

Buprenorphine Advanced Treatment 2010 Update

CA Area IHS Conference and the
American Osteopathic Academy of Addiction
Medicine

WWW.AOAAM.ORG

ALSO the 2010 AOAAM Buprenorphine Waiver Course

Welcome

- Greetings and welcome to the Advances in Indian Health and the American Osteopathic Academy of Addiction Medicine Update for the Buprenorphine Advanced Training (BAT), Evaluation and Treatment of Opioid Dependence and OBOT Program. This eight hour program will review up to date information on the treatment of prescription drug and heroin abuse and dependence. It will also provide eligibility for the Drug Abuse Treatment Act (DATA) 2000 Waiver consistent with the present law. Understanding the DATA 2000 and its updates, the pharmacology of opioids and buprenorphine, medical and psychiatric co-morbidities to opioid dependence, patient selection and assessment, office management, critical decisions in chronic pain management and Special Populations are critical to completion of the program. Recent concerns of the DEA and CSAT will also be covered.
- NVidmer@AOAAM.ORG or Anthony.dekker@ihs.gov for any questions

Goals and Objectives

- a. To understand the federal Drug Abuse Treatment Act (DATA) of 2000 that identifies the criteria needed for Office Based Opioid Treatment(OBOT) utilizing buprenorphine and its updates. To appreciate the new concerns of Buprenorphine to the DEA and CSAT
- b. To distinguish between spontaneous withdrawal and precipitated withdrawal
- c. To describe and contrast the functions of full agonists, partial agonists and antagonists
- d. To describe the basic approach used different types of non-pharmacological treatment
- e. To describe symptoms of opioid withdrawal or intoxication that mimic symptoms of a psychiatric disorder

Goals and Objectives-cont.

- f. To list the criteria for establishing the diagnosis of opioid dependence**
- g. To describe at least three factors to consider in determining if the patient is an appropriate candidate for office-based treatment with buprenorphine**
- h. To describe at least three areas that should be covered in the rules and expectations that are communicated to patients during the patient assessment process**
- i. To list at least three situations in which patient information, with patient identity, can be shared under current laws protecting the patient's confidentiality**
- j. To understand the buprenorphine induction process**
- k. To be aware of diversion, misuse and toxicology of BUP**

Disclosures

- This program is provided by the Indian Health Service and the American Osteopathic Academy of Addiction Medicine. This program has been approved by the American Osteopathic Association and has been approved by the American Academy of Family Practice (AAFP) for prescribed credit for the live didactic portion of the OBOT. The UNM also provides CE via the ANCC.
- Anthony Dekker, DO, Course Director has disclosed that he does not have a conflict and has disclosed no business affiliations to pharmaceuticals. The program is supported with an educational grant from the Centers for Substance Abuse Treatment, a division of the Substance Abuse and Mental Health Services Administration and the Indian Health Service. The opinions of Dr Dekker are not necessarily the opinions of the Indian Health Service, the HHS or the USPHS.

The Problem: Prescription Analgesics: Non-Medical Use

- **30 million persons (13%)**, used prescription analgesics non-medically at least once in their lifetime
 - **First time users: Increased from 600,000 (1990) to 2 million (2002)**
- **2002: 1.5 million either abused or were dependent on prescription pain relievers**
- According to the 2003 National Survey on Drug Use and Health, 6.3 million Americans aged 12 and older have used prescription medications for nonmedical purposes in the prior 30 days.

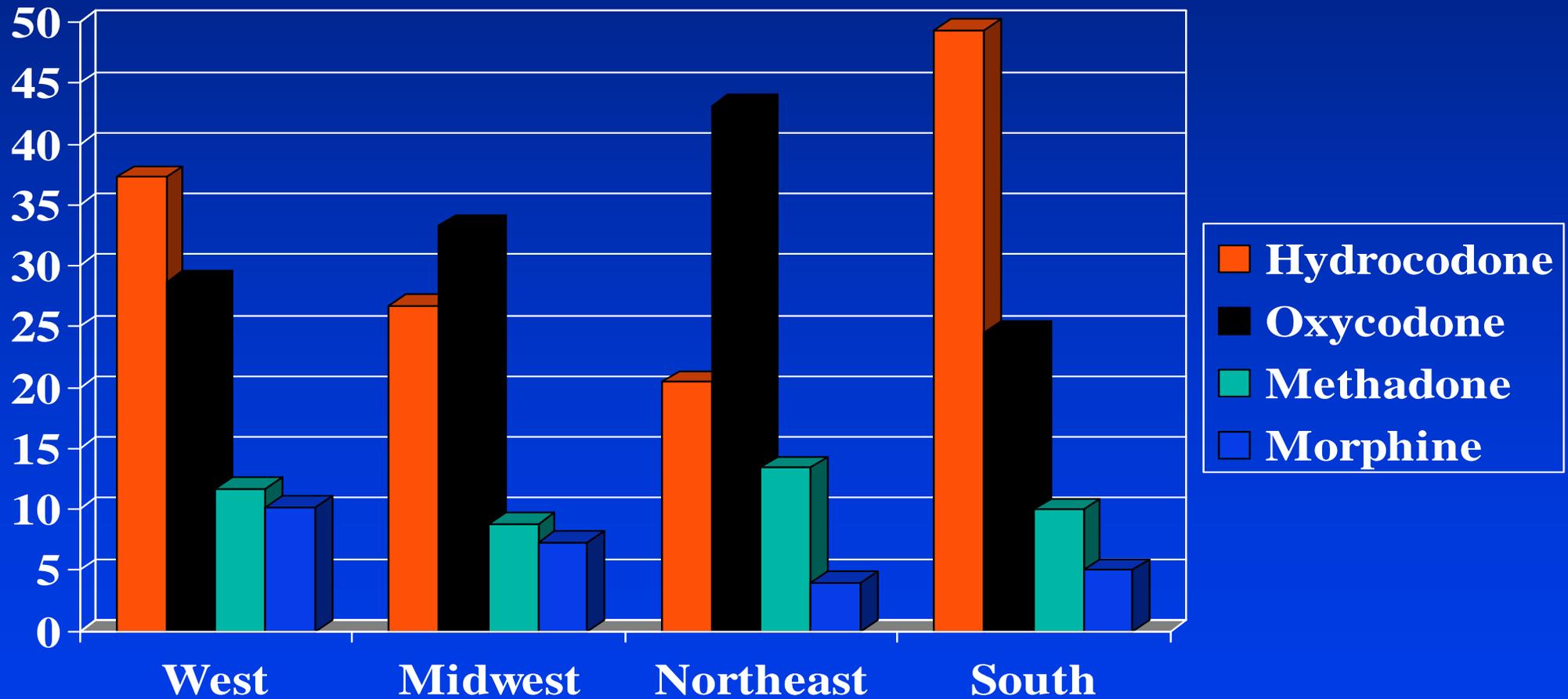
NFLIS National Data - 2007 Narcotic Analgesics

	Number	Percent
Hydrocodone	30,504	39.66%
Oxycodone	24,029	31.24%
Methadone	7,496	9.75%
Morphine	4,202	5.46%
Codeine	2,674	3.48%
Propoxyphene	1,306	1.70%
Hydromorphone	1,559	2.03%
Dihydrocodeine	957	1.24%
Fentanyl	732	0.95%
Buprenorphine	2,094	2.72%

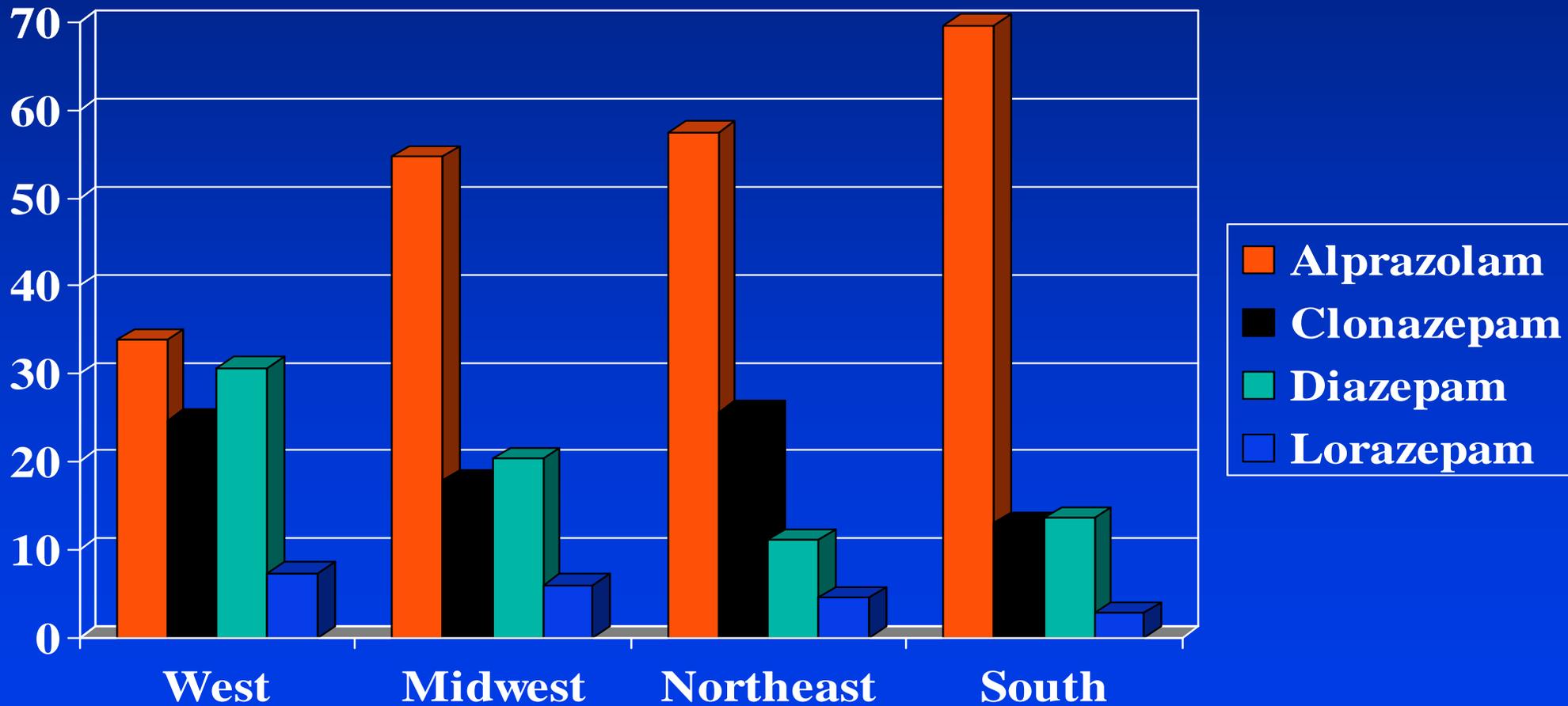
NFLIS National Data - 2007 Benzodiazepines

