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# **Clinical Aspects of Risk Management in Opioid Prescribing**

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# Disclosures

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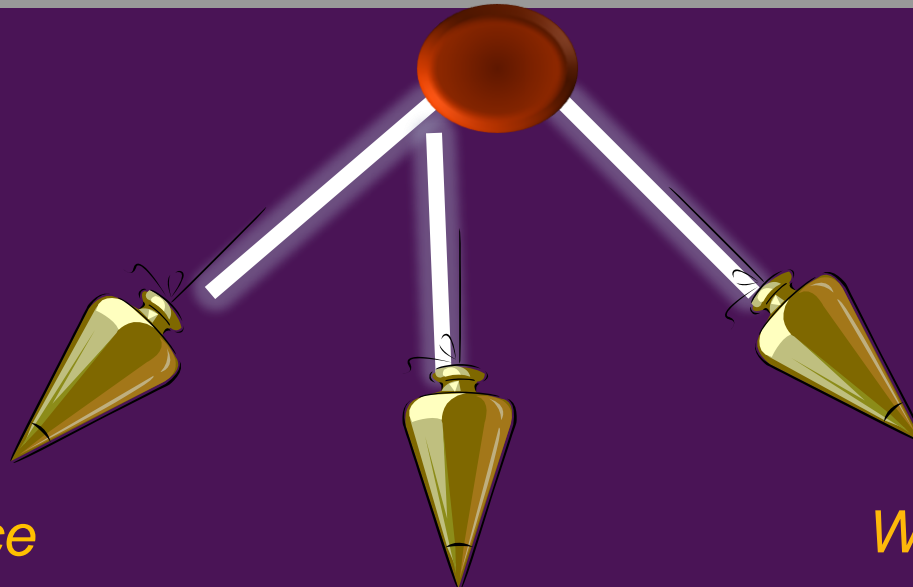
- Speaker and Consultant (Honoraria)
  - Cephalon, Pfizer (King), Ameritox, Millenium, Quest
- Consultant (Honoraria)
  - Purdue, Pharmacofore, Pricara

# Disclosures

- As a psychologist, I feel that in the interest of truly full disclosure I should tell you that I also had a highly conflicted relationship with:



# The Opioid Pendulum



## *Avoidance*

Even dying people  
at risk of addiction

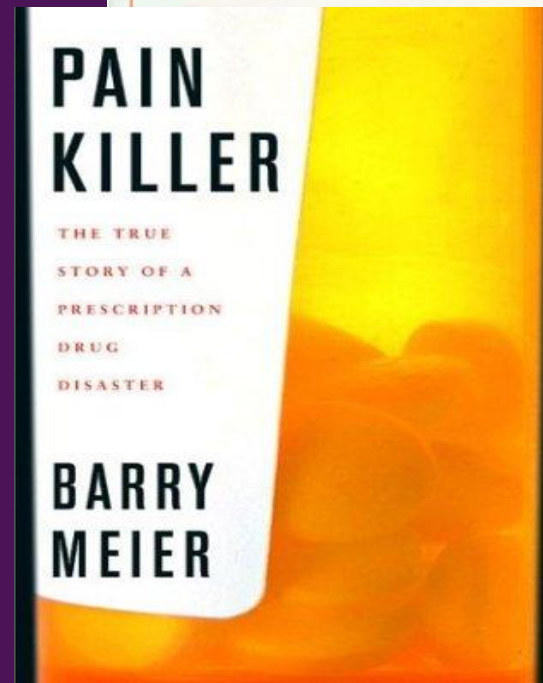
## *Balance*

Risk stratification and  
principles of addiction  
medicine applied to  
opioid prescribing  
regardless of the pain  
problem at hand

## *Widespread Use*

Opiophobia must go

# The OxyContin Story



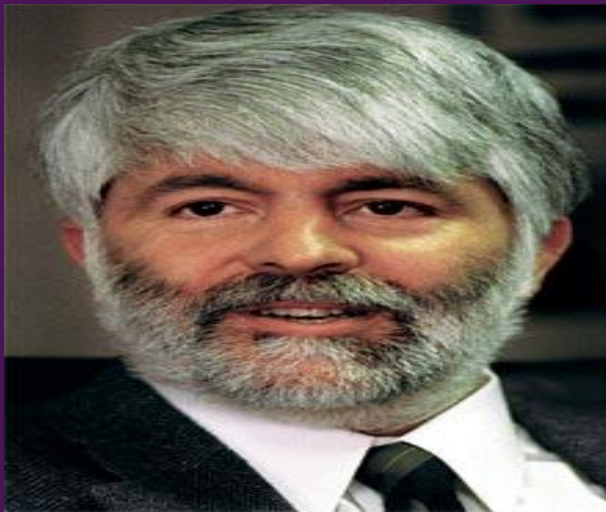
# Base Rates of Addiction/Abuse

- 6-10% Illicit drugs
- 15% Alcohol
- 25% Nicotine
- 33% Have experimented with illicit drugs at least once
  
- 50%



(Colliver & Kopstein, 1991; Gfroerer et al, 1992; Regier et al, 1984)

# Doctors on Trial: Pain Docs or Drug Dealers?



**1. DISTRIBUTION SYSTEM**  
(lawful distribution)

**2. PRIMARY DIVERSION**  
(unlawful; supplies some abusers and re-distribution)

**3. REDISTRIBUTION**  
(Layers of re- distribution; illicit industry)

**4. NON MEDICAL USES**

**5. MEASUREMENT OF IMPACTS**

Wholesale  
Retail  
Ultimate

Manufacturers  
Distributors

(Common Carriers)  
•Pharmacies  
•Hospitals/Clinics  
•Internet w/Rx  
•Practitioners  
✓Prescribers  
✓Dispensers  
•Nursing homes  
•Hospices

(Prescribed medication)  
Patients  
(Lawful medical use)

▪Theft from manufacturers and distributors\*

▪Theft in transit \*

•Theft from hospitals\*  
▪Pharmacies/robbery\*  
▪Employee/customer Pilferage \*

▪Internet sales without Rx

▪International smuggling

▪Theft of Rx/forgery

•Script docs/pill mills  
•Inappropriate prescribing  
•Doctor shopping

•Patient sells or gives  
•Theft from home  
•Theft from patient  
•Improper disposal

Abusers, addicts, impaired health care professionals use what they steal

Unprescribed drugs  
Dealers

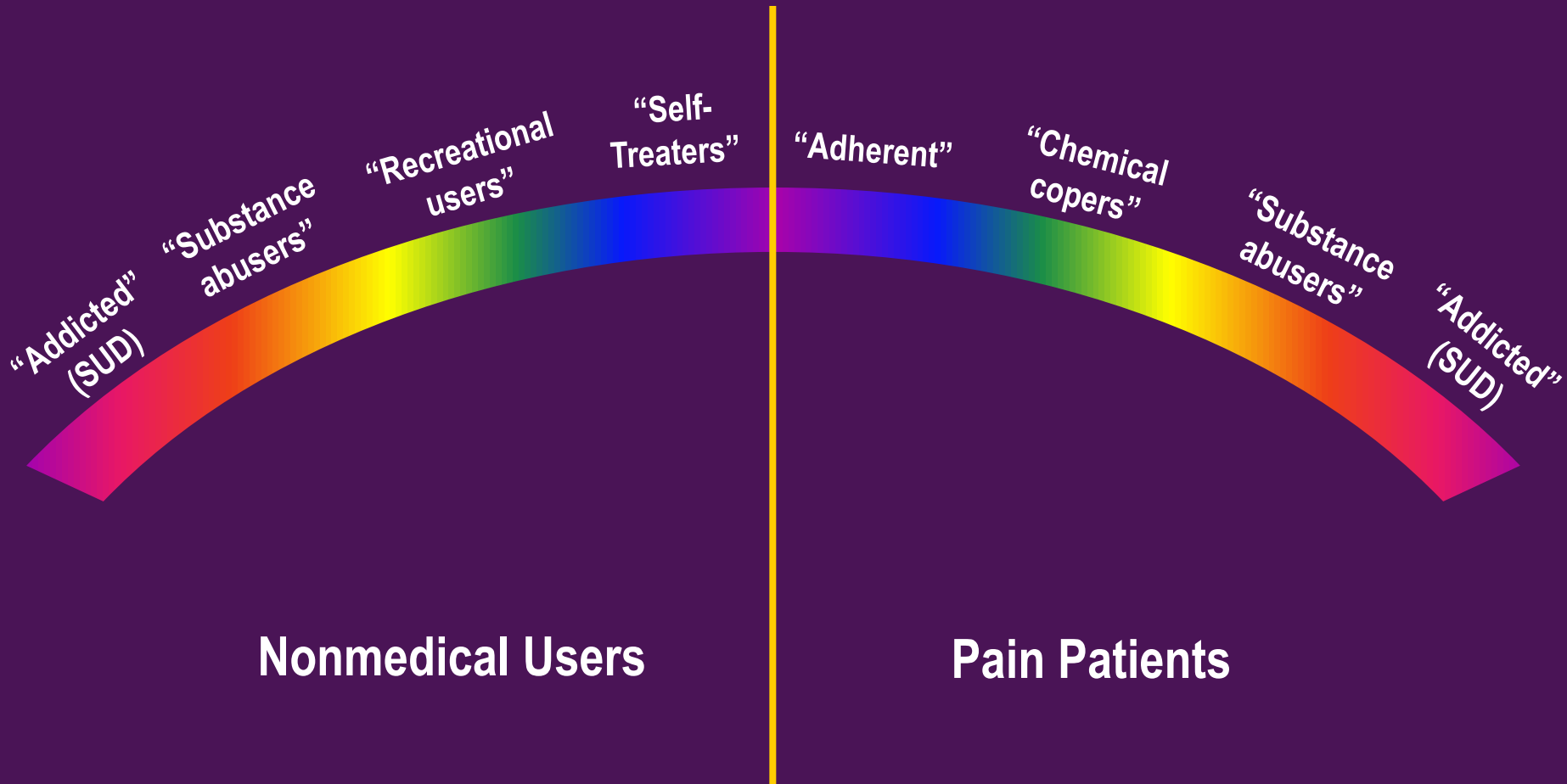
Prescribed medications  
Peers  
Relatives

