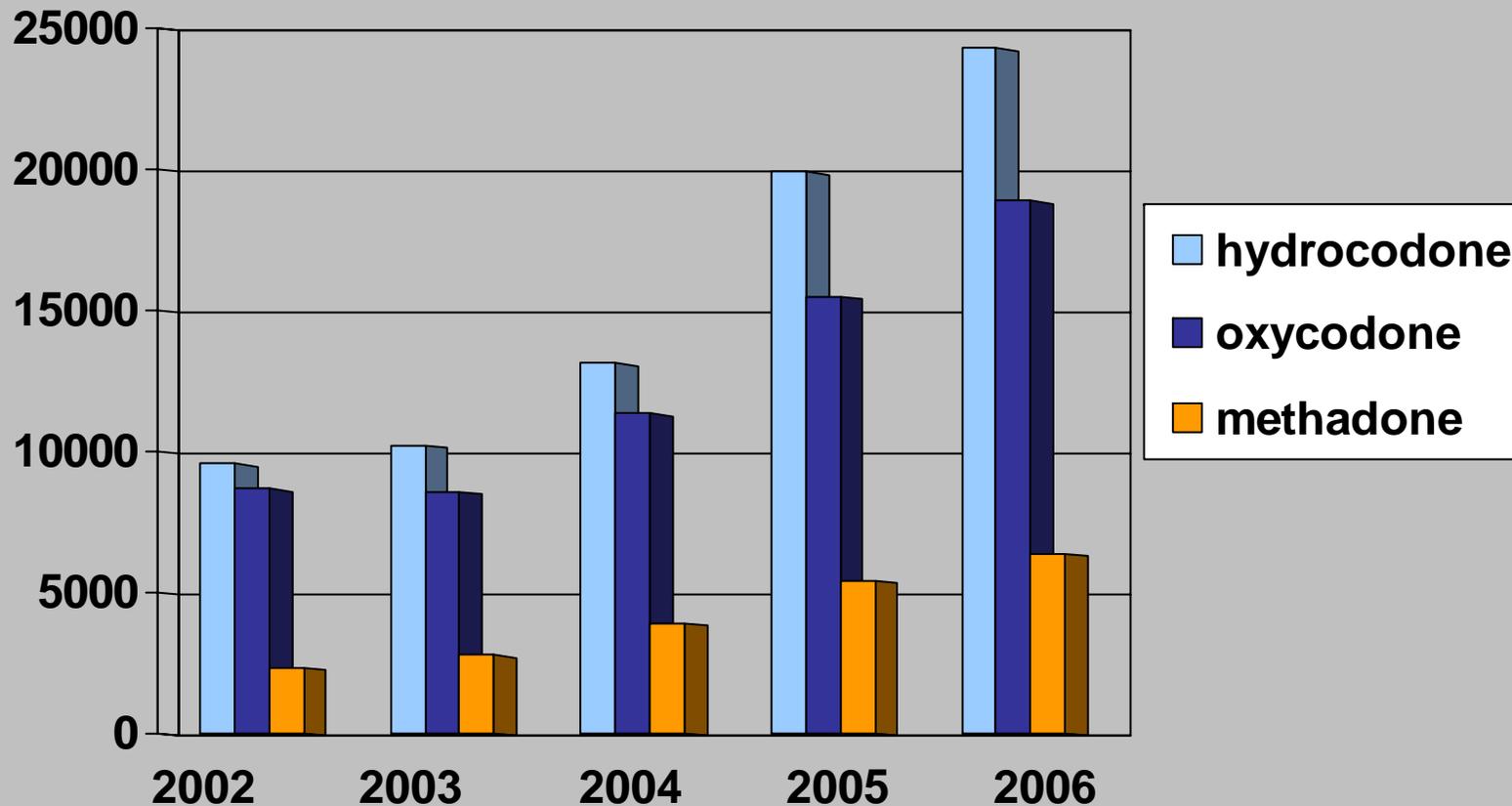
2005 AAPCC Deaths/100 Exposures



Source: National Association of Poison Control Centers (AAPCC)