	Number	Percent
Alprazolam	29,187	65.86%
Clonazepam	7,015	15.83%
Diazepam	6,110	13.79%
Lorazepam	1,527	3.45%
Temazepam	307	0.69%
Chlordiazepoxide	88	0.20%
Triazolam	50	0.11%
Flunitrazepam	24	0.05%
Midazolam	9	0.02%

NFLIS Narcotic Analgesics 2006 Regional Distribution



NFLIS Benzodiazepines 2006 Regional Distribution



NFLIS 2007 Annual Report

From 2001 – 2007

- Hydrocodone increased 133%
- Oxycodone increased 100%
- Alprazolam increased more than 94%

DEA Diversion Website

U.S. DEPARTMENT OF JUSTICE
DRUG ENFORCEMENT ADMINISTRATION
OFFICE OF DIVERSION CONTROL

HOME PRIVACY POLICY CONTACT US WHAT'S NEW HOT ITEMS SITEMAP SEARCH

DIVERSION PROGRAMS
APPLICATIONS & ON-LINE FORMS
ARCOS
CHEMICALS
CONTROLLED SUBSTANCE SCHEDULES
IMPORT AND EXPORT
IFLIS
QUOTAS
REGISTRATION SUPPORT
REPORTS REQUIRED BY 21 CFR

RESOURCES
CAREER OPPORTUNITIES
DRUGS/CHEMICALS OF CONCERN
e-COMMERCE INITIATIVES
FEDERAL REGISTER NOTICES
MEETINGS & EVENTS
OFFICES & DIRECTORIES
PROGRAM DESCRIPTION
PUBLICATIONS
QUESTIONS & ANSWERS
REGULATIONS & CODIFIED CSA

LINKS
FEDERAL AGENCIES & RELATED
INDUSTRY RELATED
PUBLIC INTEREST

REGISTRATION VALIDATION

CASES AGAINST DOCTORS

WELCOME TO THE DIVERSION CONTROL PROGRAM

Registration Number
Toll Free: 1-800-882-9539

REGISTRATION SUPPORT

Save time by applying for and/or renewing your DEA Registration on-line. Data will be entered through a **secure connection** to the **ODWIF** on-line web application system. Minimum requirements: Credit Card and a web browser that supports **128-bit encryption**.

NEW REGISTRATION FEE EFFECTIVE NOVEMBER 1, 2006

- To Apply for Renewal Applications for Registration On-Line
- To Apply for New Applications for Registration On-Line
- To Apply for Registration by Mail
- For Registration Changes
(Address, Drug Codes, Name, Schedules)
- Duplicate Certificates
- Order Forms

For Registration Matters
1-800-882-9539

WHAT'S NEW

RENEWAL
Apply On-Line
REGISTRATION APPLICATIONS
Renewal Applications

NEW APPLICATIONS FOR REGISTRATION
New Registration Applications

DEA FORM 106 ONLINE
REPORT THEFT OR LOSS OF CONTROLLED SUBSTANCES

COMBAT METH ACT 2005
Combat Methamphetamine Epidemic Act 2005

For Additional
Information

www.DEAdiversion.usdoj.gov

Rates of lifetime non-medical use of prescription analgesics

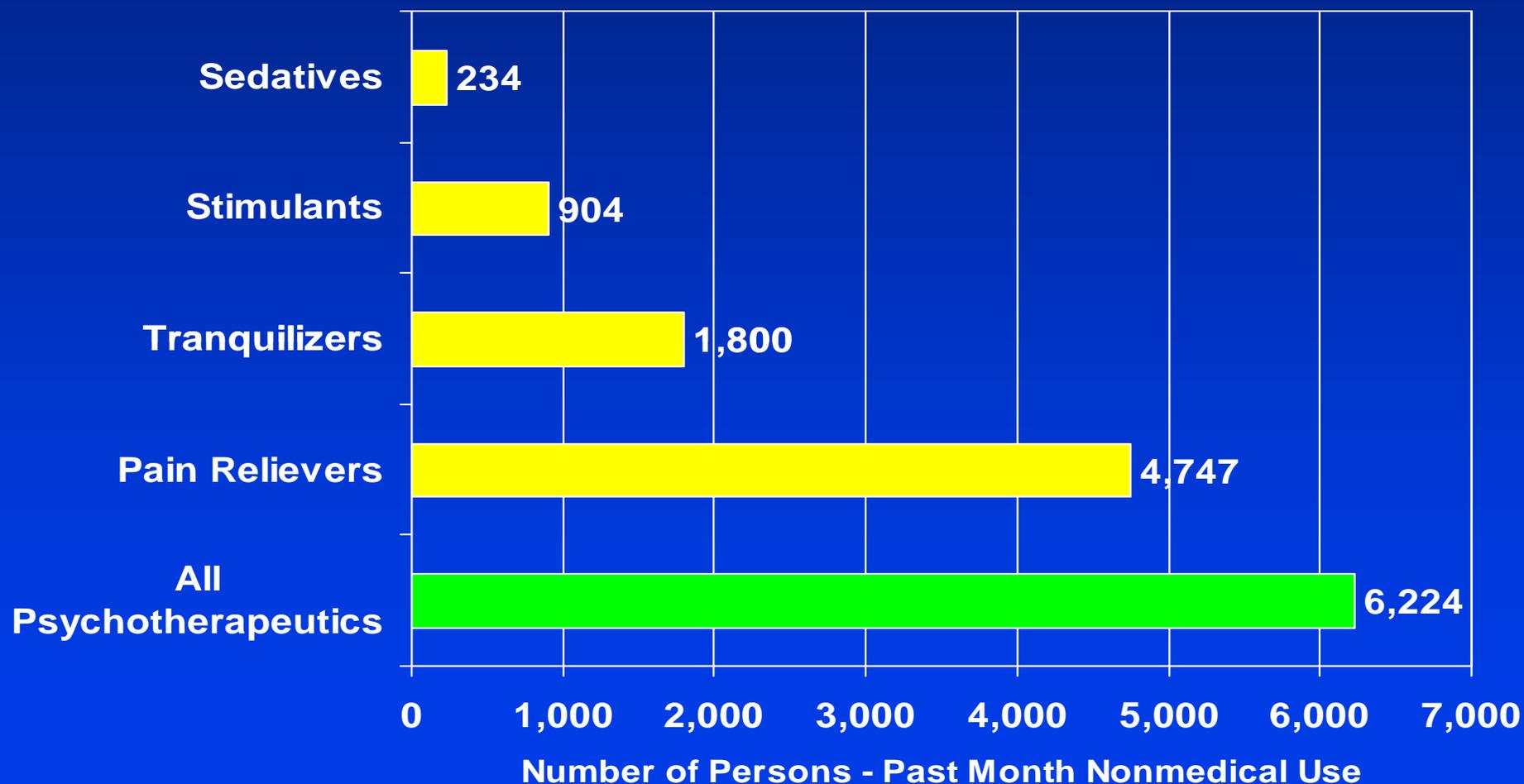
Rates of lifetime oxycodone abuse increased significantly from 2002 to 2003 while heroin rates are stable

- **1.9 million** had used only **heroin** at least once in their lifetime
- **11 million** had used **oxycodone** non medically at least once in their lifetime
- **1.7 million** had used **both** in their lifetime at least once