All Nonmedical users:  
Used for reward, high, recreation; compulsive use due to addiction; treatment of withdrawal; Self medication for mood, sleep, pain

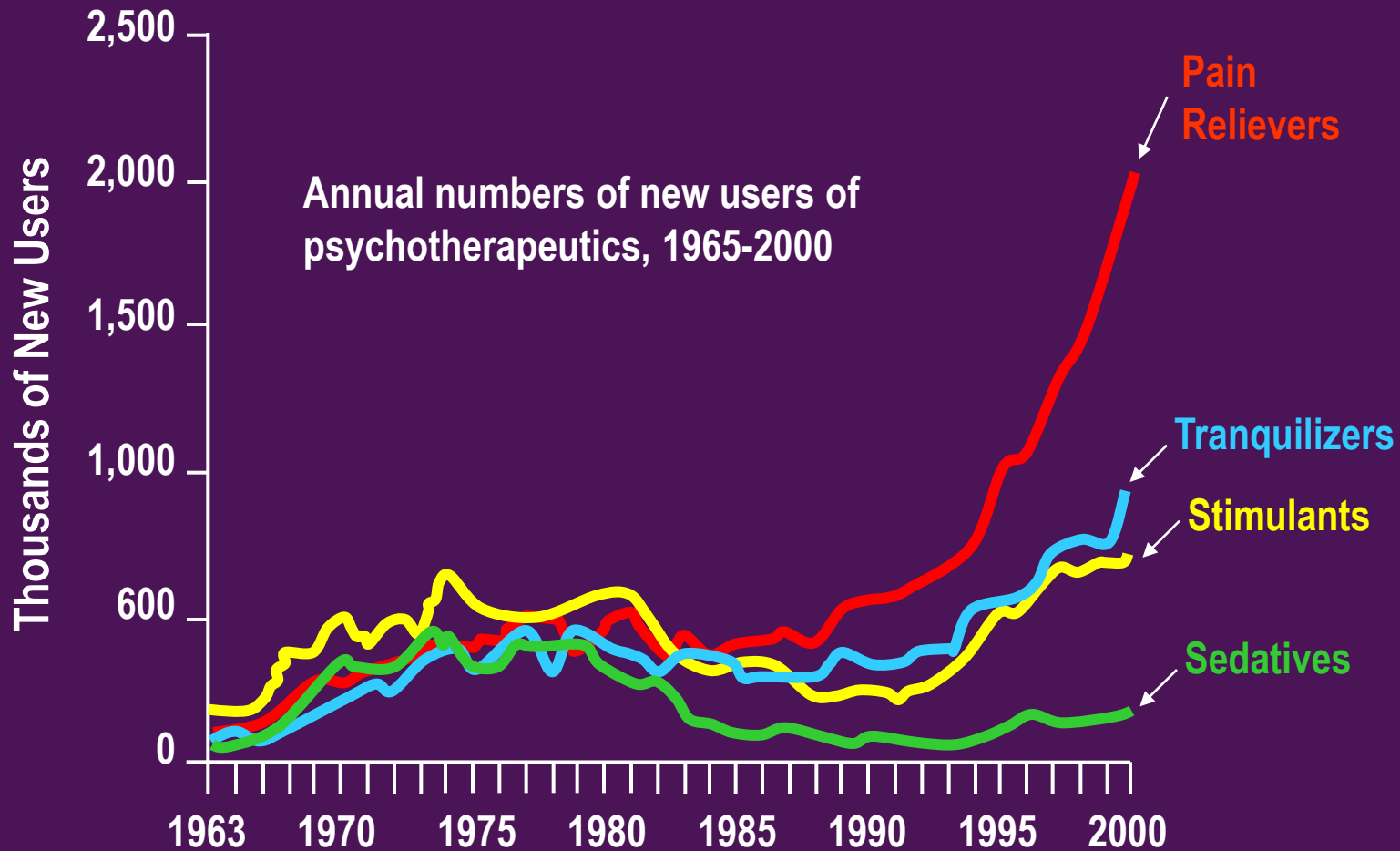
- Surveys
  - ✓ Postmarketing
  - ✓ Nonmedical use
    - ✓ Abuse
    - ✓ Addiction
  - ✓ Addiction treatment
  - ✓ Key informants
  - ✓ Pain patients
- Reporting systems
  - ✓ Adverse events
  - ✓ Accident/Poisoning
  - ✓ Emergency Dept
  - ✓ Internet surveillance
  - ✓ Medical Examiner
  - ✓ Treatment episodes
    - ✓ Arrests
  - ✓ Literature
  - ✓ Misuse, abuse, addiction
  - ✓ Self medication

**Diversion Schematic: Lawful distribution; primary diversion; layers of redistribution, non medical uses; measurement of impacts**

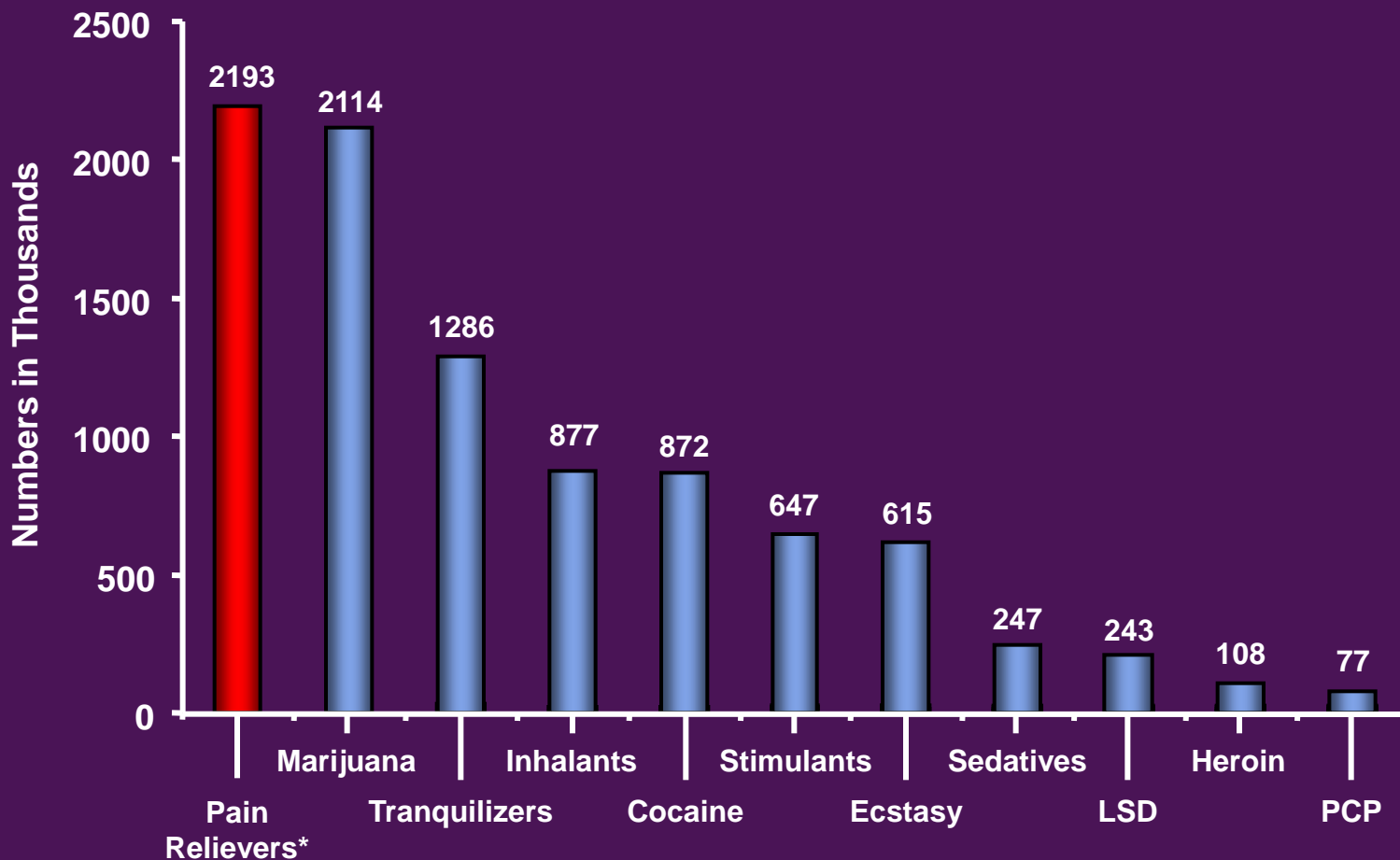
# Population of Rx Opioid Users Is Heterogeneous



