

# Post-Marketing Surveillance of Controlled Substance Abuse and the Emergence of REMS



**THEODORE J. CICERO, PHD.  
DEPARTMENT OF PSYCHIATRY  
WASHINGTON UNIVERSITY IN ST. LOUIS  
SCHOOL OF MEDICINE  
SEPTEMBER 24 & 25, 2009**

# What are REMS?



- Risk Evaluation and Mitigation Strategies
- The FDA now mandates that a new opioid analgesic must have a program to:
  - Identify, localize and characterize abuse and diversion, and other adverse events with newly marketed drugs.
  - Once this information is in hand, develop a plan to “mitigate” the abuse.

# Why are REMS Needed?



- Phase I-III studies tend to be small relative to general population so that relatively rare events will be missed or underestimated.
- Data over the past decade indicates a sharp increase in Rx abuse and diversion.



**Why has Rx abuse increased so markedly in the past decade?**

# Why has Rx Abuse Increased?



- Arguably, errors in the labeling of OxyContin and the enormous quantity of drug in a single tablet led to its widespread abuse
- Rx drugs are considered legal and therefore it is believed there are no penalties for usage.
- Taking them is safe because of authenticity and dose certainty.

# Why has Rx Abuse Increased?



- Easily available from doctors, friends and/or family.
- No perceived stigma associated with use.
- Don't consider themselves addicts.



- **The RADARS™ System is composed of five signal detection systems:**
  - Drug Diversion
  - Survey of Key Informants' Patients (SKIP)
  - Poison Center
  - Opioid Treatment Program
  - College Survey

# Survey of Key Informant Patients (SKIP)



- **Key Informants are experts in the field of substance abuse and pain medicine, most often treatment center directors.**



# Survey of Key Informant Patients (SKIP)



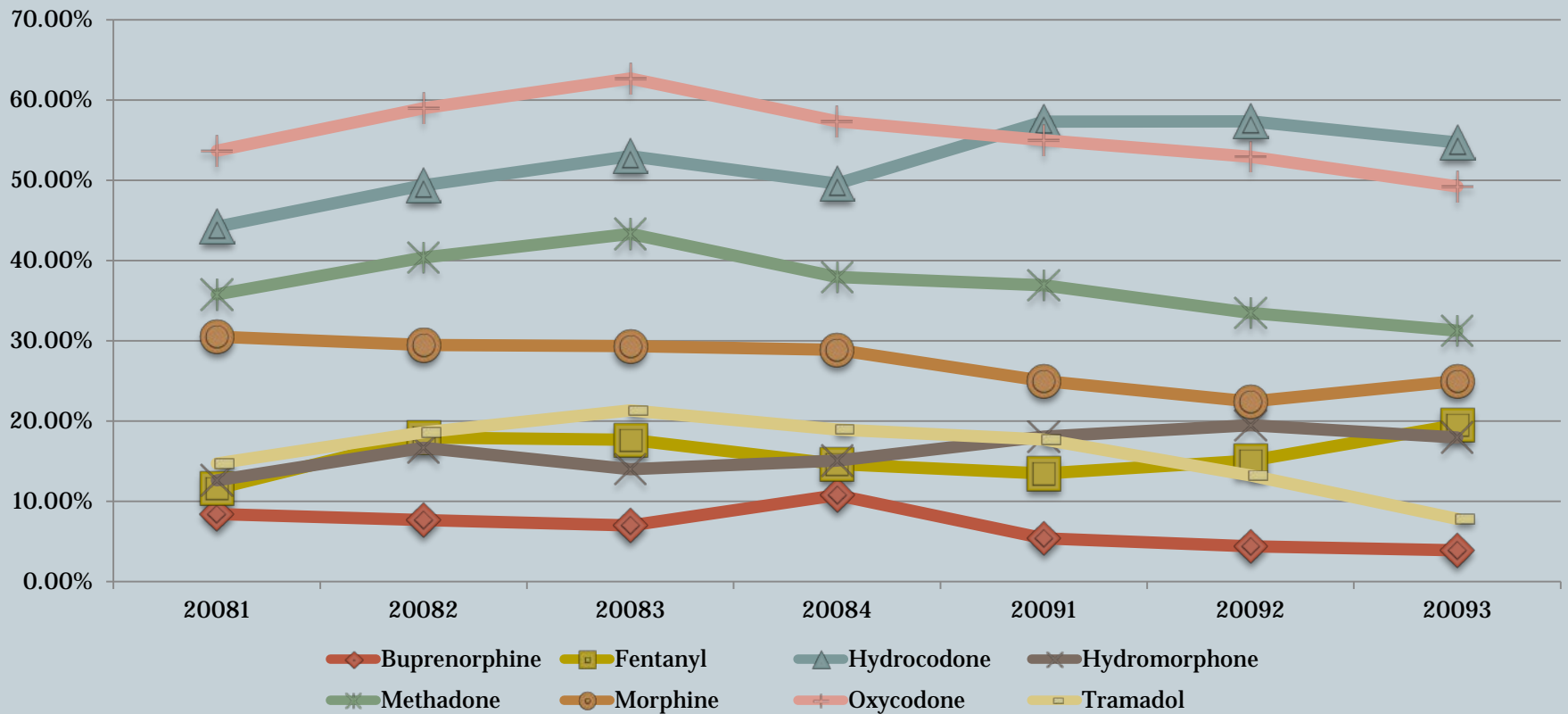
- Questionnaire, self-addressed envelope and gift card are sent to Key Informants.
  - Key Informants have their patients/clients complete questionnaires which carry a specific ID #.
- Questionnaire returned directly to Washington University (treatment center does NOT see completed survey)
  - Key Informants are notified that a questionnaire has been completed.
  - Patient receives gift card for participation