NFLIS Exhibits

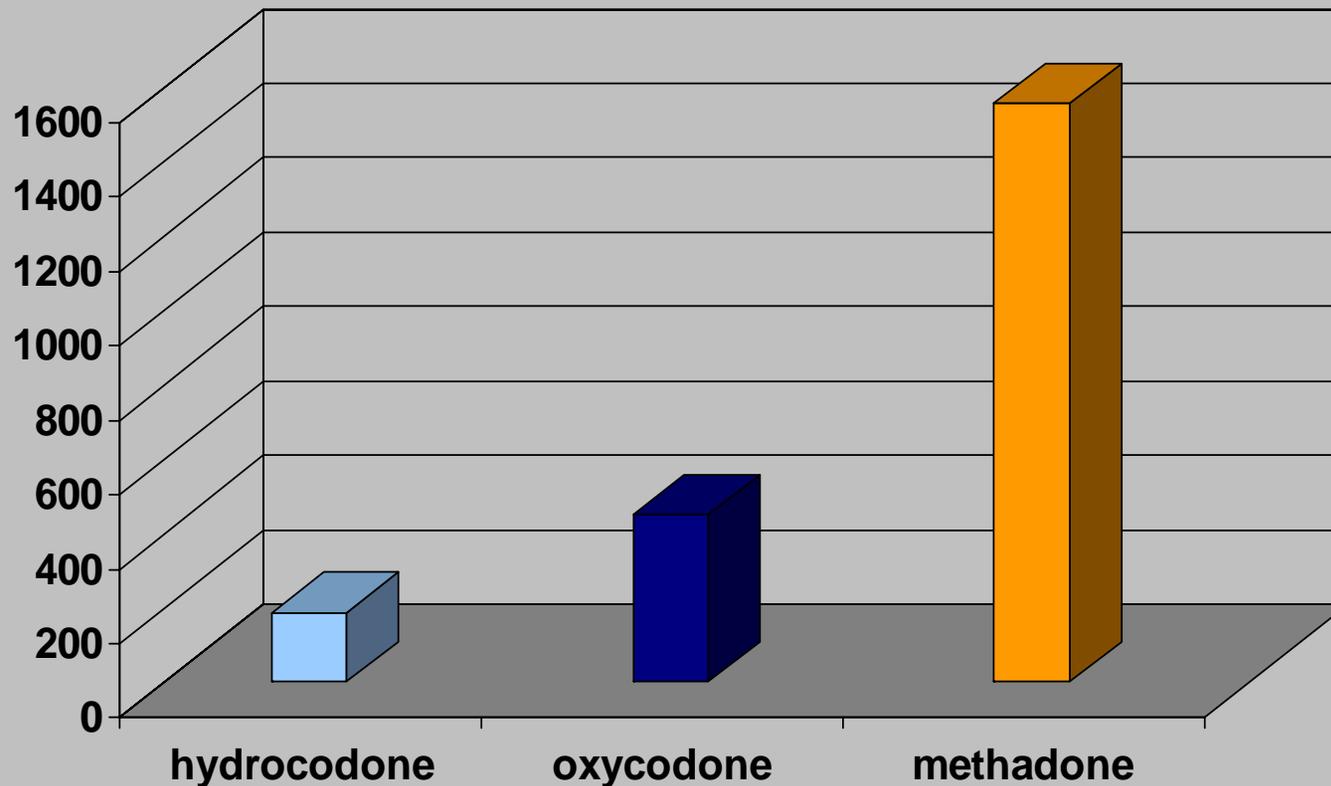
Source: DEA National Forensic Laboratory Information System



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)

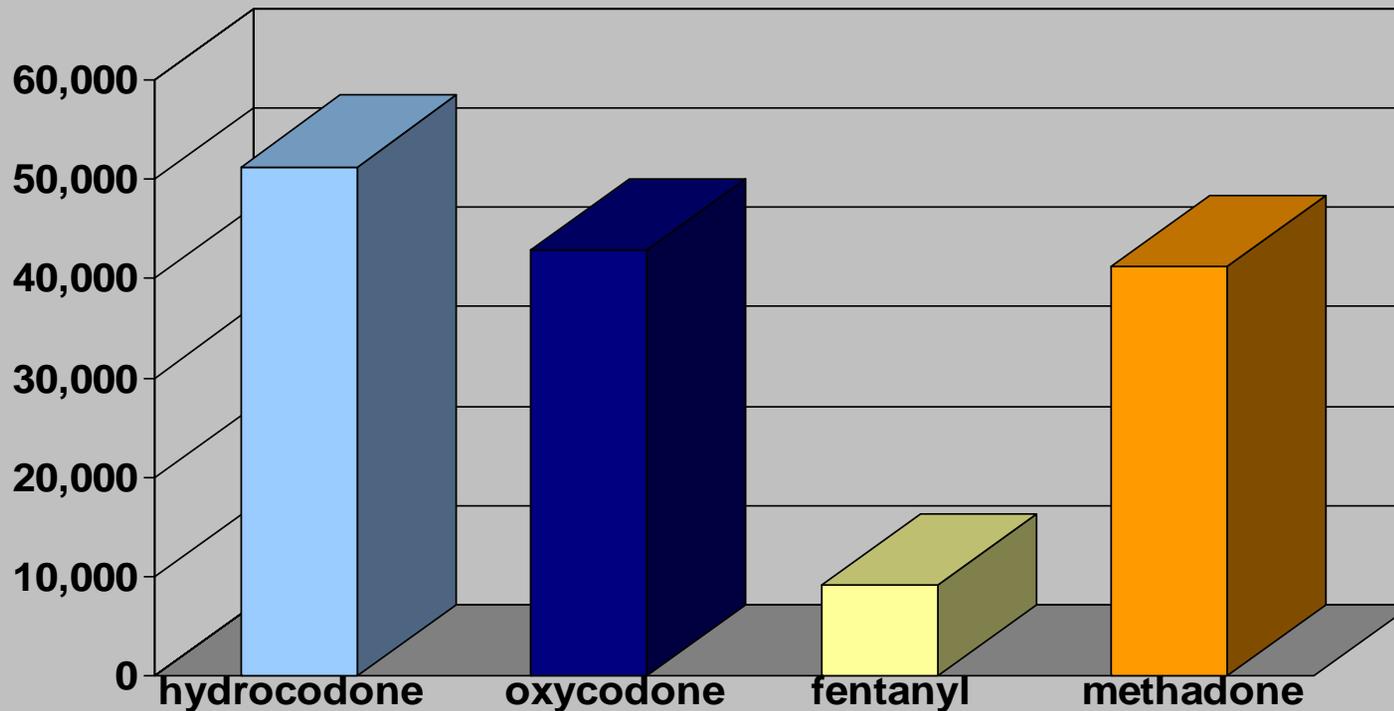
Data regarding the types of methadone formulations submitted to forensic laboratories show:

- 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)



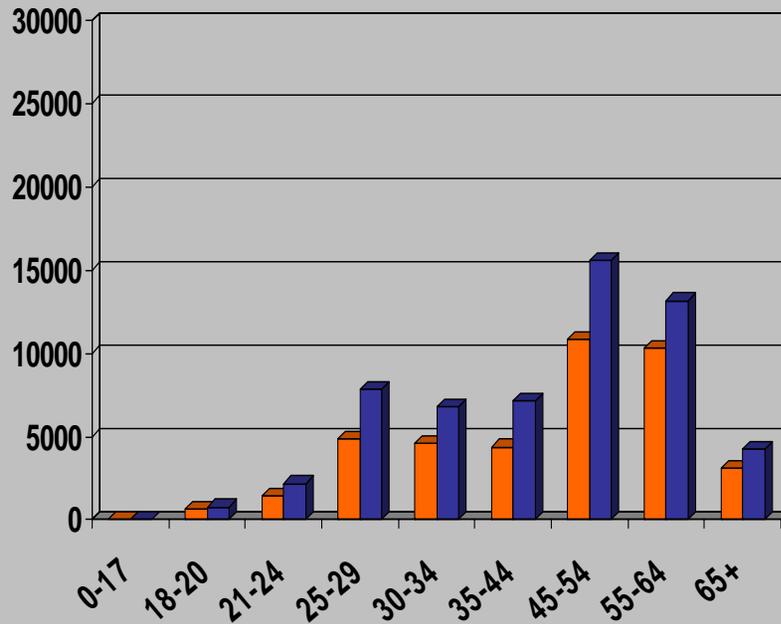
Methadone ranked 3rd among all opioid analgesics, 4th among all controlled pharmaceuticals, and 8th among all controlled substances.