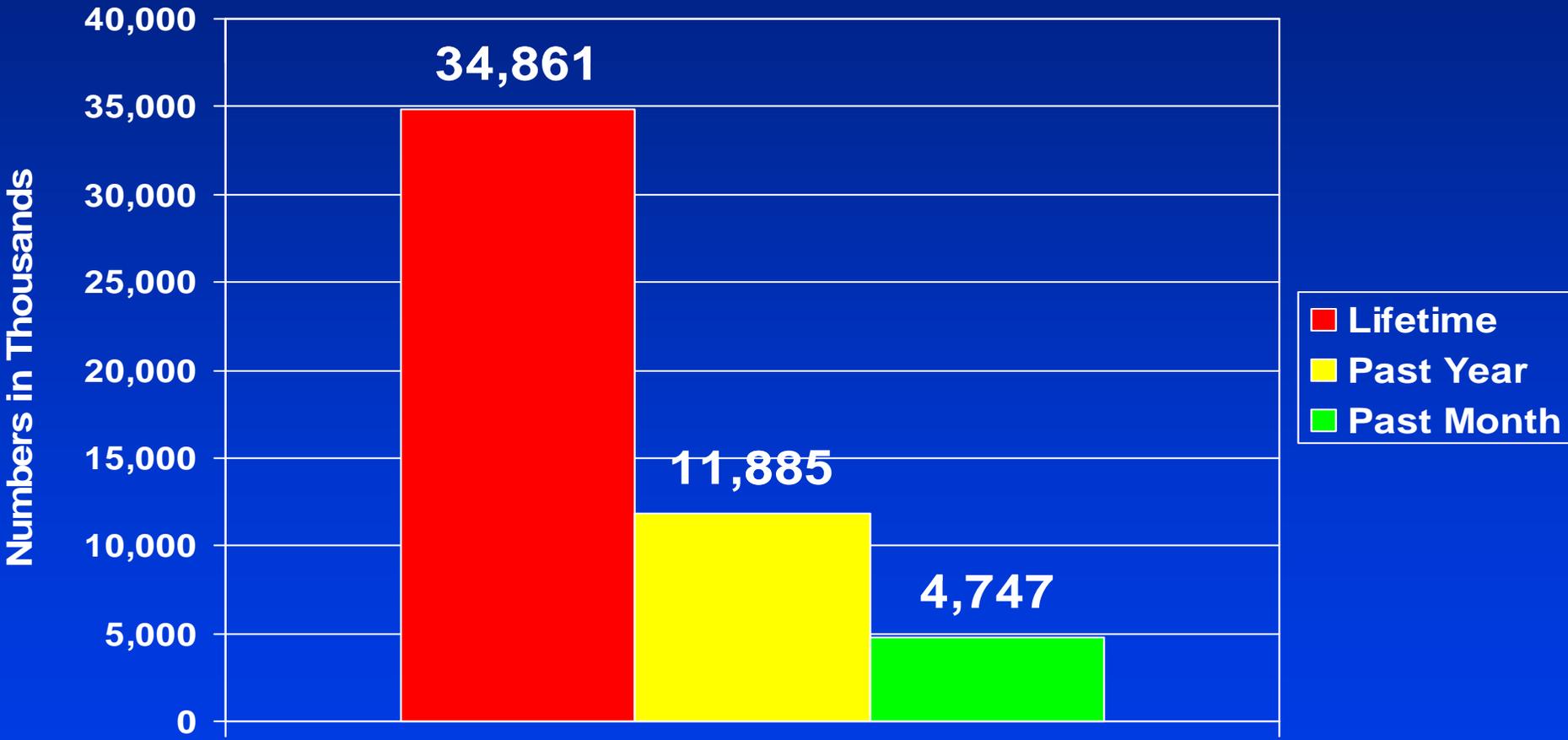
TEDS: Rural vs Urban

- Admissions for treatment of narcotic painkillers
 - 155% increase from 1992-2002
 - Greatest increase in rural areas (269%), smallest in large central metro areas (58%)
 - 15% fall in admissions for injection users
 - Increase in rural inhalant abuse from 2-12%

Past Month Nonmedical Use of Psychotherapeutics among Persons Aged 12 or Older: 2008

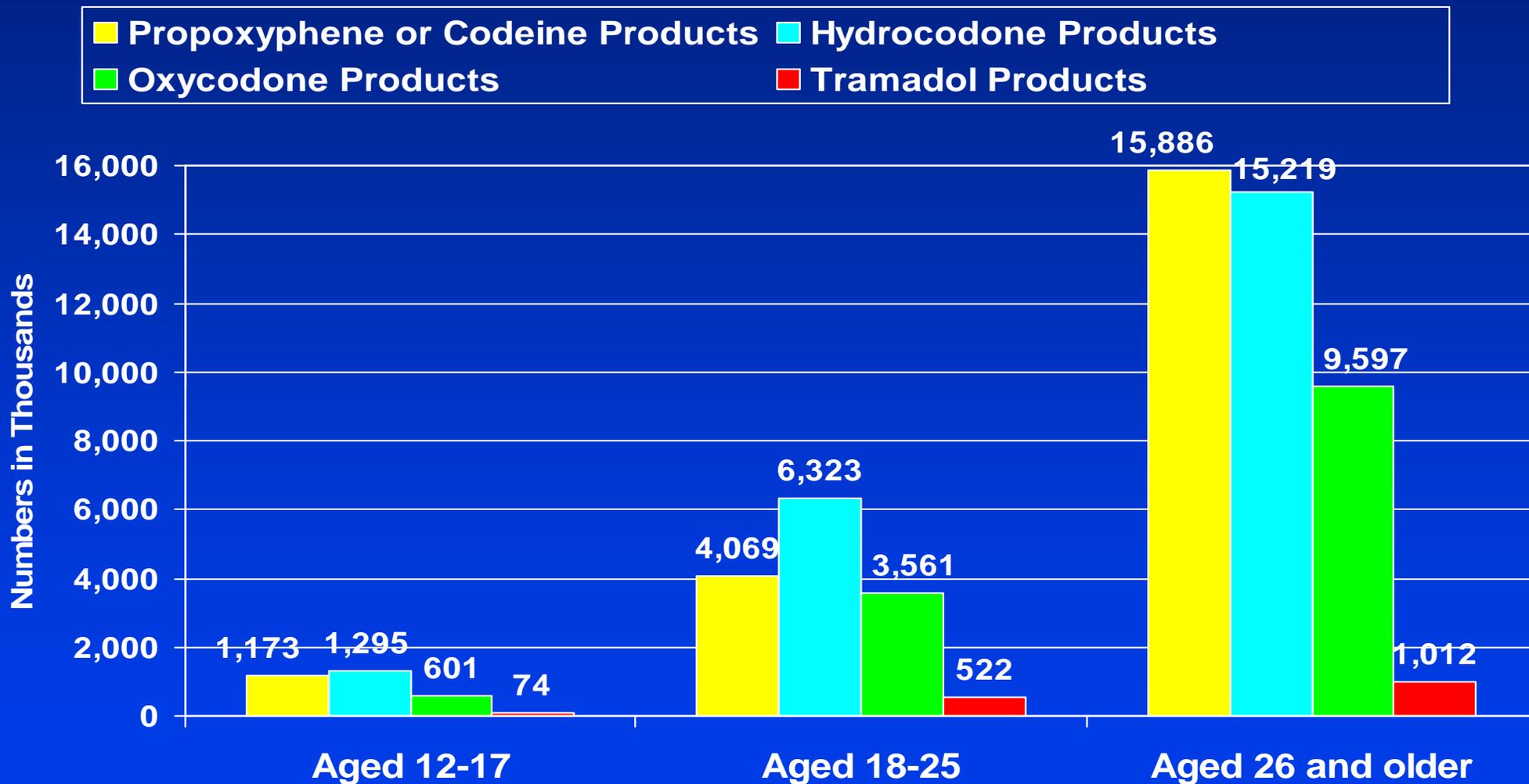


Nonmedical Use of Pain Relievers in Lifetime, Past Year, and Past Month: 2008



Source: NSDUH 2008

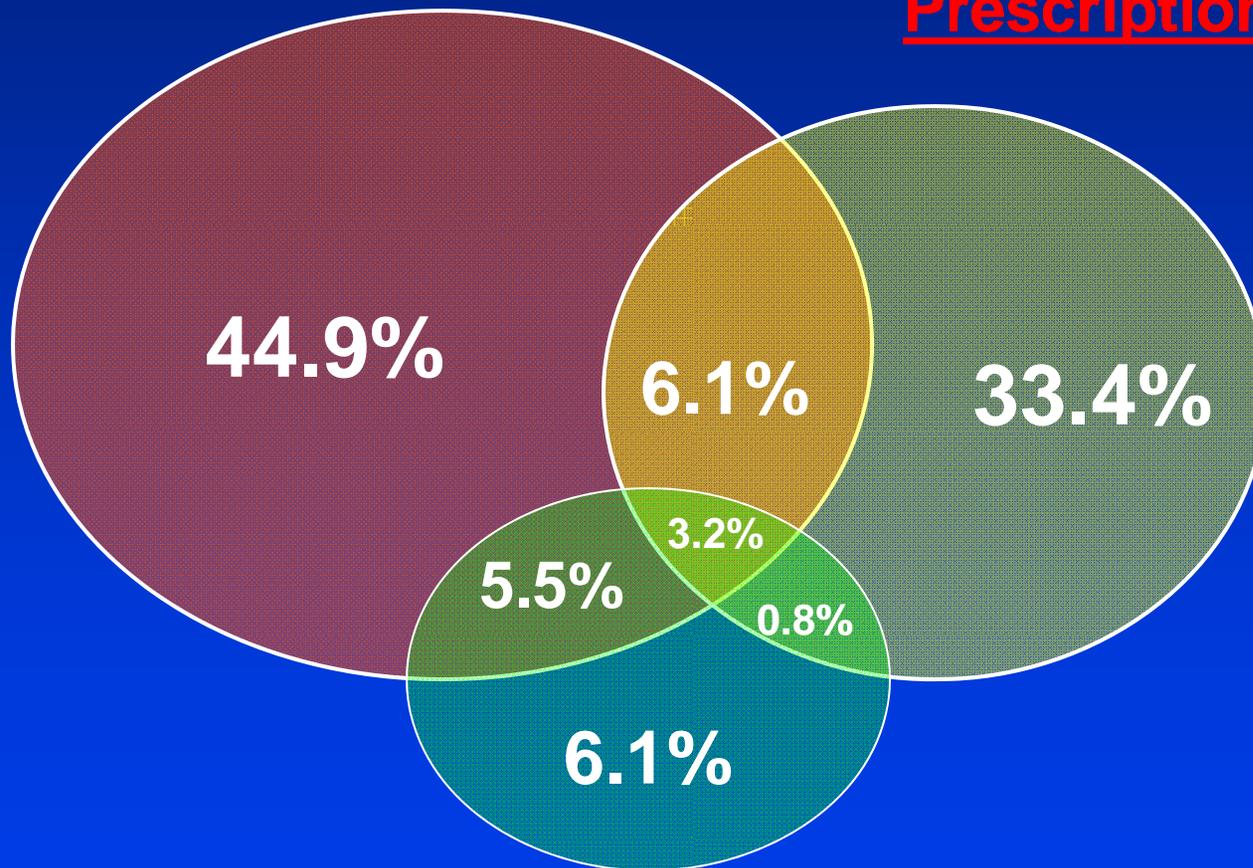
Nonmedical Use of Selected Pain Relievers in Lifetime by Age Group, Numbers in Thousands, 2007