# Use of Psychotherapeutic Agents



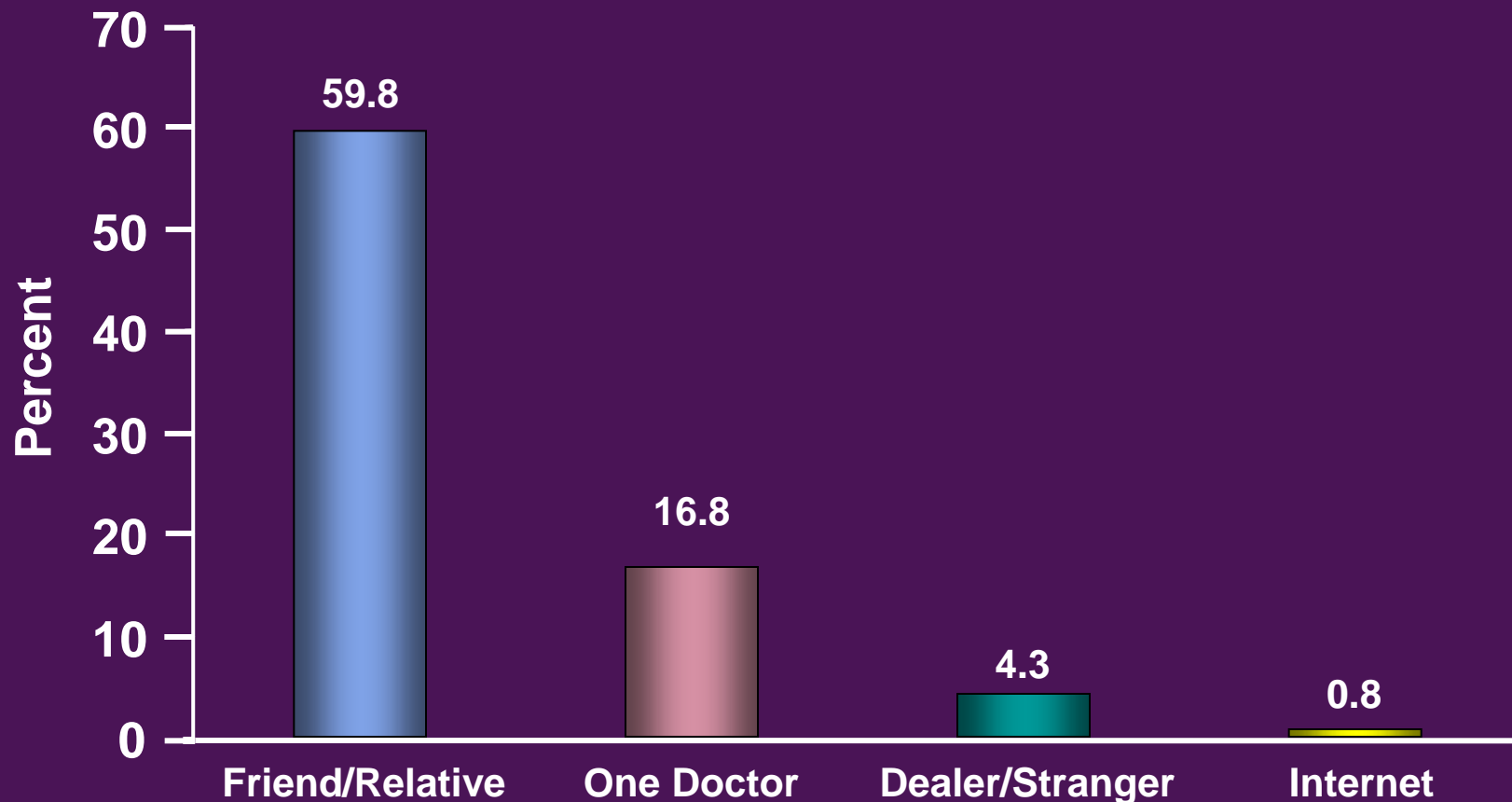
# New Illicit Drug Use in the United States: 2005



\*526,000 new nonmedical users of OxyContin®.

SAMHSA. *Results From the 2005 National Survey on Drug Use and Health*. DHHS Publication No. SMA 06-4194, 2006.

# Pain Relievers Obtained for Nonmedical Use: Sources Reported by Users\*

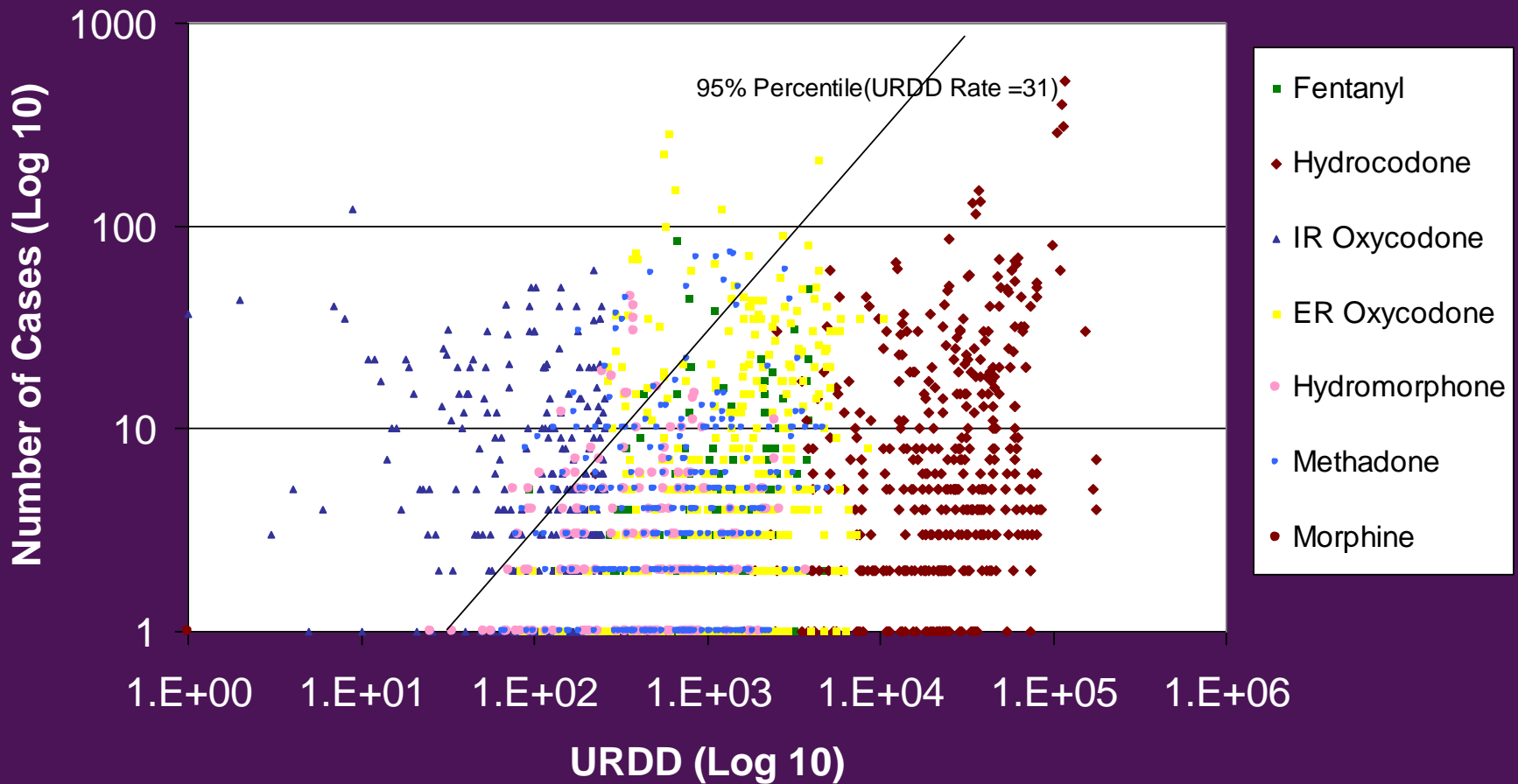


\*Source of drugs for the most recent nonmedical use of pain relievers reported by persons aged 12 or older in the United States 2005.