2005 DAWN ED Estimates by Age

Source: Office of Applied Science, SAMHSA, DAWN

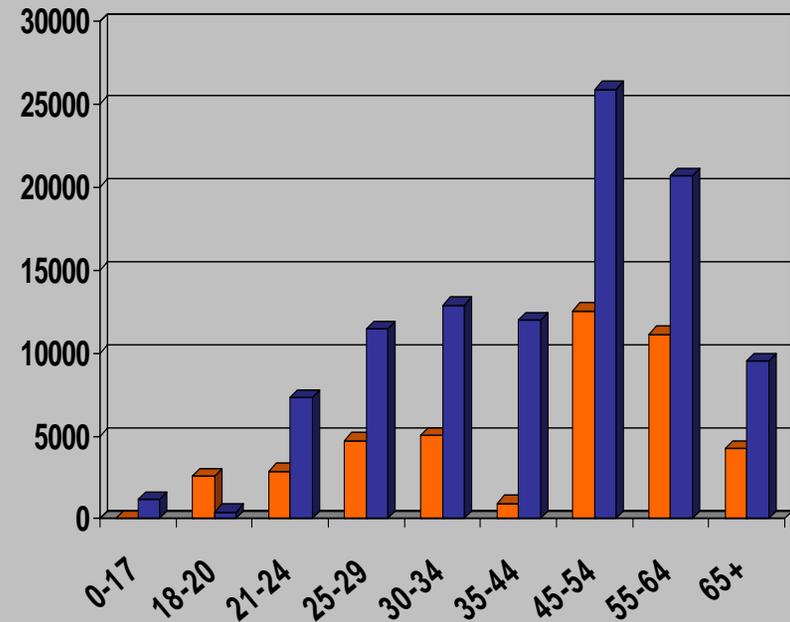
Methadone

- 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



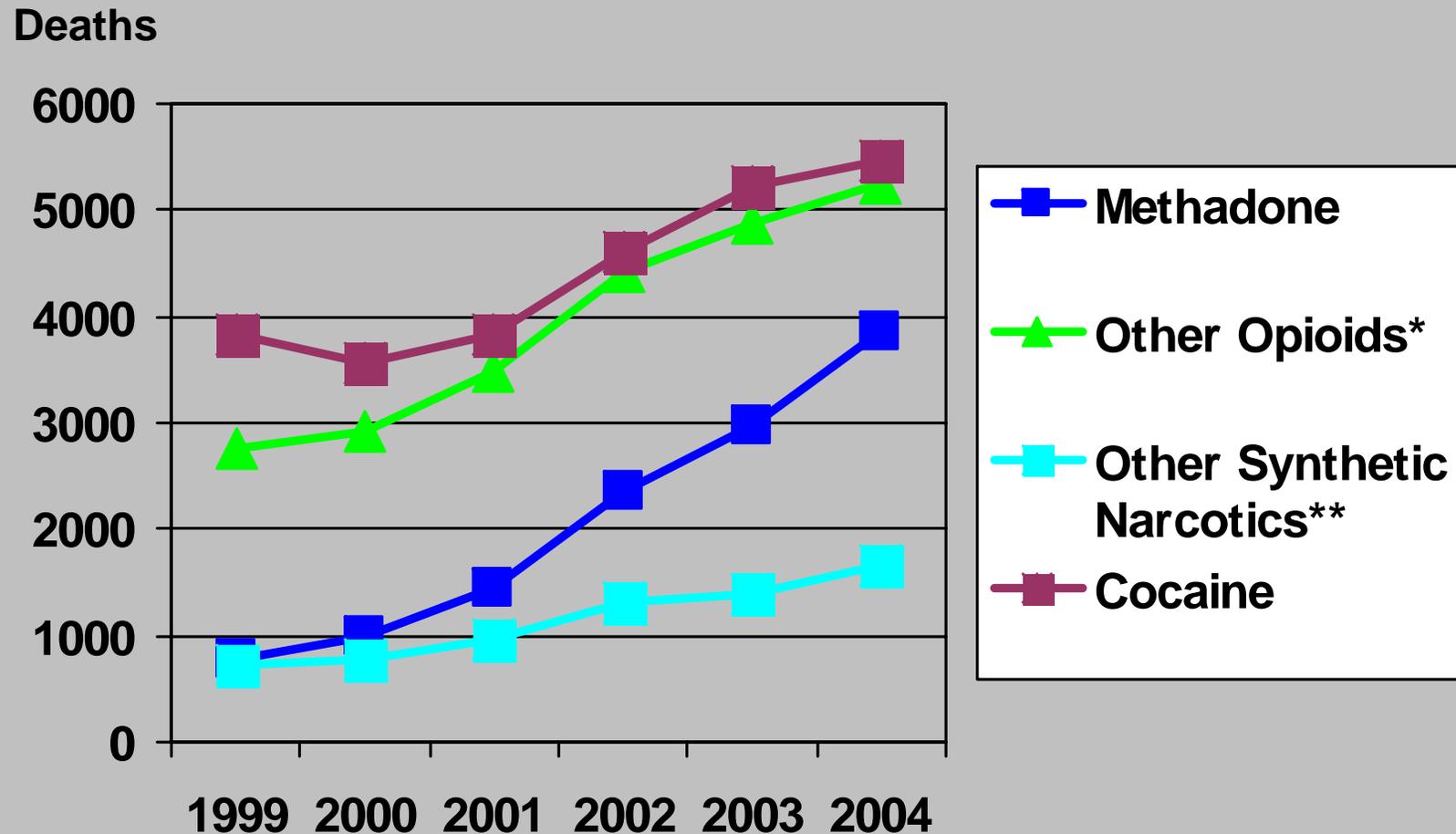
Methadone-related Deaths (1999-2004)

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)