Type of Illicit Drugs Used in Past Year: Adults 50 or Older

Marijuana Use

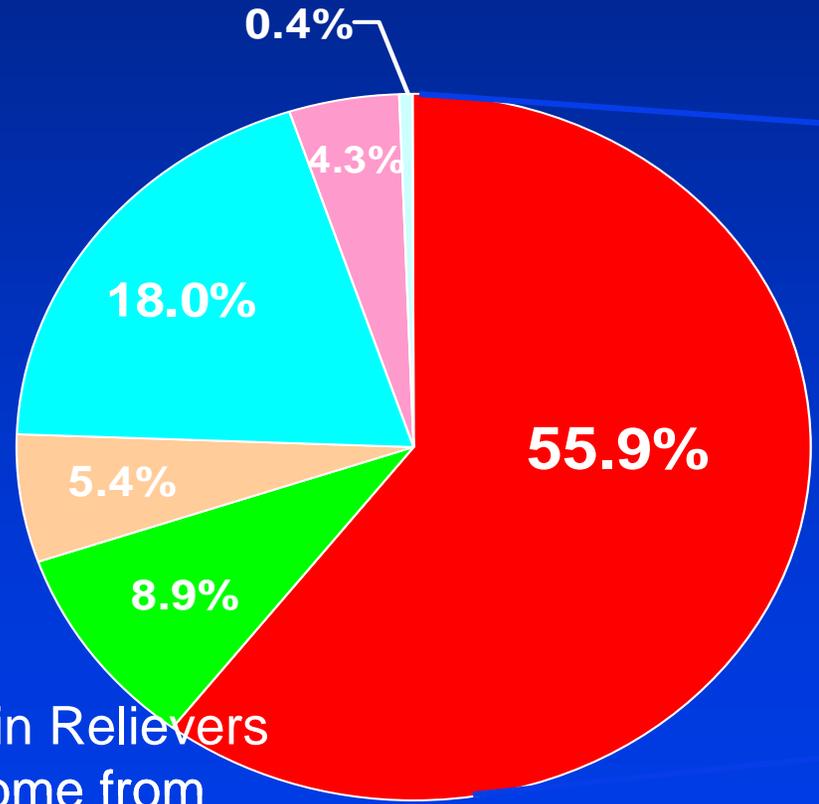
Nonmedical Use of Prescription-type Drugs



Other Illicit Drug Use

Source Where Pain Relievers Were Obtained for Most Recent Nonmedical Use among Past Year Users Aged 12 or Older: 2008

- Friend/Relative for Free
- Bought from Friend/Relative
- Took from Friend/Relative
- Prescription from One Doctor
- From Drug Dealer or Stranger
- From Internet

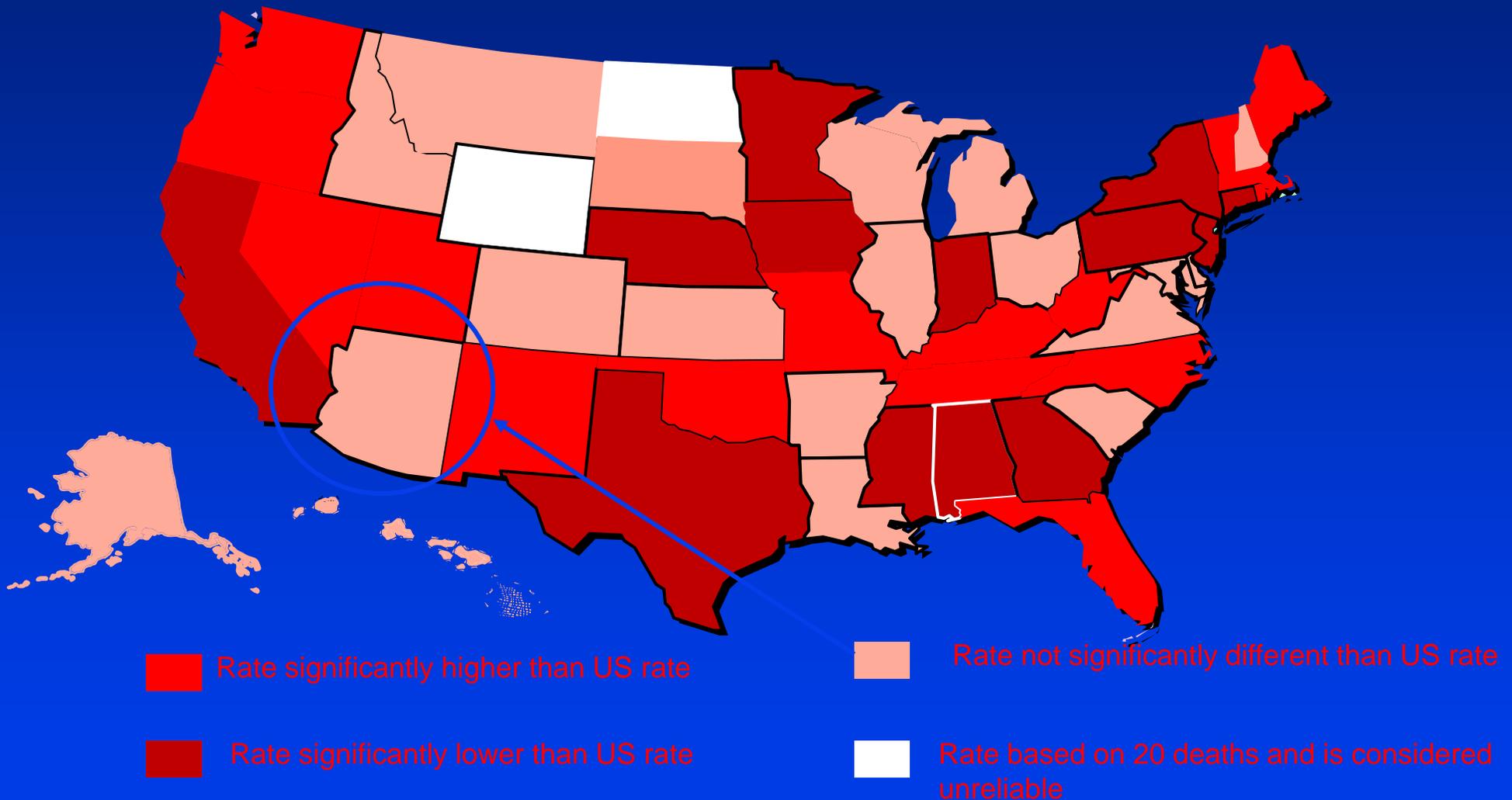


81.7% of pain relievers obtained from friend/relative for free were obtained from one doctor. **1.6%** were obtained from a drug dealer.

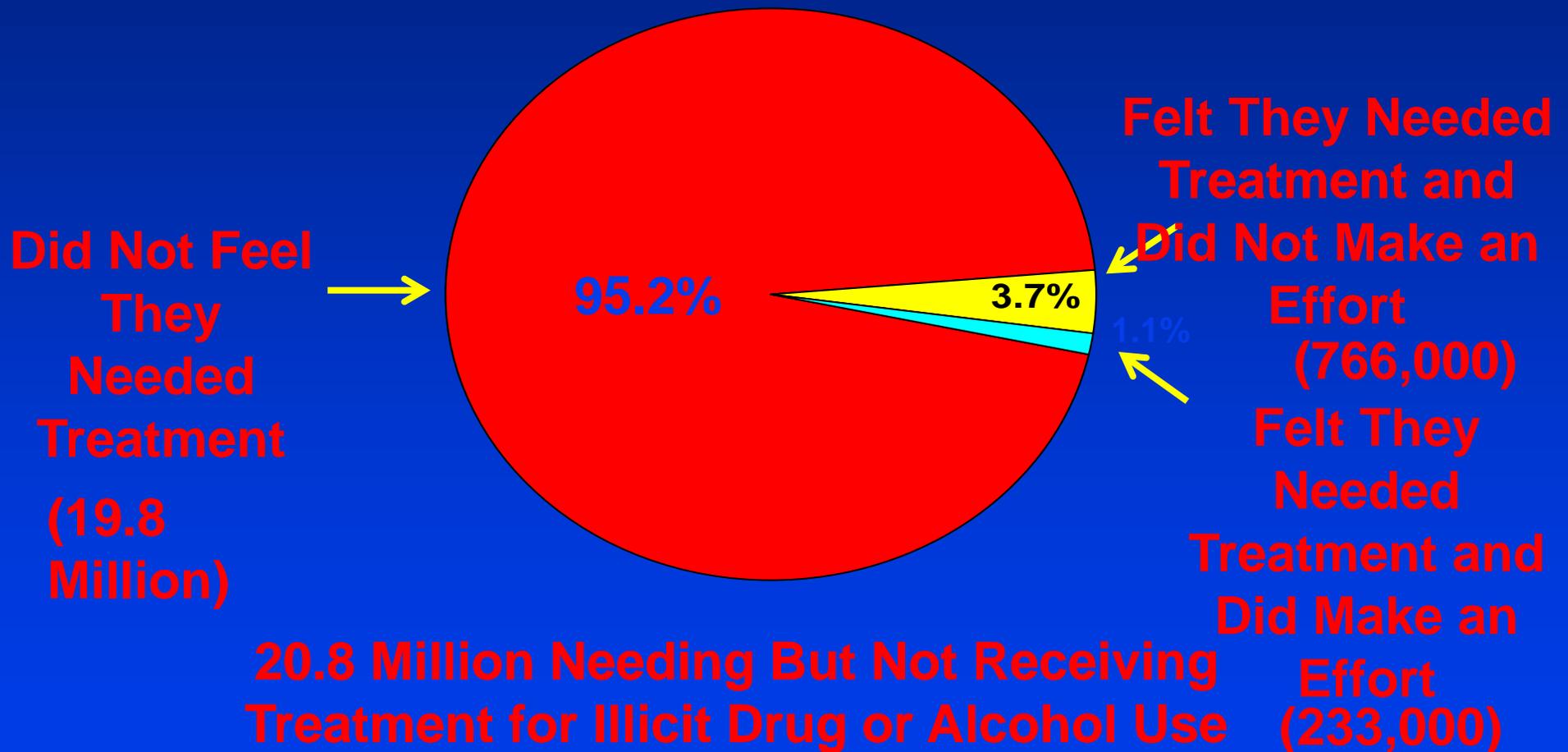
70% of Prescription Pain Relievers Used Non-Medically Come from Friends or Relatives

Note: Totals may not sum to 100% because of rounding or because suppressed estimates are not shown.
 Source: NSDUH 2008

Age Adjusted Death Rates for poisoning involving opioid analgesics: Comparison of States and US Rates: 2006



Past Year Perceived Need for and Effort Made to Receive Specialty Treatment among Persons Aged 12 or Older Needing But Not Receiving Treatment for Illicit Drug or Alcohol Use: 2008