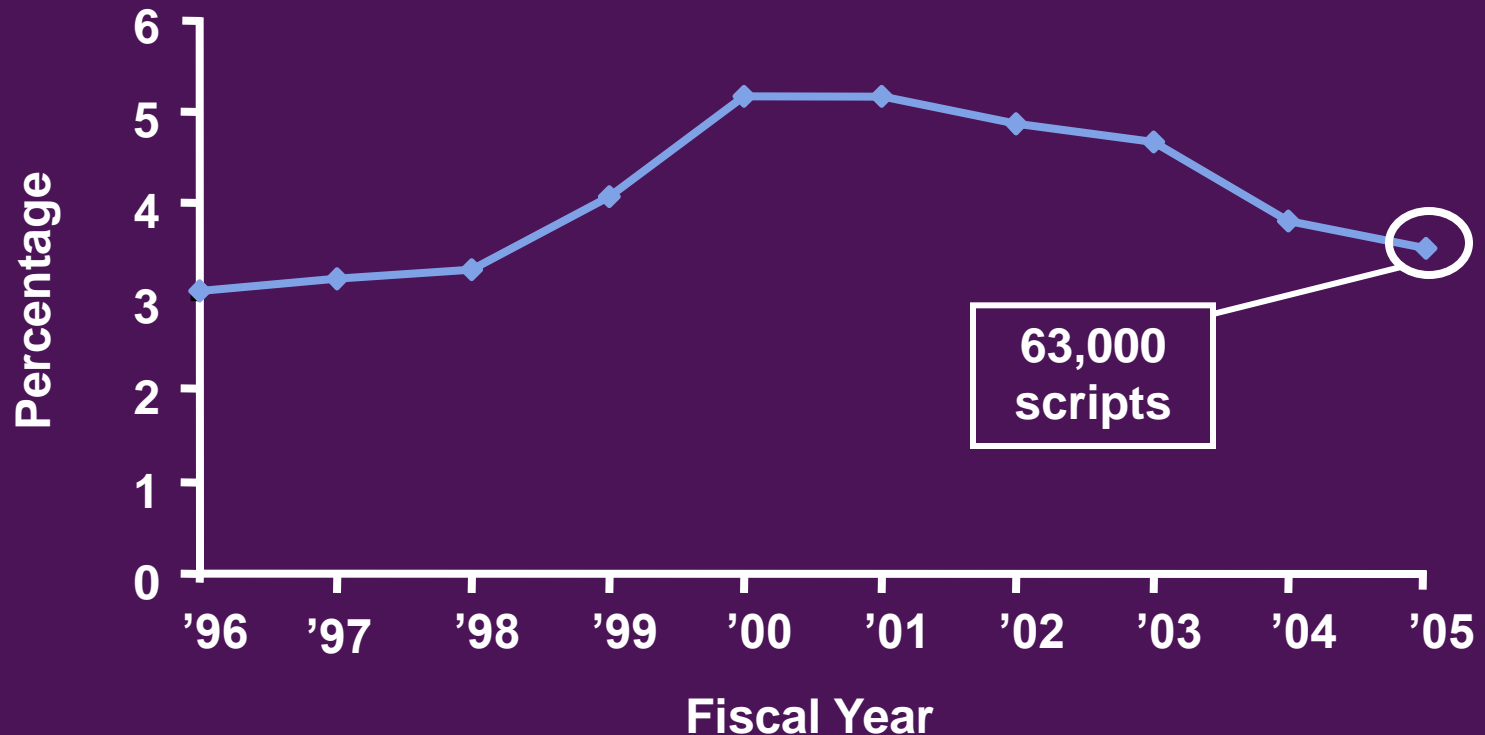
SAMHSA. *Results From the 2005 National Survey on Drug Use and Health*. DHHS Publication No. SMA 06-4194, 2006.

# Relationship Between Use & Abuse

RADARS™ Data - Key Informant Network (URDD>0)  
2006Q4 to 2007Q3



# Estimated Percentage of Schedule II Opioid Prescriptions Dispensed to Individuals Showing Questionable Activity\* by Fiscal Year



\*Questionable Activity = obtained Schedule II opioid prescriptions from  $\geq 4$  pharmacies and  $\geq 4$  physicians during the specified year.

# The Four “A’s” of Pain Treatment Outcomes

- ❑ Analgesia (pain relief)
- ❑ Activities of Daily Living (psychosocial functioning)
- ❑ Adverse effects (side effects)
- ❑ Aberrant drug-taking (addiction-related outcomes)

# My Dog on Opioids



# Aberrant Drug-taking Behaviors: The Model

- Probably more predictive
  - Selling prescription drugs
  - Prescription forgery
  - Stealing or borrowing another patient's drugs
  - Injecting oral formulation
  - Obtaining prescription drugs from non-medical sources
  - Concurrent abuse of related illicit drugs
  - Multiple unsanctioned dose escalations
  - Recurrent prescription losses
- Probably less predictive
  - Aggressive complaining about need for higher doses
  - Drug hoarding during periods of reduced symptoms
  - Requesting specific drugs
  - Acquisition of similar drugs from other medical sources
  - Unsanctioned dose escalation 1–2 times
  - Unapproved use of the drug to treat another symptom
  - Reporting psychic effects not intended by the clinician

# Differential Diagnosis: Aberrant Drug-Taking Attitudes & Behavior

- ❑ Addiction
  - *Compton*
  - *Fleming*
- ❑ Pseudo-addiction
  - *Elander*
- ❑ Other psychiatric diagnosis
  - Organic mental syndrome
  - Personality disorder
  - Chemical coping
  - Depression/anxiety/situational stressors
    - *Butler*
- ❑ Criminal intent
  - *Katz*
  - *Jung & Reidenberg*

# Management of Risk Is a “Package Deal”

- Screening & risk stratification
- Use of PMP data
- Compliance monitoring
  - Urine screening
  - Pill/patch counts
- Education re drug storage & sharing
- Psychotherapy & highly “structured” approaches
- Abuse-deterrent formulations



# Assessment of Addiction Risk

- ❑ Measures for screening for addiction risk
  - STAR/SISAP
  - CAGE AIDD
  - Opioid Risk Tool (Emerging Solutions in Pain)
  - SOAPP (see [painedu.org](http://painedu.org))
- ❑ Psychiatric interview assessment of risk
  - Chemical
  - Psychiatric
  - Social/Familial
  - Genetic
  - Spiritual

# What Kind of a Rat am I?

<b>Fisher 344</b>	<b>Abstinence</b>	<b>drug rejecting</b>
<b>Lewis</b>	<b>Polysubstance Abuse</b>	<b>drug seeking</b>
<b>Sprague-Dawley</b>	<b>Average</b>	<b>drug neutral</b>



With Permission: Lynn Webster M.D., Lifetree Clinical Research and Pain Clinic  
Salt Lake City, Utah.