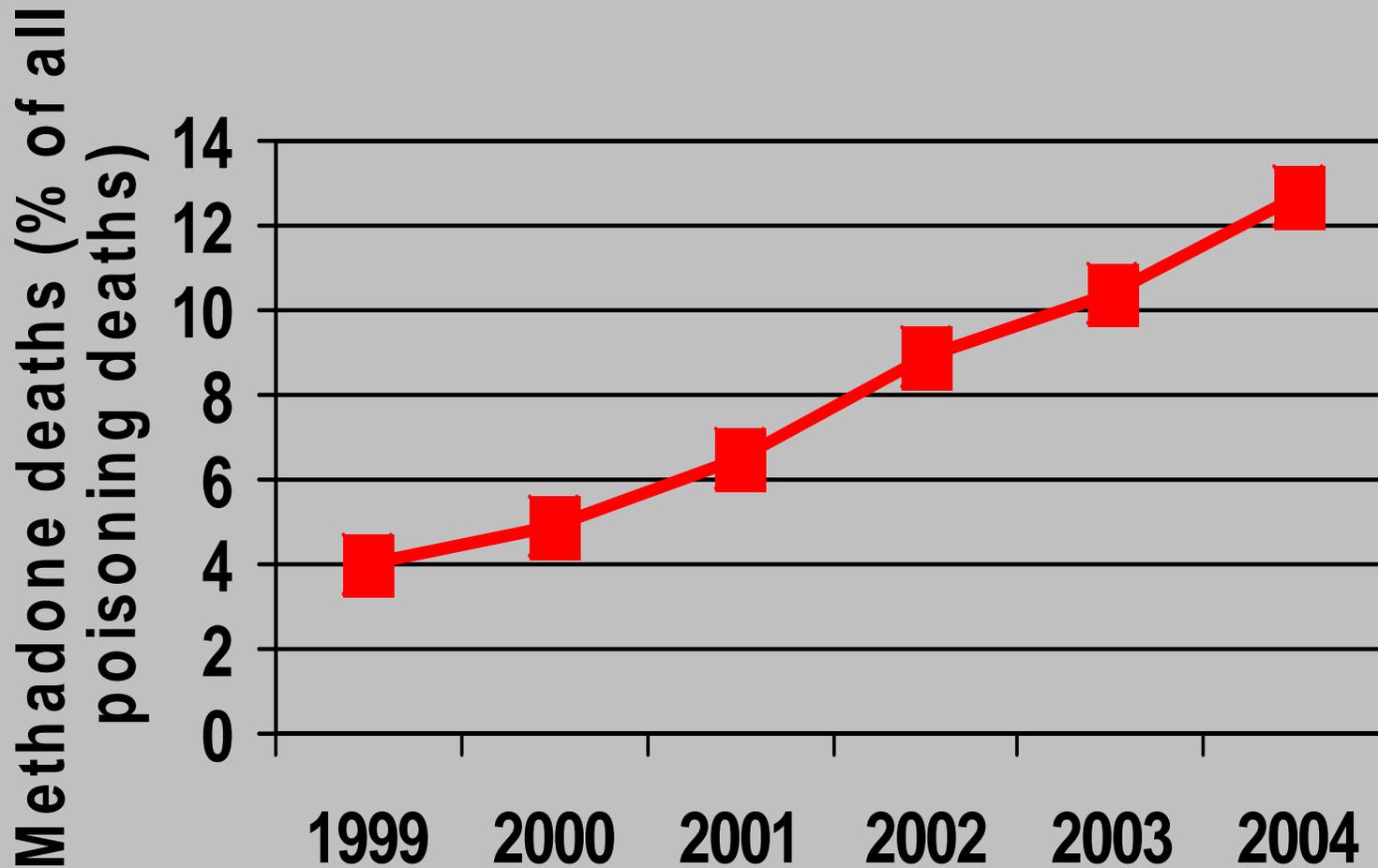


*Other Opioids include drugs like morphine, oxycodone, hydrocodone, hydromorphone