Fatal Med Errors Increase

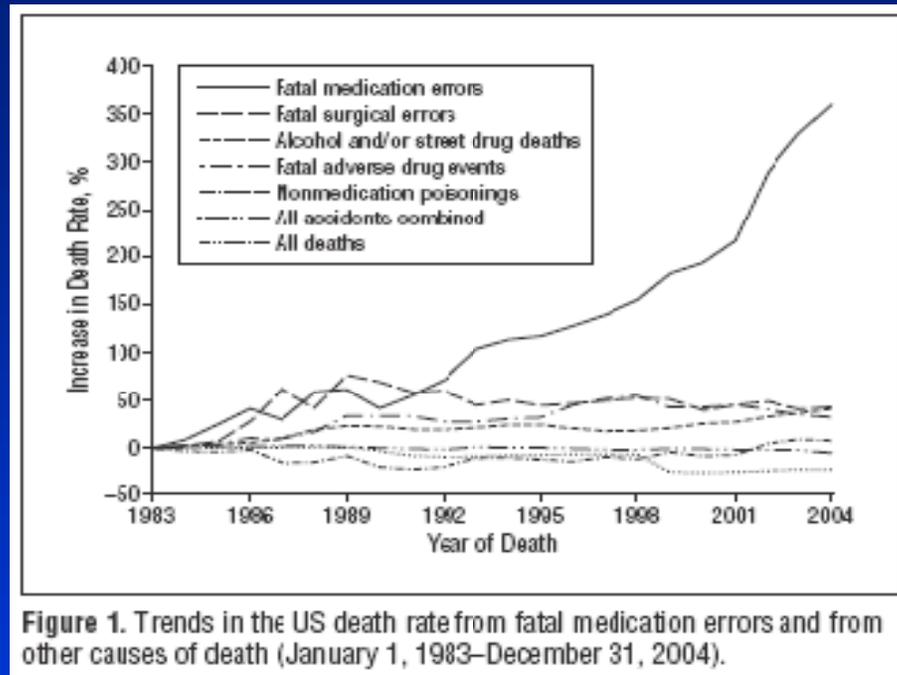
Domestic Use with Alcohol and/or Street Drugs

- Medication use has shifted
 - Past: Clinically orientated with inpatient, hospital care, supervised medication use
 - Current: Increased OTCs, increased domestic use, polypharmacy
- Consequences
 - Less professional oversight in domestic situation
 - Ease of concomitant use of EtOH and/or Street Drugs
 - Patient has increased responsibility to self-monitor drug consumption

FME death rate analysis

- Review of electronic death certificates
 - Jan 1, 1983 thru Dec 31, 2004
- FME definition: *Fatal Preventable Adverse Drug Events*
 - Listed as either primary or secondary cause of death
 - ICD-9/ICD-10 codes for FME
 - Includes Rx and OTC
 - Excludes alcohol and “*Street Drugs*”
 - Location Code
 - Home
 - If not coded “home” assigned to Non-home
- Four FME groups analyzed
 - Type 1: Home with EtOH/Street Drug
 - Type 2: Home without EtOH/Street Drug
 - Type 3: Non-Home with EtOH/Street Drug
 - Type 4: Non-Home without EtOH/Street Drug

Overall FME death rate accelerated



- Overall FME death rate increased by 360% (above; $p > 0.001$) with average age decreasing slightly (not shown)
- Figure 1 additionally demonstrates
 - Surgical errors, adverse effects of Medication and deaths from EtOH/"Street Drugs" show a slight increase
 - Other types of accidents (falls, drowning, poisoning, MVA) show a slight decrease

Upper Graph Fig 2a

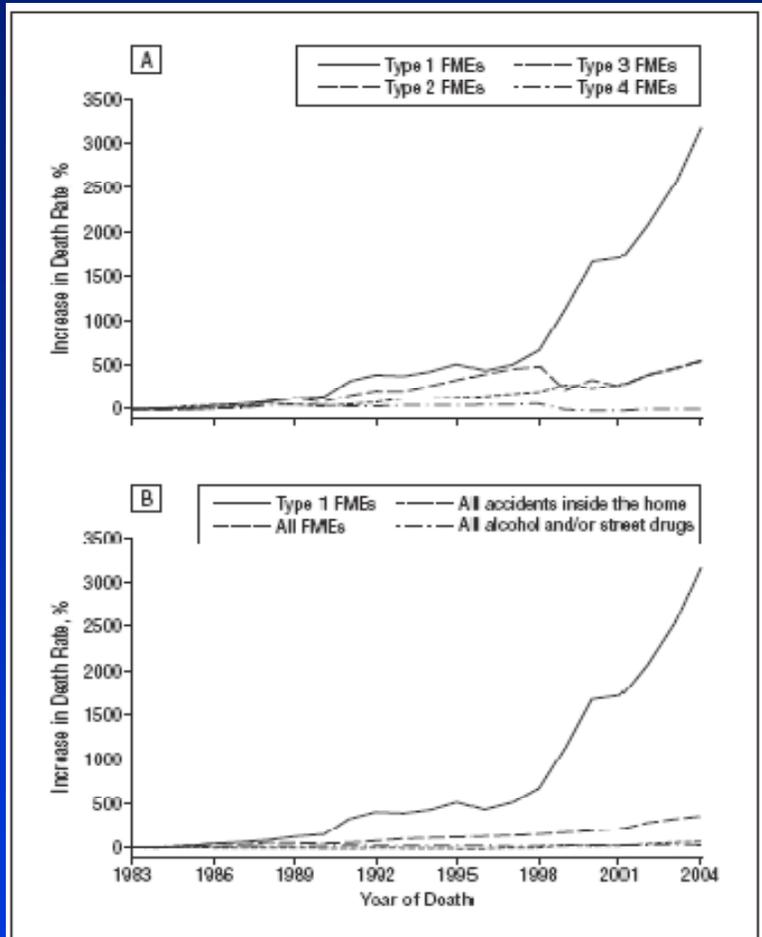


Figure 2. Trends in the US fatal medication error (FME) death rate by type of circumstance in which the FME occurs (A) and for various comparison groups (B) (January 1, 1983–December 31, 2004).

- Type 1 (*Home with “EtOH/Street”*) has increased by **3196%**
 - Steep and accelerating rate ($p < 0.001$)
- Type 2 (*Home without EtOH/Street*) and Type 3 (*Non-Home with EtOH/Street*) increased 564% and 555%, respectively
- Type 4 (*Non-Home without “EtOH/Street”*) only increased 5%

Lower Graph Fig 2b

- Type 1 has three components:
 - Fatal Medication Errors
 - Occurring at home
 - In conjunction with EtOH/Street drugs
- The 3 components graphed separately show slight increase
- Component combined (Type 1) shows steep increase by **3196%**

FME Death Rates Vary by Age

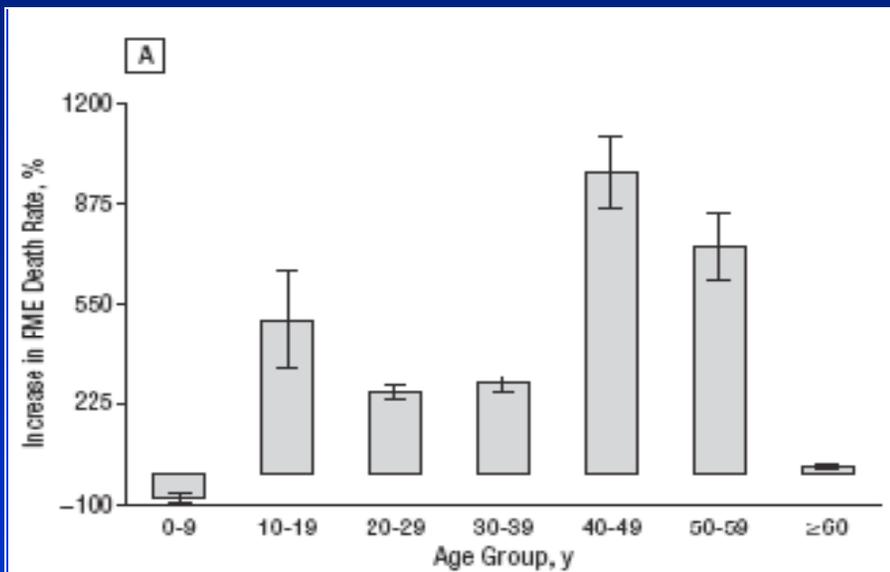


Fig 3a. Increase in US fatal medication error (FME) death rates by age group. 95% CI error bars

Figure 3a demonstrates an increase in fatal medication errors are greater in the teen and middle age.

- Study limitations:

- Official computerized death certificates do not provide much detail about FME
- Examination is only of severe (fatal) med errors
- No coding for medical institution location (restricted to home vs non-home)
- Does not document type of med error (type of medication, Rx vs OTC, type of street drug)

Pharmacist impact on domestic FME

- Self-administration of medication at home is least likely to have professional oversight
- Improve patient care by:
 - Evaluate patients capacity to manage their own medications
 - Educate patient about risks associated with their medications
 - Monitor patient performance

Pharmacist impact on EtOH/Street Drug related FME

- Steep increase in deaths related to combination of medication with alcohol and/or street drugs
- Improve patient care by:
 - Screening patients for use, misuse, or abuse of alcohol and/or street drugs
 - Taking extra precautions when prescribing/dispensing medicines with known dangerous interactions with alcohol and/or street drugs
 - Emphasizing to the patient the risks of mixing their medications with alcohol and/or street drugs

Pharmacist impact on EtOH/Street Drug related FME

- Medication reconciliation
 - Inpatient
 - Outpatient
- Written and oral patient education counseling
 - Regardless of distribution method:
 - counsel all new and altered prescriptions
 - Provide annual to quarterly review of all medications
 - Black box warnings on drug information sheets
 - Up-to-date patient education sheets

Role of Medications in the Treatment of Opioid Dependence

- Pharmacologic withdrawal (medically supervised taper)
- Maintenance Therapy
- Initially prevents withdrawal/diminishes drug craving until stable dose is achieved
- Blocks or attenuates the effects of abused opioids
- Increases retention rates in treatment
- Allows patient to participate in comprehensive rehabilitation
- Decreases infectious disease transmission rates

Public Expectations of Substance Abuse Treatment Interventions

- Safe, complete “detox”
- Reduced use of medical services
- Eliminate crime!
- Return to employment/ self support
- Eliminate family disruption
- No return to drug use
- “CURE”

Methadone Maintenance: The “Gold” Standard

- A Comprehensive Rehabilitation Program...
 - Improves overall survival
 - Increases retention in treatment
 - Decreases illicit opioid use
 - Decreases seroconversion of hepatitis and HIV
 - Normalizes immune and endocrine systems
 - Decreases criminal activity
 - Increases employment
 - In Perinatal Addiction: Improves birth outcomes