# Opioid Risk Tool (ORT)

Mark each box that applies:

1. Family history of substance abuse

	Female	Male
Alcohol	<input type="checkbox"/> 1	<input type="checkbox"/> 3
Illegal drugs	<input type="checkbox"/> 2	<input type="checkbox"/> 3
Prescription drugs	<input type="checkbox"/> 4	<input type="checkbox"/> 4

2. Personal history of substance abuse

Alcohol	<input type="checkbox"/> 3	<input type="checkbox"/> 3
Illegal drugs	<input type="checkbox"/> 4	<input type="checkbox"/> 4
Prescription drugs	<input type="checkbox"/> 5	<input type="checkbox"/> 5

3. Age (mark box if between 16-45 years)

<input type="checkbox"/> 1	<input type="checkbox"/> 1
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4. History of preadolescent sexual abuse

<input type="checkbox"/> 3	<input type="checkbox"/> 0
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5. Psychological disease

ADO, OCD, bipolar, schizophrenia	<input type="checkbox"/> 2	<input type="checkbox"/> 2
Depression	<input type="checkbox"/> 1	<input type="checkbox"/> 1

Scoring totals:

\_\_\_\_\_

## Administration

- On initial visit
- Prior to opioid therapy

## Scoring

- 0-3: low risk (6%)
- 4-7: moderate risk (28%)
- $\geq 8$ : high risk (> 90%)

# How Do Different Risk Measures Compare?

- A recent study at a pain practice in Tennessee
  - A retrospective study of discharged patients
  - N= 48
  - Risk rating of each patient with all four measures:
    - Clinical semi-structured interview by a psychologist
    - DIRE (Belgrade et al, 2006)
    - ORT (Webster & Webster, 2005)
    - SOAPP (Butler et al, 2004)
  - “Medium” or “High” risk rating = Accurate prediction
  - This assesses measure sensitivity (not specificity)

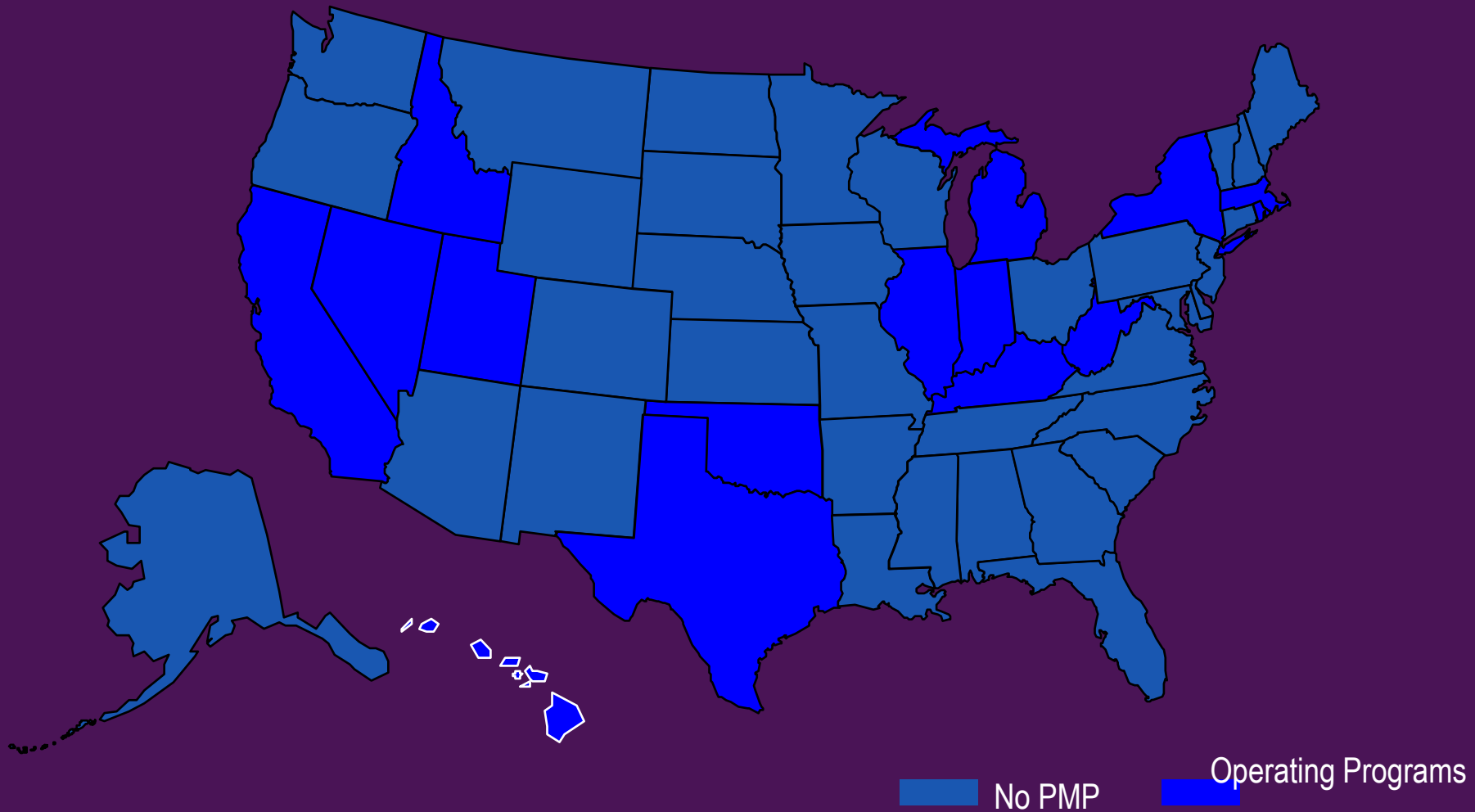
# Accuracy in Predicting Discharge (Aberrant Drug-Related Behaviors)

<u>Measure</u>	<u>% Accuracy Rate</u>
Interview	77%
SOAPP	72%
ORT	45%
DIRE	17%

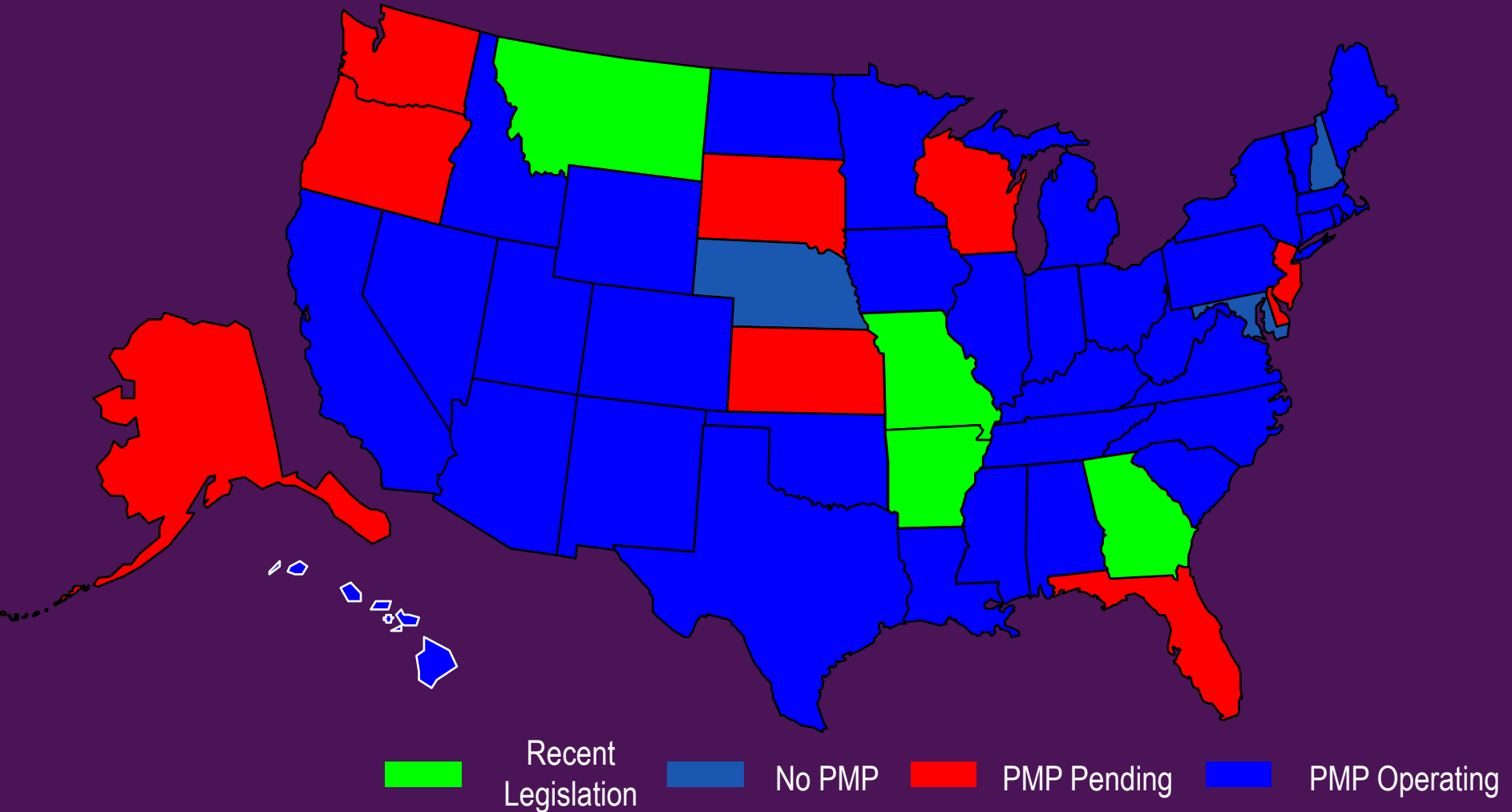
# Why the Difference?