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

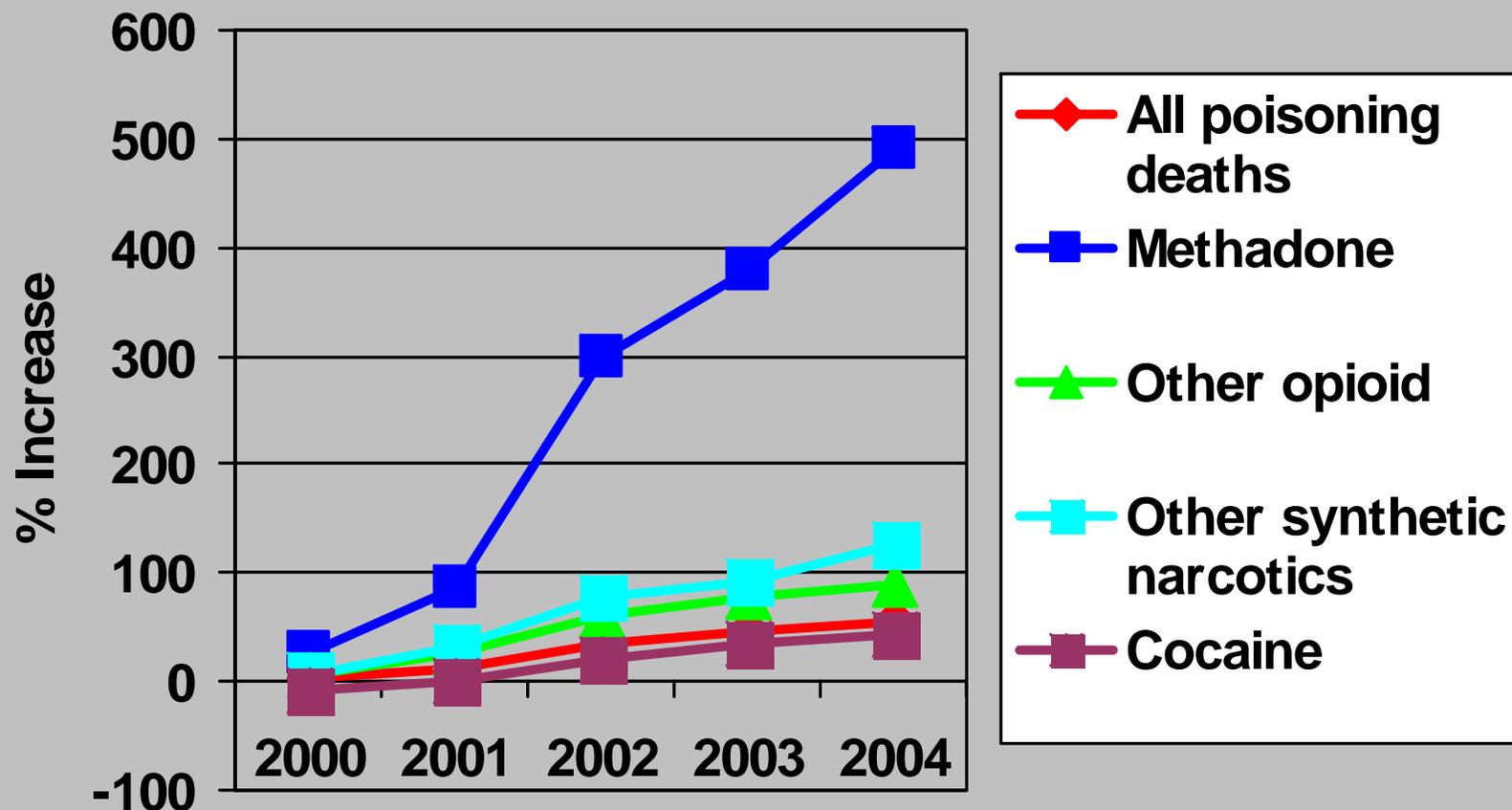
DEA/OD

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)

Ranking	State	Deaths
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

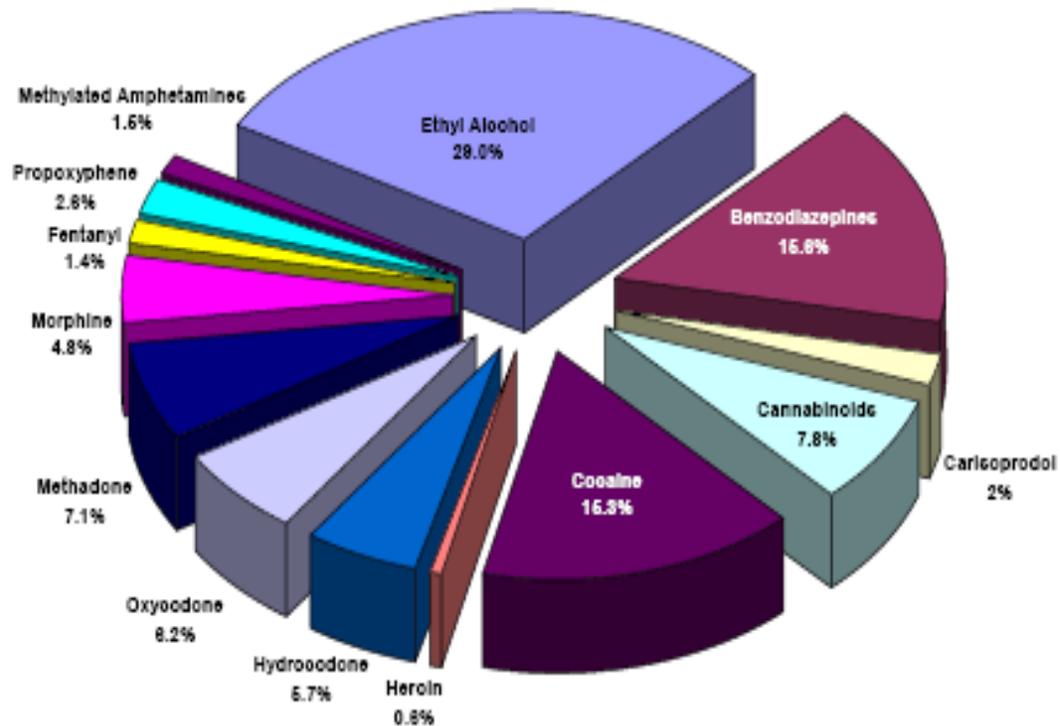
States With the Largest Rate of Increase in Methadone Deaths 1999 to 2004

Source: Center for Disease Control (CDC)