Medication choice: Methadone vs Suboxone

- Full agonist: Methadone
 - Easier induction
 - Less safety
- Oral liquid
 - Observed dose easy
 - Computerized dispensing easy
- Cheaper
- Tox screen easy
- Partial agonist-Buprenorphine
 - Induction easy for short acting, but less so for methadone
 - Safe for takehome
- Sublingual tablet
 - Observed dose takes longer
 - Manual pill counting
- Expensive
- Tox screen expensive

SUBOXONE®



SUBUTEX®

Rationale for opioid agonist medications

Biologic changes in the brain with opioid dependence

Provide insight into the chronic and relapsing nature of opioid dependence

Result from repeated exposure to opioids

Lead to neuronal adaptations in brain resulting in tolerance, physical dependence, craving

Form the basis for pharmacotherapies

Rationale for opioid agonist medications

Opioid agonist maintenance treatment

Targets biological factors perpetuating opioid administration

Prevents withdrawal

Reduces craving

Blocks or attenuates euphoric effects of exogenous opioids

Rationale for opioid agonist medications

Advantages of opioid agonist medication over heroin

Non-parenteral administration

Known composition

Gradual onset and offset

Long-acting

Mildly reinforcing

Medically supervised

Purpose of this curriculum and disclosure

This curriculum includes the core information unique to buprenorphine and its use in the pharmacological management of opioid dependence, as well as a comprehensive overview of treatment for opioid dependence. It does not describe a standard of care. Treatment decisions should be made based upon the individual patient and the level of available resources. The standard of care constantly evolves and this course will review the current status. Physicians who use buprenorphine are responsible for their decisions and this course, the AOAAM and CSAT do not assume any patient care responsibilities.

Purpose of this curriculum

Office-based treatment for opioid dependence is being developed to address several needs in accordance with public health objectives:

1. to increase access to treatment
2. to offer treatment to patients outside the traditional methadone clinic system
3. to mainstream the treatment of opioid dependence by coordinating it with treatment of other medical conditions

Summary

The need for opioid dependence treatment far exceeds what is currently available; office-based buprenorphine is intended to address unmet treatment need, and to place it in the mainstream of medical care

This curriculum provides content to aid the clinician preparing to treat opioid dependent patients in the office.

Primary Opioid of Abuse in 30 Days Prior to Treatment

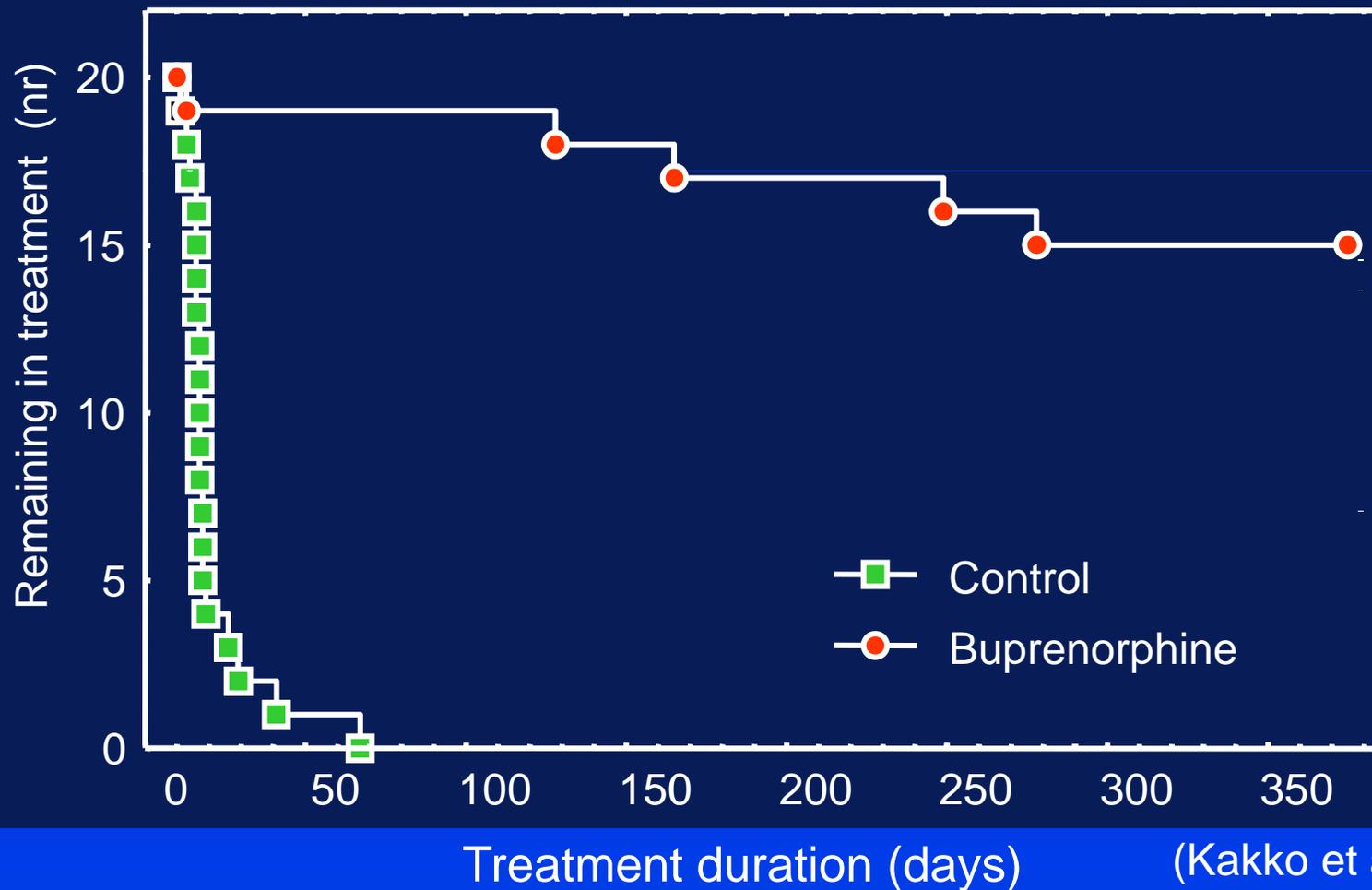
<u>Primary Opioid of Use*</u>	<u>Frequency</u>	<u>% Sample</u>
Heroin	174	40%
Oxycodone	124	29%
Hydrocodone	74	17%
Street Methadone	18	4%
Multiple Rx Meds	10	2%
Hydromorphone	9	2%
None Specified	8	2%
Morphine	5	1%
Rx Methadone	4	1%
Fentanyl	3	1%
Other	5	1%

60% reported primarily using opioids other than heroin in the 30 days prior to treatment.

*The primary drug of abuse was determined by an item asking for the opioid used most often in the last 30 days. The primary drug of abuse for 9% of the sample in a controlled environment such as jail or inpatient treatment in the 30 days prior to treatment was determined by the drug with the longest lifetime use.

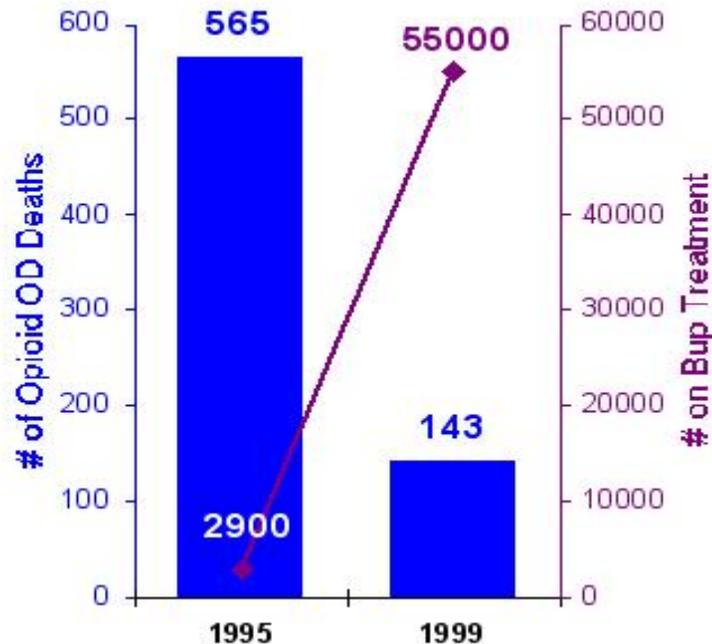
Other = Propoxyphene, Meperidine, Tramadol, Codeine, Opium

Buprenorphine Maintenance/Withdrawal: Retention



(Kakko et al., 2003)