- Psychologist had access to all written risk assessment scores as well interview data
- Different methods (clinician rating vs. patient self-report)
- Different questionnaire styles (shorter transparent questions vs. longer more subtle questions)

# State PMP Status, 2003



# State PMP Status, September 2010



# Aberrant Behaviors Versus Urine Toxicology Testing

Urine Toxicology	Aberrant Behaviors		Total
	Yes	No	
Positive	10 (8%)	26 (21%)	36 (29%)
Negative	17 (14%)	69 (57%)	86 (71%)
Total	27 (22%)	95 (78%)	122

53/122 (43%) of patients had “problems” (positive urine screen or behavioral issues)

# Predicting Abnormal Urine Drug Testing in Patients on Chronic Opioid Therapy

Bronstein K<sup>1</sup>, Passik S<sup>2</sup>, Munitz L<sup>1</sup>, Leider H<sup>1</sup>

<sup>1</sup>Ameritox, Ltd., Baltimore MD, USA <sup>2</sup> Memorial Sloan Kettering Cancer Center, New York, NY, USA



## BACKGROUND

The American Pain Society and the American Academy of Pain Medicine Guidelines for the Use of Chronic Opioid Therapy (COT) in Chronic Noncancer Pain state "In patients who are on COT who are at high risk or who have engaged in aberrant drug-related behaviors, clinicians should periodically obtain urine drug screens. In patients on COT not at high risk and not known to have engaged in aberrant behaviors, clinicians should consider periodically obtaining urine drug screens" (Chou et al., 2009). Several retrospective studies demonstrated that physicians are often unable to accurately assess the likelihood of drug misuse, abuse or diversion in patients on COT. In a study investigating urine drug toxicology results in 122 patients receiving chronic opioids over a three year period, aberrant drug-related behaviors were discordant with urine toxicology. Twenty seven percent of patients with no behavioral issues had an illicit or non-prescribed controlled substance in their urine (Katz & Fanciullo, 2002). Michna (2007) reported on 470 patients where 45% were found to have an illicit drug, a non-prescribed controlled substance, or the absence of the prescribed medication. No clear predictors of abnormal drug screens were identified based on the variables of gender, pain site, type of opioid, opioid dose, number of opioids prescribed, or prescribing physician.

## PURPOSE

This study was designed to assess how accurately clinicians can predict which patients on COT will have abnormal urine drug test results.

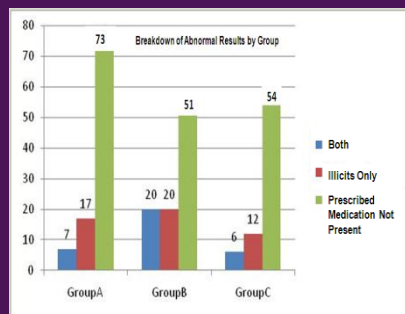
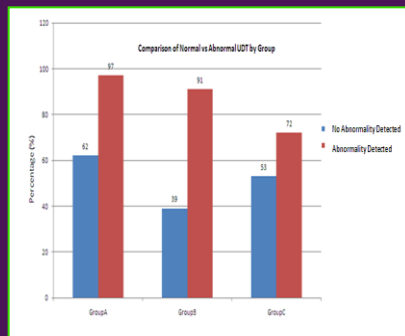
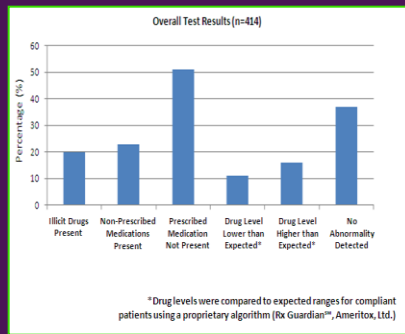
## DESIGN

Clinicians prospectively classified COT patients who were about to have a random urine drug test into one of 3 groups: Group A: those patients thought to be compliant with prescribed therapy, Group B: those patients thought to be misusing medications or using illicit drugs, and Group C: a random, unclassified group of patients for comparison. The clinics assessed risk in patients by whatever methods they normally used in that practice. Over a 2 month period 51 prescribers from 39 clinics submitted urine samples for analysis. Data was analyzed on 414 unique patient samples. Urine drug monitoring results were categorized as normal or abnormal, with abnormal consisting of samples with the prescribed opioid medication not found and/or an illicit drug present

## RESULTS

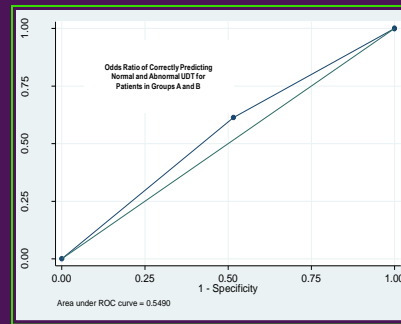
Of the 414 samples, 159 were classified as coming from patients thought to be compliant (Group A), 130 classified as coming from patients suspected of medication misuse (Group B), and 125 random samples (Group C). In Group A (N=159), clinical assessment was correct in the 62 patients (39%) who had a normal urine drug screen and incorrect in 97 patients (61%) who had either illicit present, prescribed drug absent from the urine or both. Prediction accuracy increased in the group suspected of misusing their medications. Predictions of misuse from Group B (N=130) were correct in 91 samples (70%) that had abnormal urine drug monitoring, again classified as having illicit present, missing prescribed drug or both. Results of the unclassified samples in Group C (N=125) showed 72 (58%) were abnormal. In the group thought to be compliant (Group A), the prescribed medication was missing in 73 patients; illicit drugs were present in 17 patients and 7 patients had an illicit drug present and were also missing prescribed opioid medication. Clinical accuracy in this group was comparable to the data from the random group

## RESULTS CONTINUED



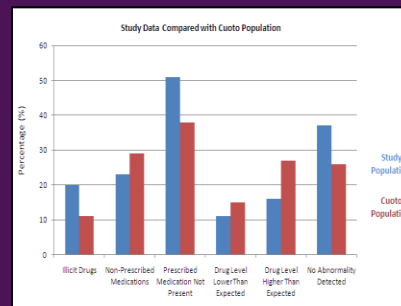
Group A = NOT Suspected of medication misuse  
Group B = Suspected of medication misuse  
Group C = Randomly selected

## RESULTS CONTINUED



For any given patient, the clinician has a 50-50 chance of being right in correctly identifying which group the patient should be placed, A or B. In terms of odds ratios, the Receiver Operating Characteristic curve demonstrates that physician categorization of patients into Group A or B was only slightly better (.54) than by chance (.50)

- Prevalence = all actual non-compliants divided by total population N
- Sensitivity is the proportion of actual non-compliant patients correctly identified = a/(a+b)
- Specificity is the proportion of actual compliant patients correctly identified = d/(c+d)
- The ROC (Receiver Operating Characteristic) curve area is (for this sample test) the average of sensitivity and specificity.
- The likelihood ratio of a positive "guess" (LR+) is the ratio of the probability (likelihood) of a positive "guess" result in an actual non-compliant patient and in a compliant patient = Sensitivity/(1 - specificity)
- The odds ratio (OR) defined as is (AB)/(CD) is also equal to LR+\*LR-
- The positive and negative predictive values (PPV & NPV) show the probability of the patient actually being non-compliant following a + or a - "guess".



In comparing this data with previously published information on rates of inappropriate drug use, the rates of illicit drugs, medication not present and no abnormality detected were higher than those reported by Couto (2009). All other categories were lower than those reported in that study. This data finding may be due to clinicians being asked to specifically identify patients they thought were taking their medication correctly and those that were misusing their medications.

## CONCLUSIONS

- It is difficult to predict which patients are likely to be misusing opioids or taking an illicit drug. Clinicians who suspected patients of medication misuse were correct 70% of the time when urine drug testing was abnormal. In patients who were not suspected of medication misuse, clinicians were correct only 39% of the time. Thus, if a clinician suspects a patient of misusing medications urine drug testing will commonly confirm medication misuse or use of illicit drugs.
- However, clinicians only testing patients suspected of misusing medications based on clinical judgment are missing a significant group (61% in this study) of patients that are misusing their medications without any identifiable risk behaviors. Overall, clinician accuracy in correctly identifying patient categorization was only slightly better than by chance alone. This data reinforces the need for physicians to test all patients on chronic opioid therapy.

## LIMITATIONS

- This study utilized a small sample size and a limited number of clinics. It should be replicated with a larger sample and include more clinics.
- Clinicians categorized patients for risk of medication abuse or misuse by whatever methodology their practice currently utilizes. As this was not a uniform process across clinicians, some methods may work better than others at categorizing risk, but this was not able to be analyzed in this study.