	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

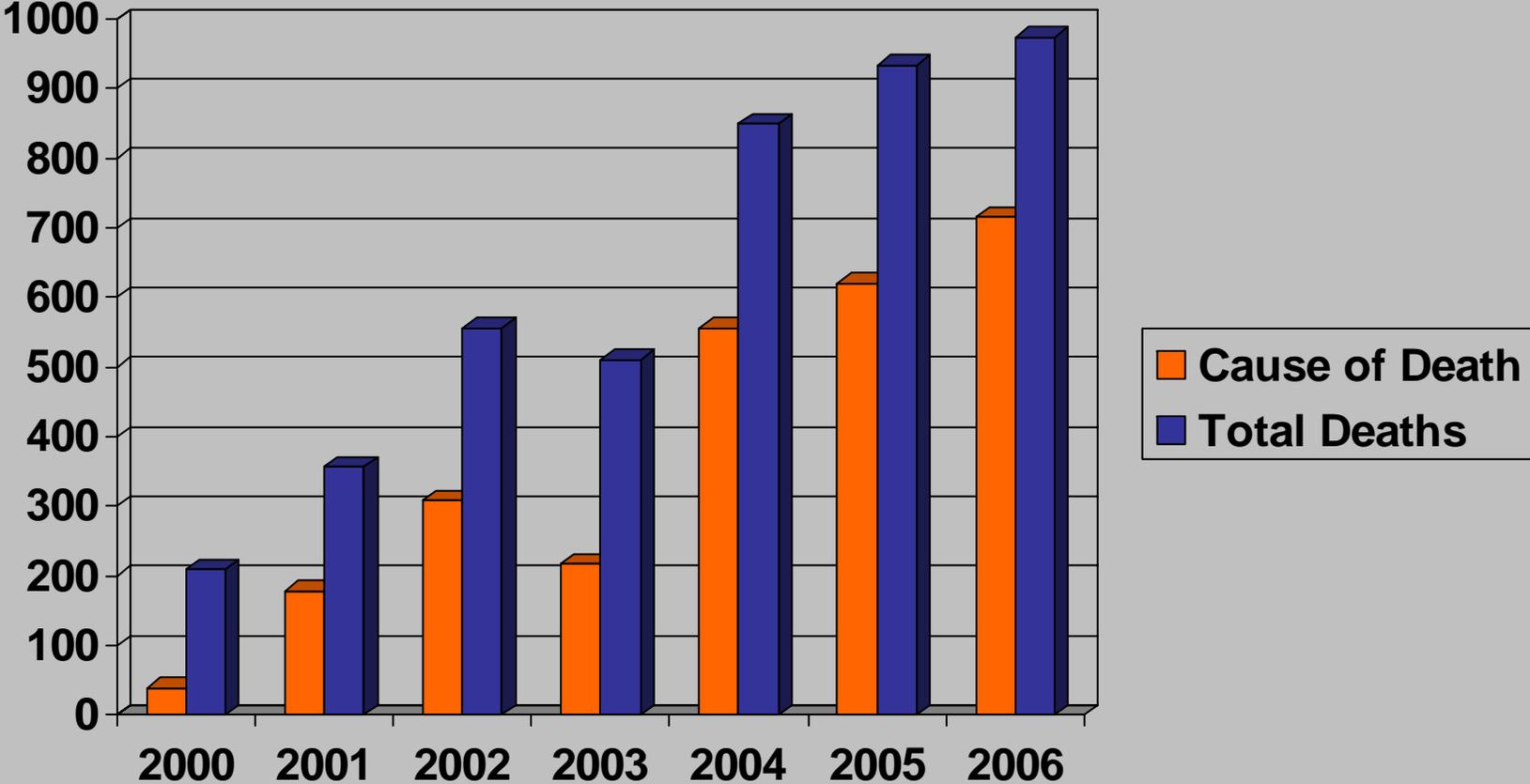
Florida Medical Examiner Data Drug-Deaths

**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



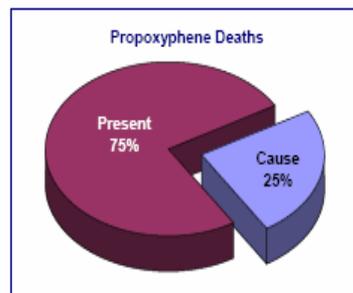
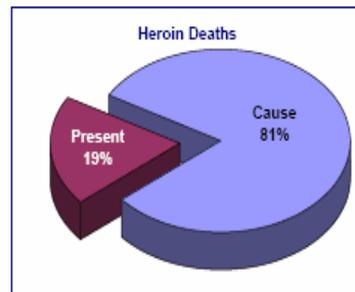
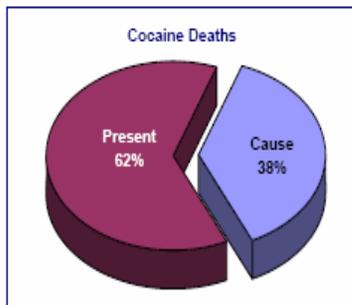
Florida Medical Examiners Report January – June 2006