Opioid Overdose Deaths Decline 79% After Introduction of Buprenorphine in France

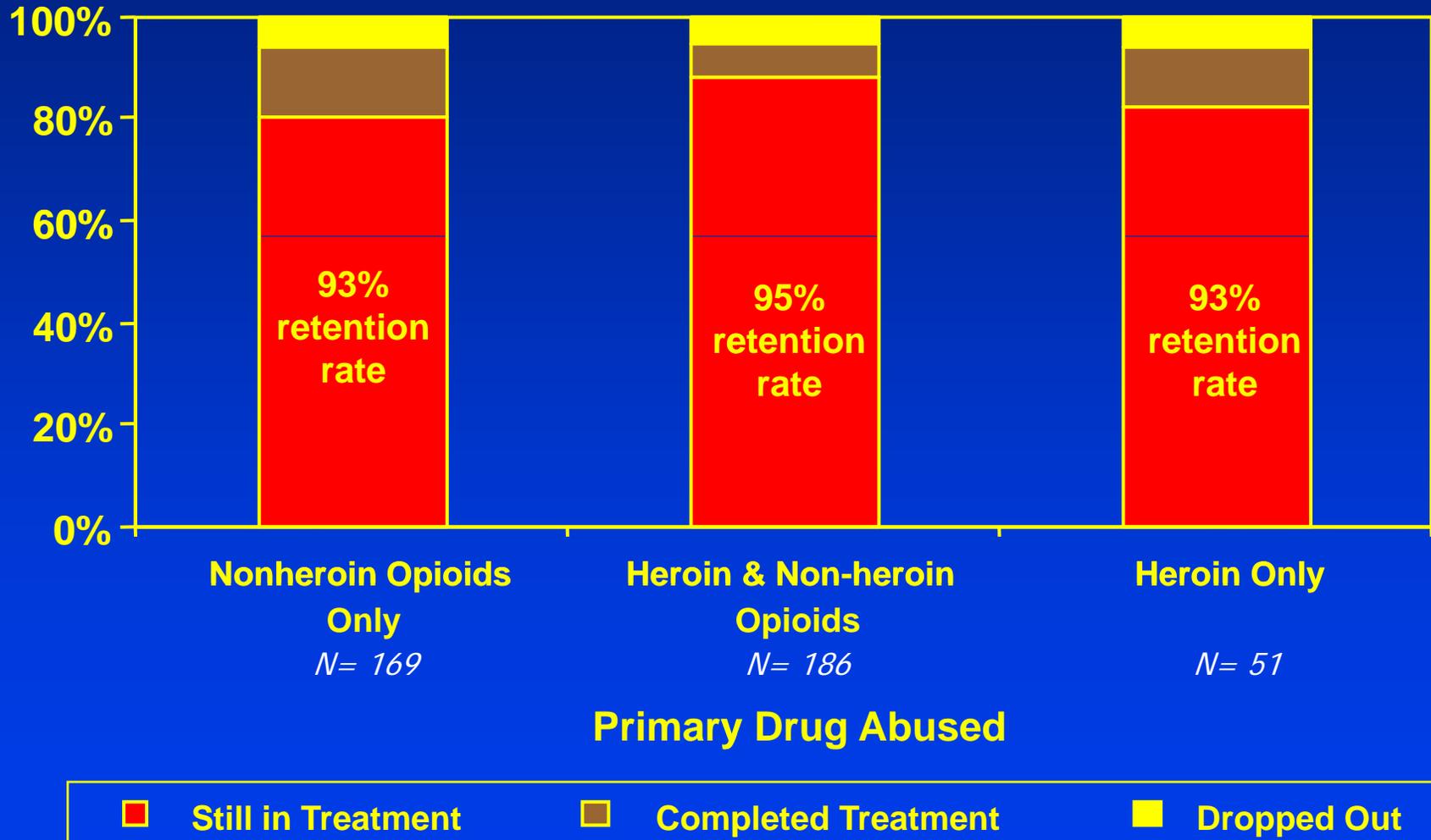


Ling et al. J Subst Abuse Treat 2002;23:87-92.
Auriacombe et al. JAMA 2001;285:45.

- French primary care MDs permitted to prescribe without special education or licensing since 1995
- Extensive certification requirements and practice limits continue in force in the U.S.

30 Day BUP Treatment Outcomes: Treatment Retention at 30 Days

(Self-Reported)



Overview to the
Drug Addiction Treatment Act of 2000 –
An Amendment
to the Controlled Substances Act

(October, 2000 signed into law by President
Clinton)

(amended by President Bush in 2005 and 2006)

This section provides an overview to the legislative changes that allow for office-based treatment of opioid dependence with controlled substances (i.e., buprenorphine).

It is important for the practitioner to understand these changes, since the clinician will be required to comply with them and to notify the Secretary of Health and Human Services (HHS) before beginning to use buprenorphine in the office setting for the treatment of opioid dependence.

Amended Controlled Substances Act (CSA)

Revision in legislation allows practitioner to prescribe narcotic drugs in schedule III, IV, V, or combinations of such drugs, for the treatment of opioid dependence

Drugs and practitioner must meet certain requirements

Amended Controlled Substances Act

Practitioner requirements:

“Qualifying physician”

Has capacity to refer patients for appropriate counseling and ancillary services

No more than 30 patients (individual practice) by revision signed into law by President Bush August 2005 and on December 29, 2006 President Bush approved a limit of 100 for physicians with one year of waiver.

Amended Controlled Substances Act

“Qualifying physician”:

A licensed physician who meets one or more of the following:

1. Board certified in Addiction Psychiatry
2. Certified in Addiction Medicine by ASAM
3. Certified in Addiction Medicine by AOA
4. Has completed 8 hours training provided by ASAM, AAAP, AOA, APA. This course qualifies.

Amended Controlled Substances Act

Practitioner:

Violations will put the physician's DEA registration at risk

Amended Controlled Substances Act

Narcotic drug:

Approved by the FDA for use in maintenance or detoxification treatment of opioid dependence

Schedule III, IV, or V

Drugs or combinations of drugs

Amended Controlled Substances Act

Methadone treatment programs:

Practitioner can also prescribe these drugs (i.e., schedule III, IV, or V; approved for maintenance or detoxification treatment) under a methadone program registration

No limit on number of patients when used in the methadone treatment program setting (OTP)

Summary

Legislation sets up relatively minor requirements for a physician to provide office-based buprenorphine treatment of opioid dependence

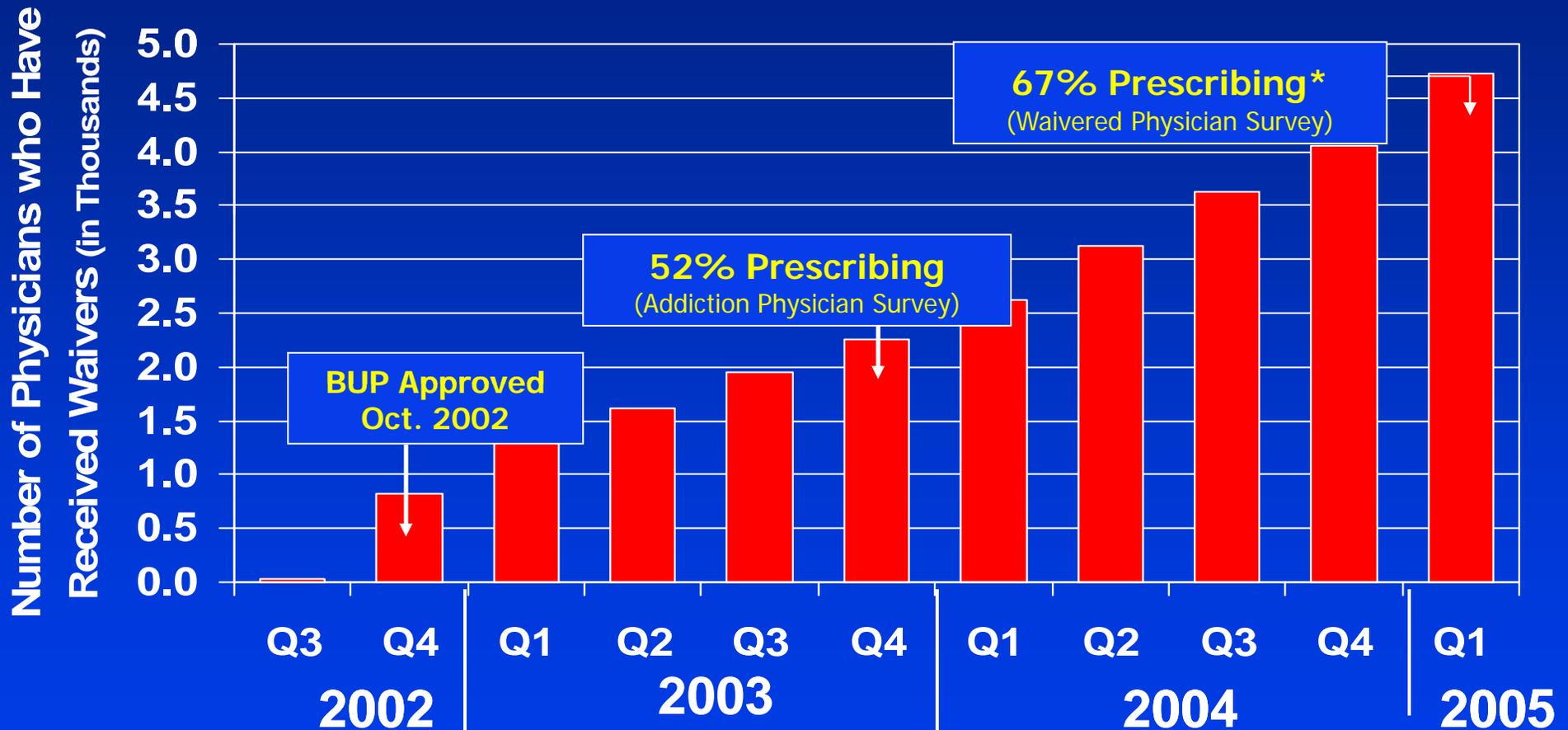
However, if difficulties arise with buprenorphine (e.g., diversion, misuse), it will be relatively easy for government agencies to end office-based treatment of opioid dependence with buprenorphine

Important for physicians to know and abide by the rules – not risk losing this valuable treatment option

Physician Clinical Support System (PCSS)