## MEETING INFORMATION

PAIN Week '10  
September 8 – 11, 2010  
Red Rock Casino, Las Vegas, NV  
Contact Information: Kathryn.Bronstein@ameritox.com

## REFERENCES



# New Technology for Urine Screening

*Tests for 12 Drugs*

- ▶ Amphetamine
- ▶ Barbiturates
- ▶ Benzodiazepines
- ▶ Buprenorphine
- ▶ Cocaine
- ▶ Methadone
- ▶ Methamphetamine
- ▶ MDMA (Ecstasy)
- ▶ Opiates
- ▶ Oxycodone
- ▶ THC
- ▶ Propoxyphene



*Results you can see in less than 5 minutes.*

*Split Chamber*

The image shows a portable urine screening device. It has a white plastic body with a clear lid on top. The front panel features a control area with three indicator lights labeled 'C', 'M', and 'T'. Below these lights is a display screen showing '1 1 1 1 1 1' and '2 2 2 2 2 2'. The device is designed for quick and accurate drug testing in various settings.

# Teaching About Medication Storage and Sharing

- Sharing prescription meds seen as safe by “self-treaters”
- Need to educate patients about medication storage
- New devices being developed to help only the patient have access and on a schedule programmed in by the MD or RN



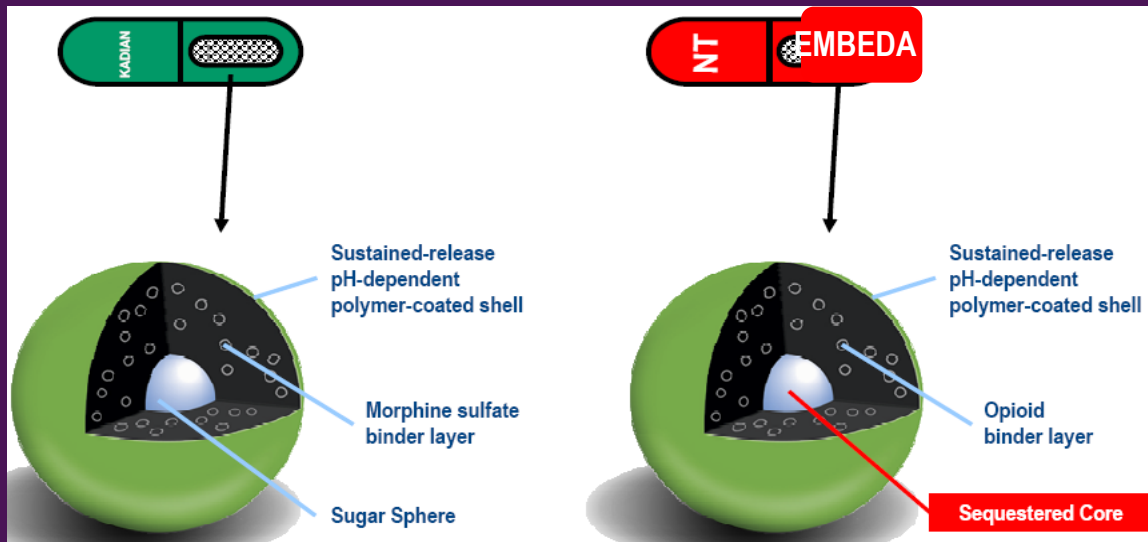
# Remoxy™

- SR oxycodone formula in viscous gel base
  - Deters dose dumping: as gelatin capsule dissolves, SR oxycodone released via GI tract
  - Difficult to crush, break, freeze, heat, dissolve
    - Cannot inject viscous gel-cap base
    - Resists crushing & dissolution in alcohol, water, acidic beverages



# EMBEDA™: Pivotal Trial

- Phase III double-blind, randomized, placebo-controlled, 12-wk, multicenter trial
  - >500 OA (hip/knee) pts moderate-severe pain
  - Primary endpoint: significant pain relief ( $P<.05$ )
- NDA filed February 2008



Alpha Pharma Press  
Releases. Oct 15, 2007;  
Nov 29, 2007; Feb 28,  
2008.  
ClinicalTrials.gov:  
NCT00420992.

# Opioid Renewal Clinic

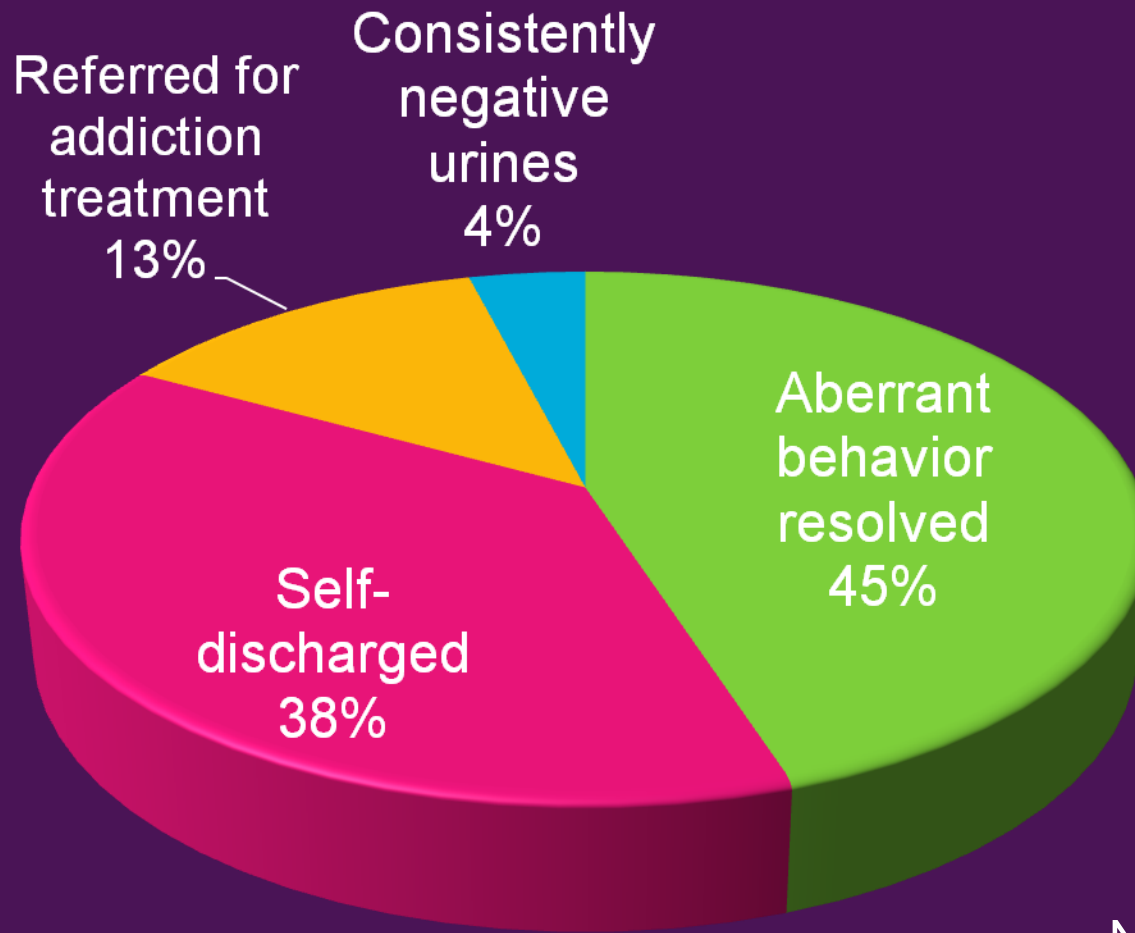
## Procedure

- Consult from PCP
- Eligibility
  - Workup & pain dx
  - Opioid Treatment Agreement
  - Baseline urine drug test
- PCP CONTINUES TO BE RESPONSIBLE TO PRESCRIBE OPIOIDS

## Strategy

- Opioid Treatment Agreement
  - Second Chance Agreement
- Frequent visits
- Prescribing opioids on short-term basis
  - ie, weekly or bi-weekly
- Random UDT
- Pill counts
- Co-management with addiction services