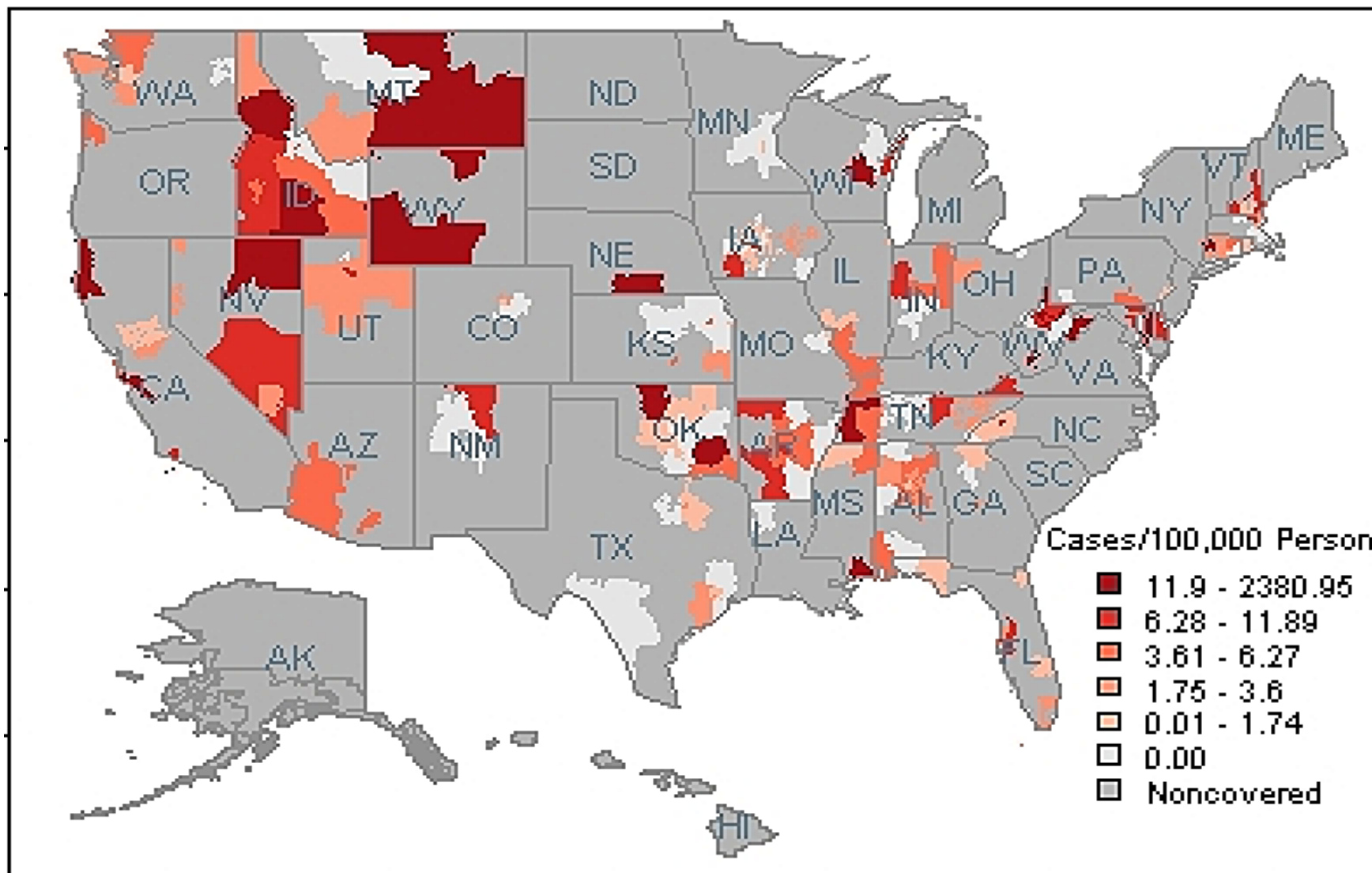
# Characteristics and Patterns of Abuse

# What Drugs are Used Most Frequently?