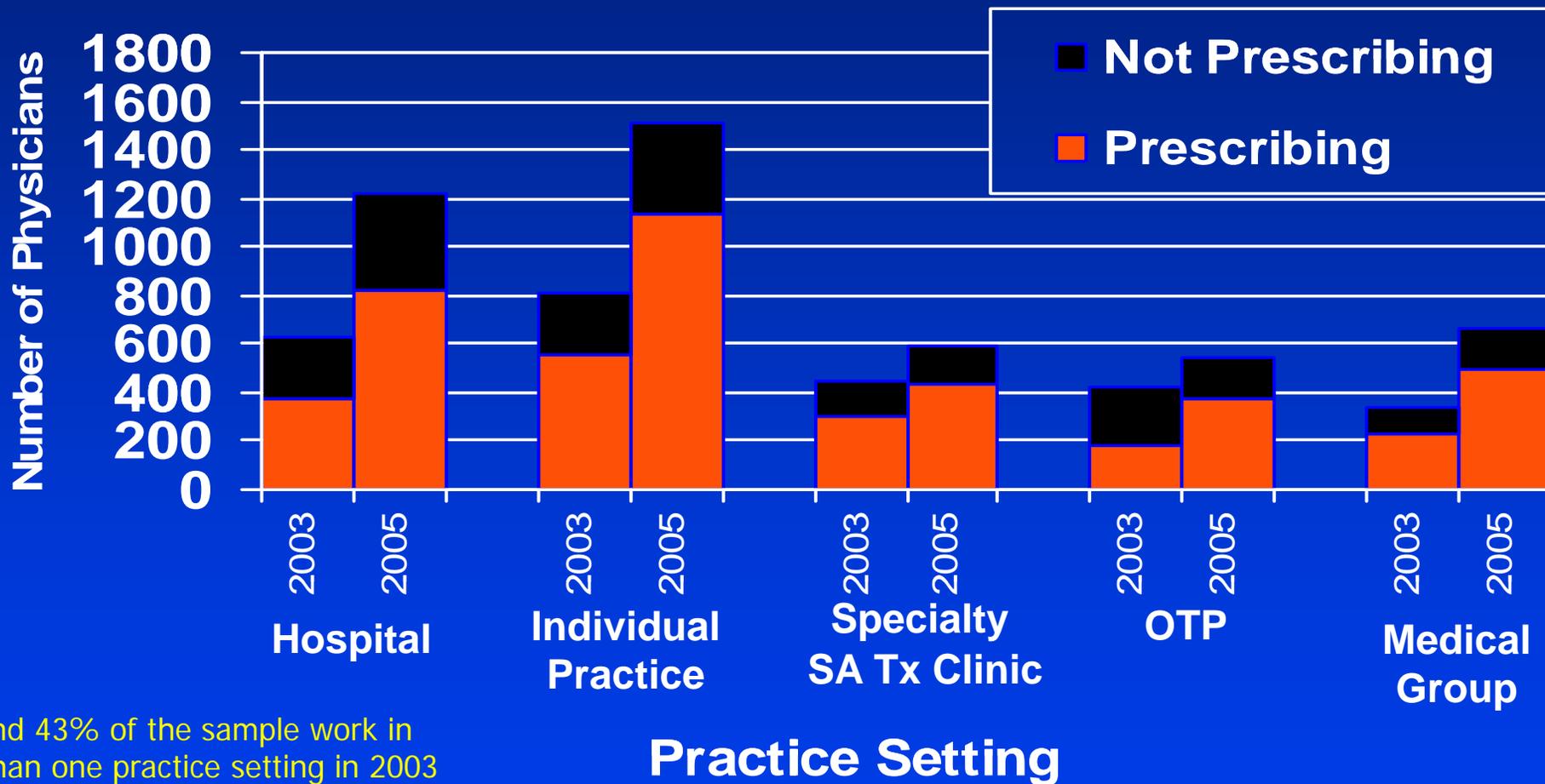
- A national mentoring network for physicians treating opioid dependence with buprenorphine
- To get involved or for assistance, either:
 - **Fill out Registration Form located in the syllabus**
 - **Pick up a PCSS brochure at the registration desk**
 - **Call: 1-877-630-8812**
 - **Email: PCSSproject@asam.org**
 - **Go to the website: www.PCSSmentor.org**
- ❖ Your information will be automatically provided to the PCSS if you approve. In order to best match you to a mentor please complete the form in its entirety. If you do not wish your information to be provided to the PCSS please indicate this on the Participant Registration form in your syllabus.

Number of Waivered Physicians Estimated Number Prescribing



* An estimated 2,353 physicians were providing treatment under the Waiver Program in early 2005

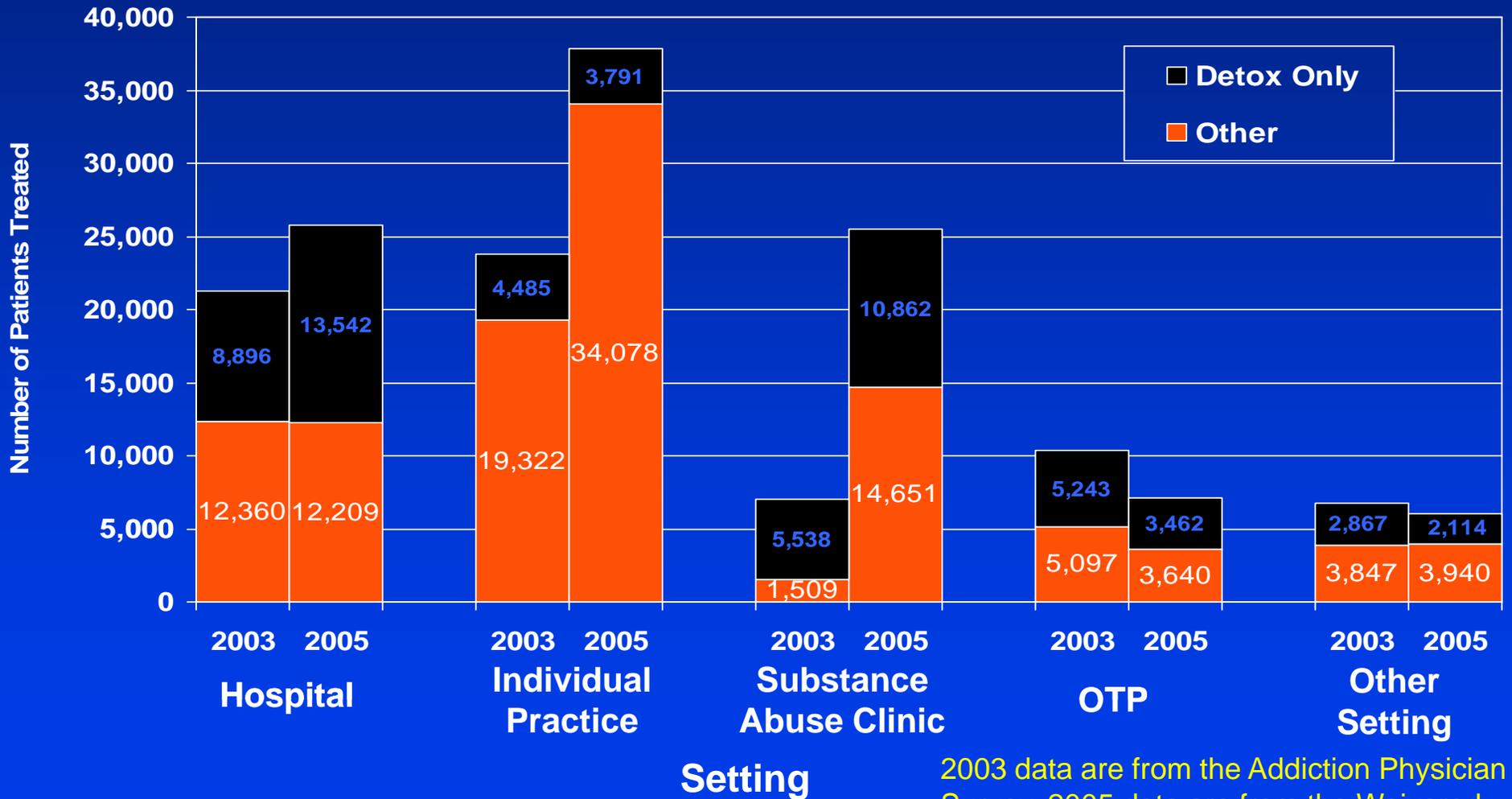
Practice Setting of Waivered Physicians



40% and 43% of the sample work in more than one practice setting in 2003 and 2005 respectively

2003 data are from the Addiction Physician Survey, 2005 data are from the Waivered Physician Survey

Patients Inducted by Setting & Treatment Offered



2003 data are from the Addiction Physician Survey, 2005 data are from the Waivered Physician Survey

2004 DAWN REPORT

- 2004 the Drug Abuse Warning Network data estimated 495,732 emergency department visits for nonmedical use of prescription medications, of which 236 (0.05%) were reports of nonmedical use of buprenorphine and or the buprenorphine/naloxone combination.
- During this same time, there were no reports of buprenorphine associated with suicide attempts.

DIVERSION ISSUES OF BUPRENORPHINE

- T Cicero, JAMA, 2006, provided information demonstrating low levels of buprenorphine diversion.
- Finland report of the street value of buprenorphine/naloxone, compared to buprenorphine mono in Finland, once buprenorphine/naloxone was introduced due to buprenorphine mono formulation abuse.
- 80% of Finnish IV users said that the IV buprenorphine/naloxone experience was "bad". The street value of buprenorphine/naloxone was less than 50% of buprenorphine mono formulation.

Buprenorphine 2001-7

John Renner MD Feb 2008 Buprenorphine Summit

- 4.1 million prescriptions
- 585,000 patients treated
- 30% Detox
- 70% Maintenance
- 16,232 Physicians trained
- 13,318 Waivered

Emerging Issues

- ED visits 2003 (1) vs 2007 (Q1-3) 368
- Compared to methadone (6000) and oxycodone (9000)
- Toxic exposures higher in children BUP 2% vs methadone, oxycodone or heroin 0.5%
- 27% of all reported toxic exposures to BUP were under the age of 6 vs methadone 7% and oxycodone 8%
- Six deaths in 2006-7 all with EtOH or sed hypnotics

Baltimore Sun Articles

- 1-17-08 ...October, its consultants found that half the doctors they surveyed were aware of an illegal trade in Buprenorphine and their numbers have been climbing”
- 1-25-08 “..addicts using the drug on the street mostly say they do so to avoid withdrawal, not to get high.”

RADARS Dasgupta Feb 2008 Bup Summit

- Governmental non-profit operation
- Rocky Mountain Poison and Drug Center
- Reckitt Benckiser did support the Pediatric data analysis in an educational grant
- 11 of 60 US Centers (18%) 2003 Q1
- 43 of 60 US Centers (72%) 2007 Q2

RADARS BUPRENORPHINE ABUSE

- 125 cases were reviewed for abuse per methodology
- Mean age 27
- Male 65%
- 7% chronic buprenorphine abuse
- 34% ingestion, 28% parenteral, 18% inhalation

RADARS Mortality Data

- “associated medical outcome”
- 2003 to 2007Q3 data set
- Not causally linked to death
- 5 deaths related to BUP with intentional use/abuse No PEDS Deaths
- Methadone has 126 deaths in the same time frame
- 3/5, 60% were intentional self harm

RADARS Peds Data 2003-6

	BUP N=176	Hydrocodone N=6003	Fentanyl N=123	Oxycodone N=2036
Age (SD)	2.1 (0.9)	2.3 (1.2)	2.0 (1.2)	2.1 (1.1)
Male (%)	99 (56.3)	3232 (53.9)	64 (52.5)	1081 (53.5)
Site Home %	169 (96)	5581 (93)	111 (90.2)	1821 (89.4)
Ingest %	174 (99.4)	5993 (99.8)	77 (62.6)	2020 (99.1)