# Aberrant-Behavior Categories (n=171)



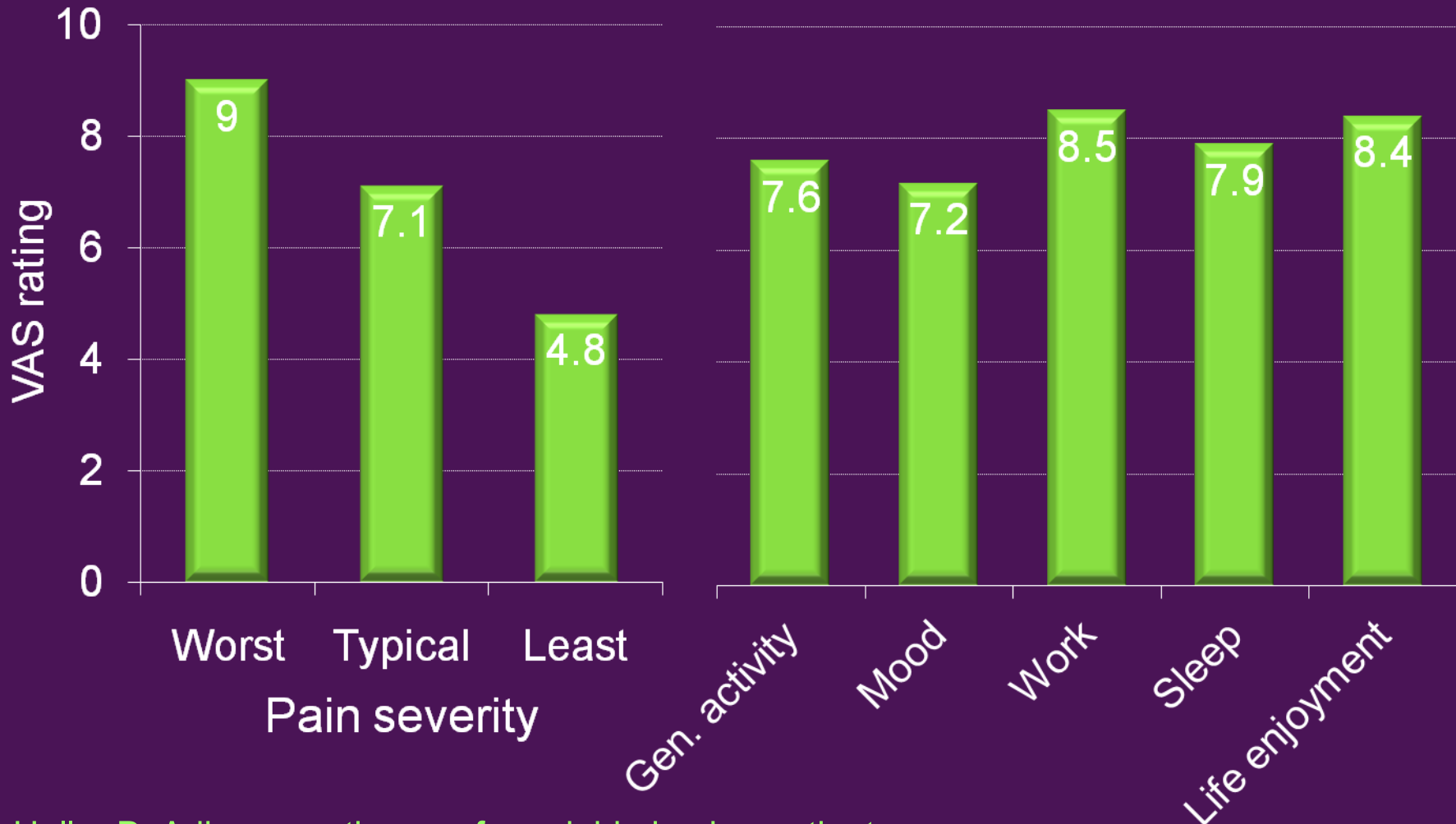
Aberrant behavior = 171  
No aberrant behavior = 164

# NIDA Study: Adherence Therapy for Opioid Abusing Pain Patients

- ❑ 40 pain patients at 2 sites in Virginia & New York
  - Evidence of opioid efficacy for diagnosis
  - >6 mo duration, constant, moderate-severe intensity (VAS >7 despite daily opioids)
- ❑ Substance abuse co-morbidity
  - Opioid abuse or dependence, >2 on “problems with pain meds”, no current substance dependence, & lifetime dependence or current abuse permissible
- ❑ Psychiatric co-morbidity
  - No unstable major psychiatric disorders, current suicidal/ homicidal ideation, or medication dose considerations
- ❑ Medical co-morbidity
  - No unstable/severe medical conditions or planned surgery within study period; no meds that interact with methadone

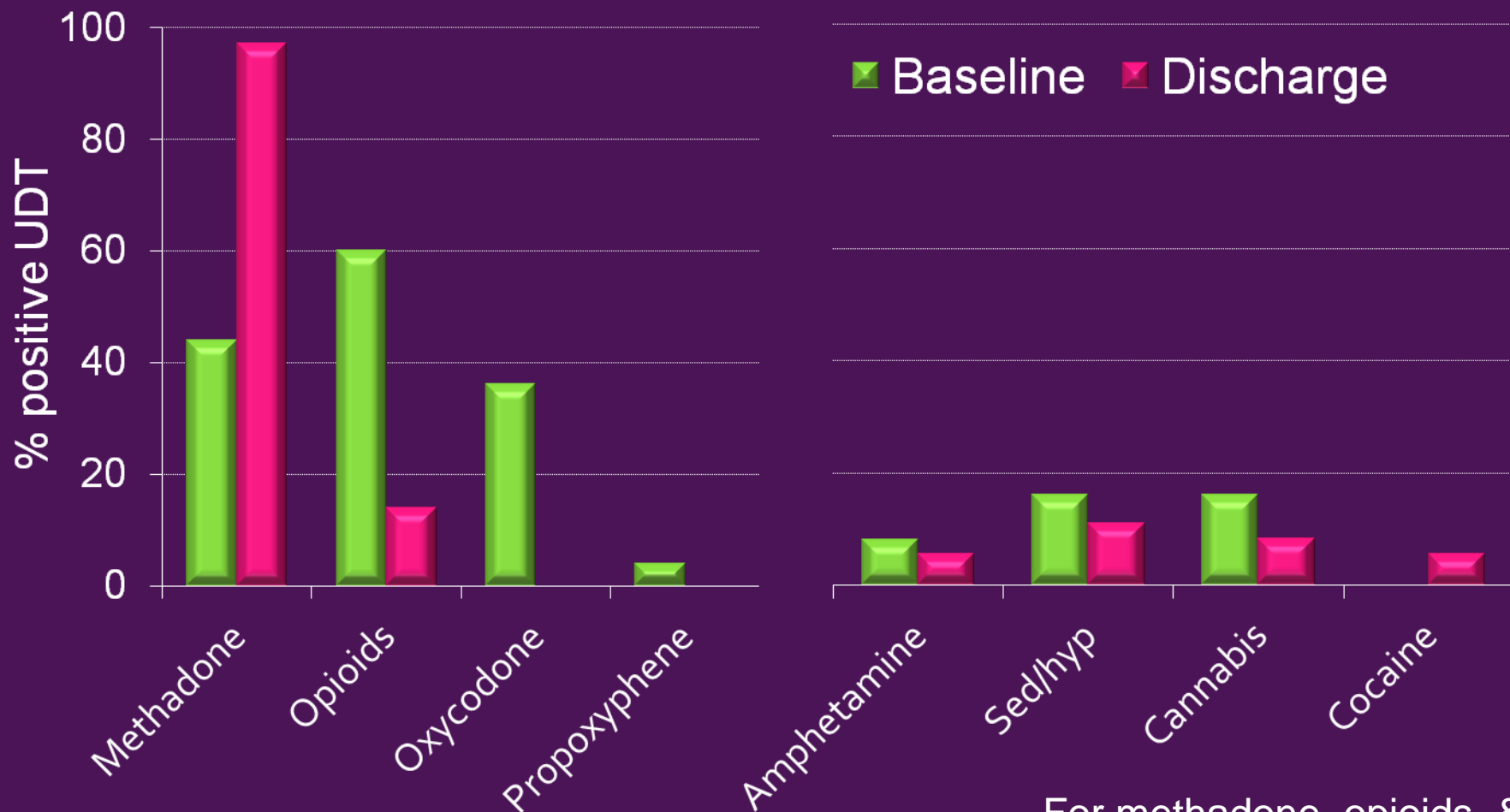
Haller D. Adherence therapy for opioid abusing patients.  
“PROJECT PAIN.” NIDA (Grant #R01DA1369). Presented at 2006 CPDD Conference.

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"PROJECT PAIN." NIDA (Grant #R01DA1369). Presented at 2006 CPDD Conference.

# Trends in Opioid & Non-opioid Use



For methadone, opioids, & oxycodone  $P < .01$

Haller D. Adherence therapy for opioid abusing patients.  
"PROJECT PAIN." NIDA (Grant #R01DA1369). Presented at 2006 CPDD Conference.

# Give a little old Jewish Lady a Break