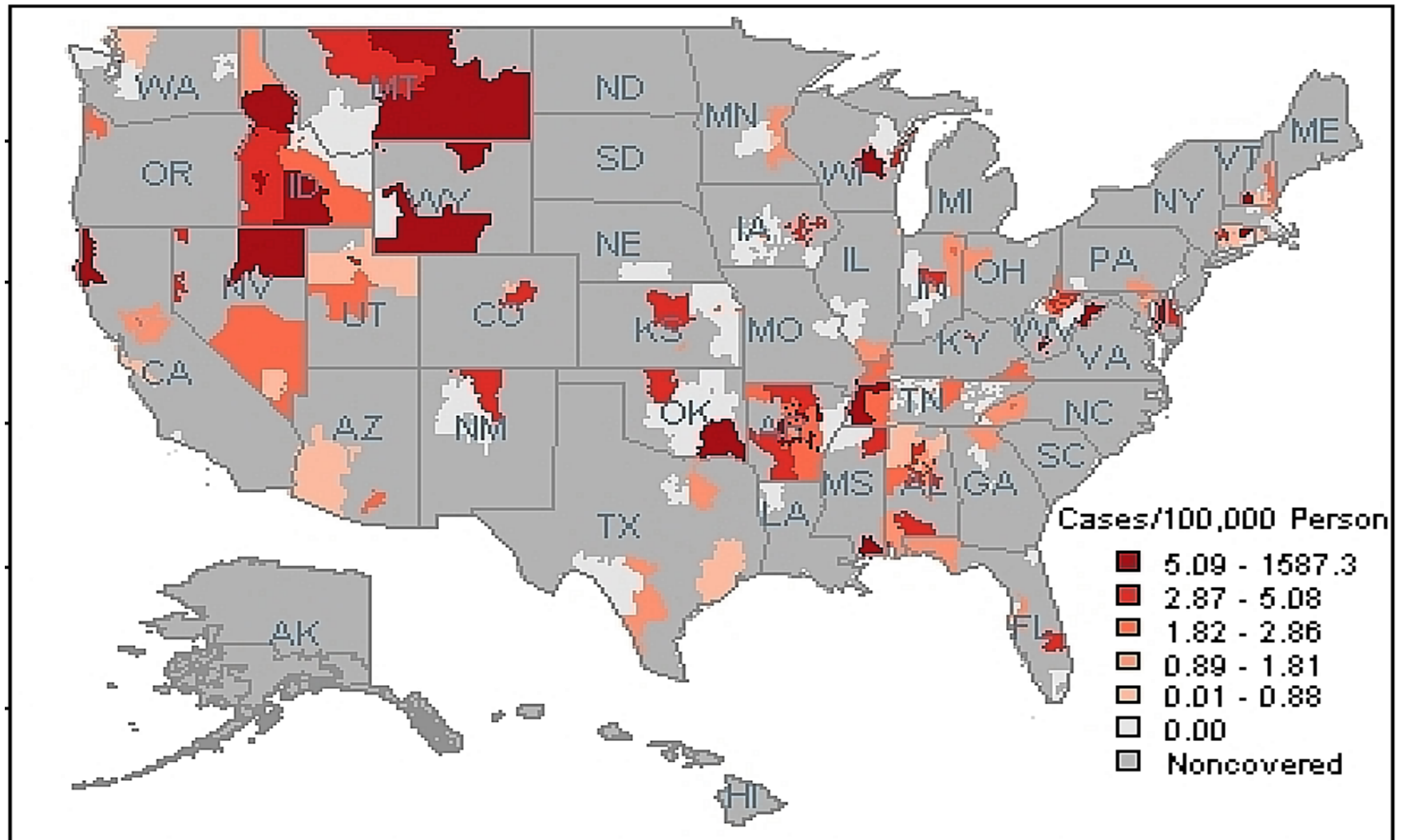
**Drugs Used in the Past 30 Days Among Rx Abusers per Quarter 20081 - 20093**