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

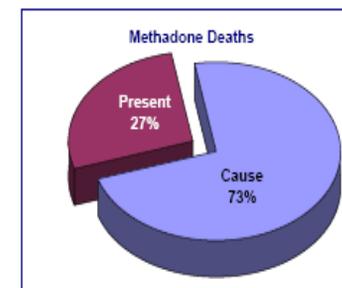
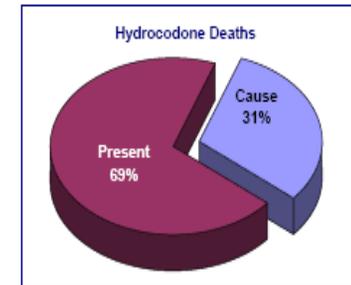
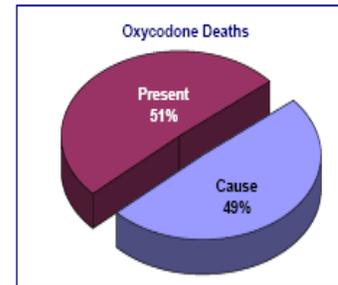
Drug Found in Body	Total Occurrences	Cause of Death
Heroin	36	29
Fentanyl	85	51
Hydrocodone	346	106
Hydromorphone	63	13
Meperidine	25	3
Methadone	428+(546)=974	312+(400)=712
Morphine	289	106
Oxycodone	377	185
Propoxyphene	155	38
Tramadol	59	18

Florida Medical Examiners Data January-June 2006

Drug Detected at Death: Lethal vs. Non-Lethal



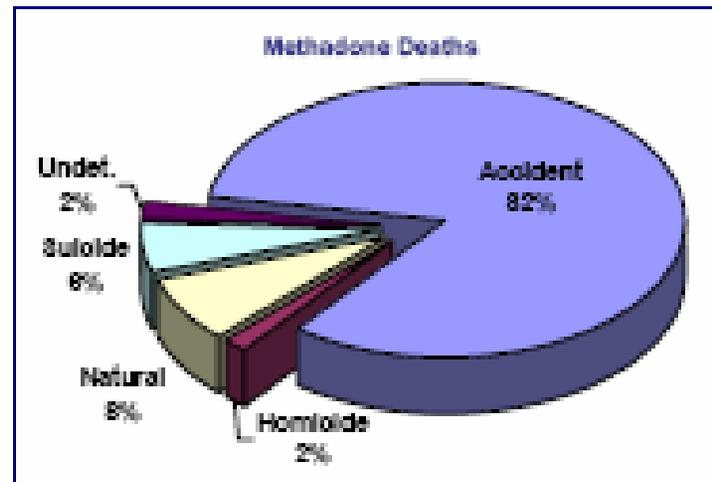
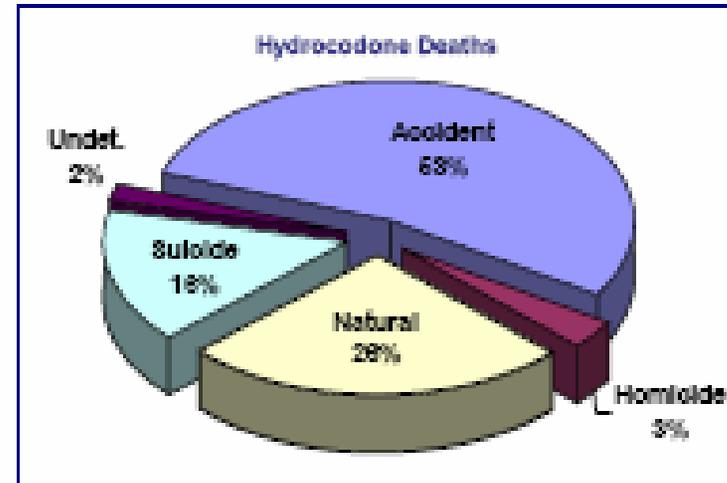
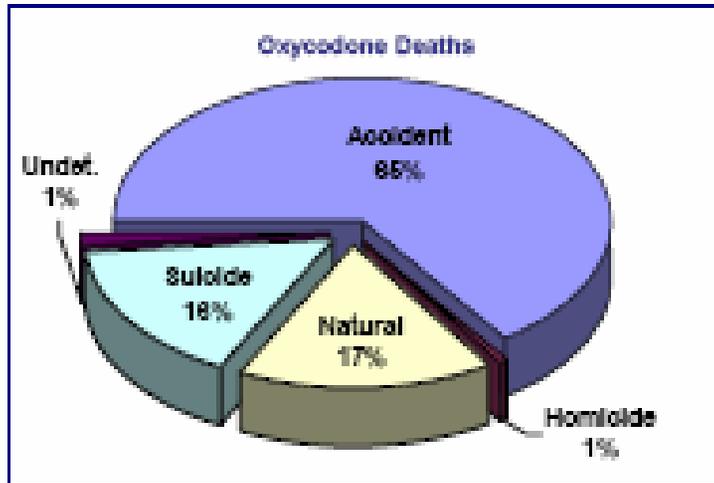
Drug Detected at Death: Lethal vs. Non-Lethal



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.