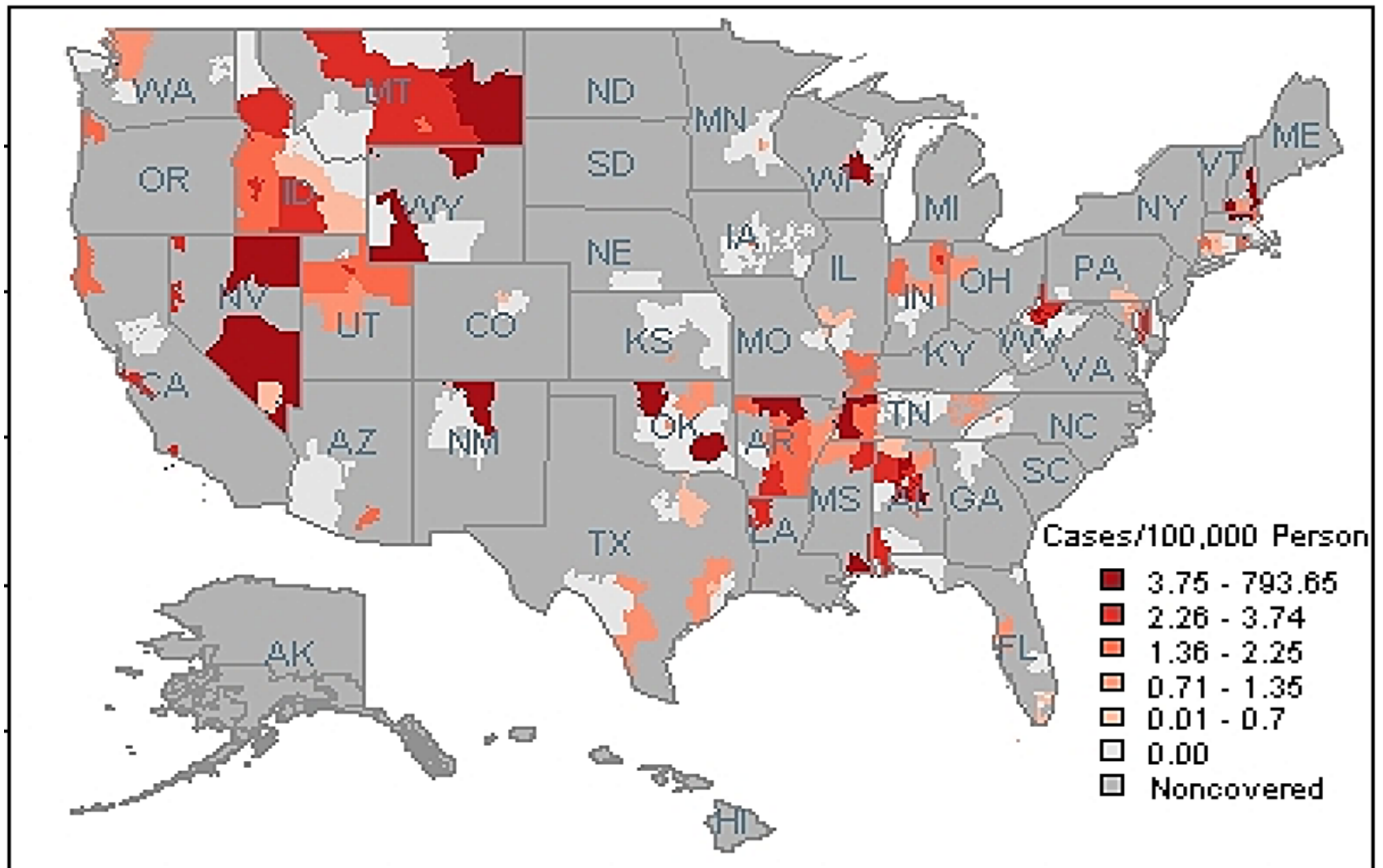
# SKIP Oxycodone Abuse Rate (per 100,000 pop) for 2008



## SKIP Hydrocodone Abuse Rate (per 100,000 pop) for 2008



# Methadone SKIP Abuse Rate (per 100,000 pop) for 2008



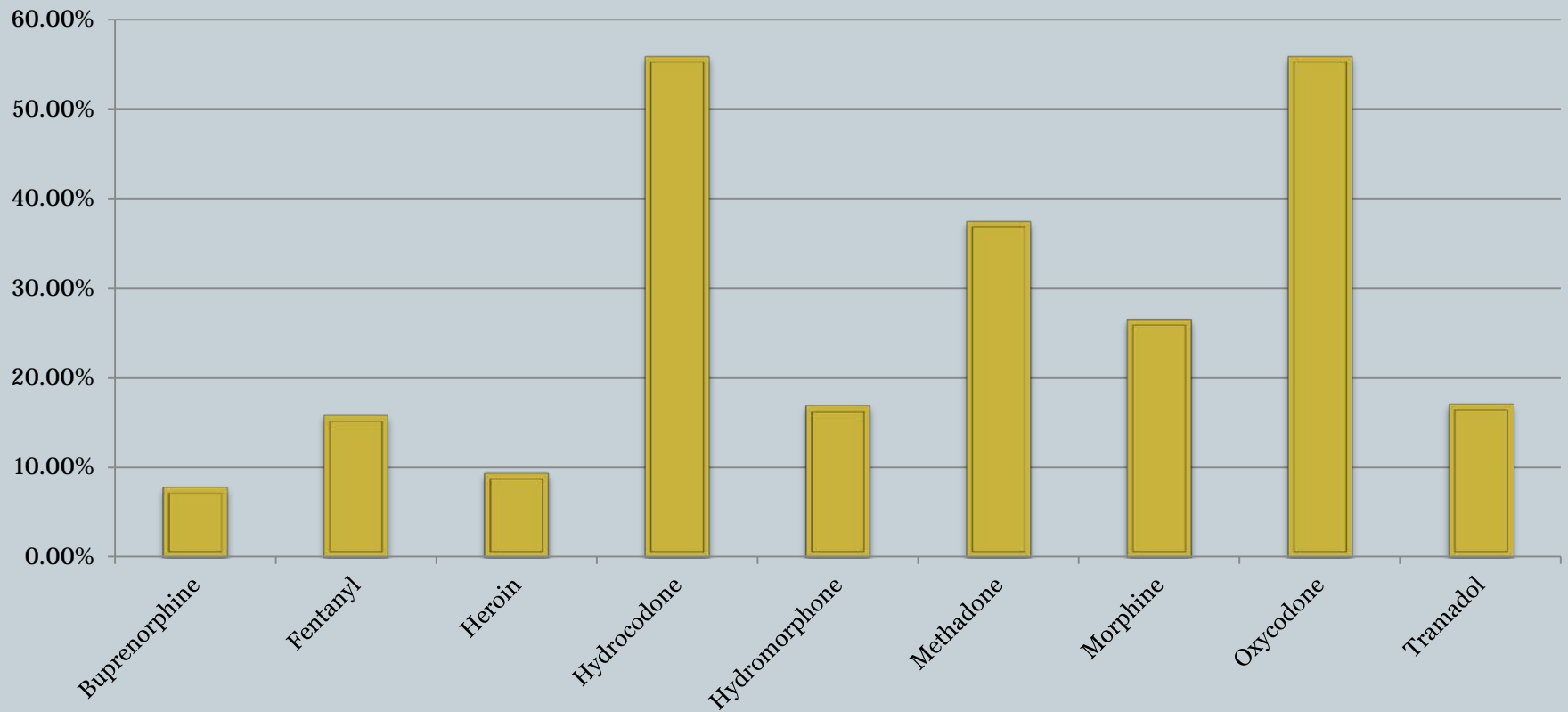


**What drugs are used  
most frequently?**

# What Drugs are Used Most Frequently?



## Drugs Used in the Past 30 Days Among Rx Abusers 2007 - 2009

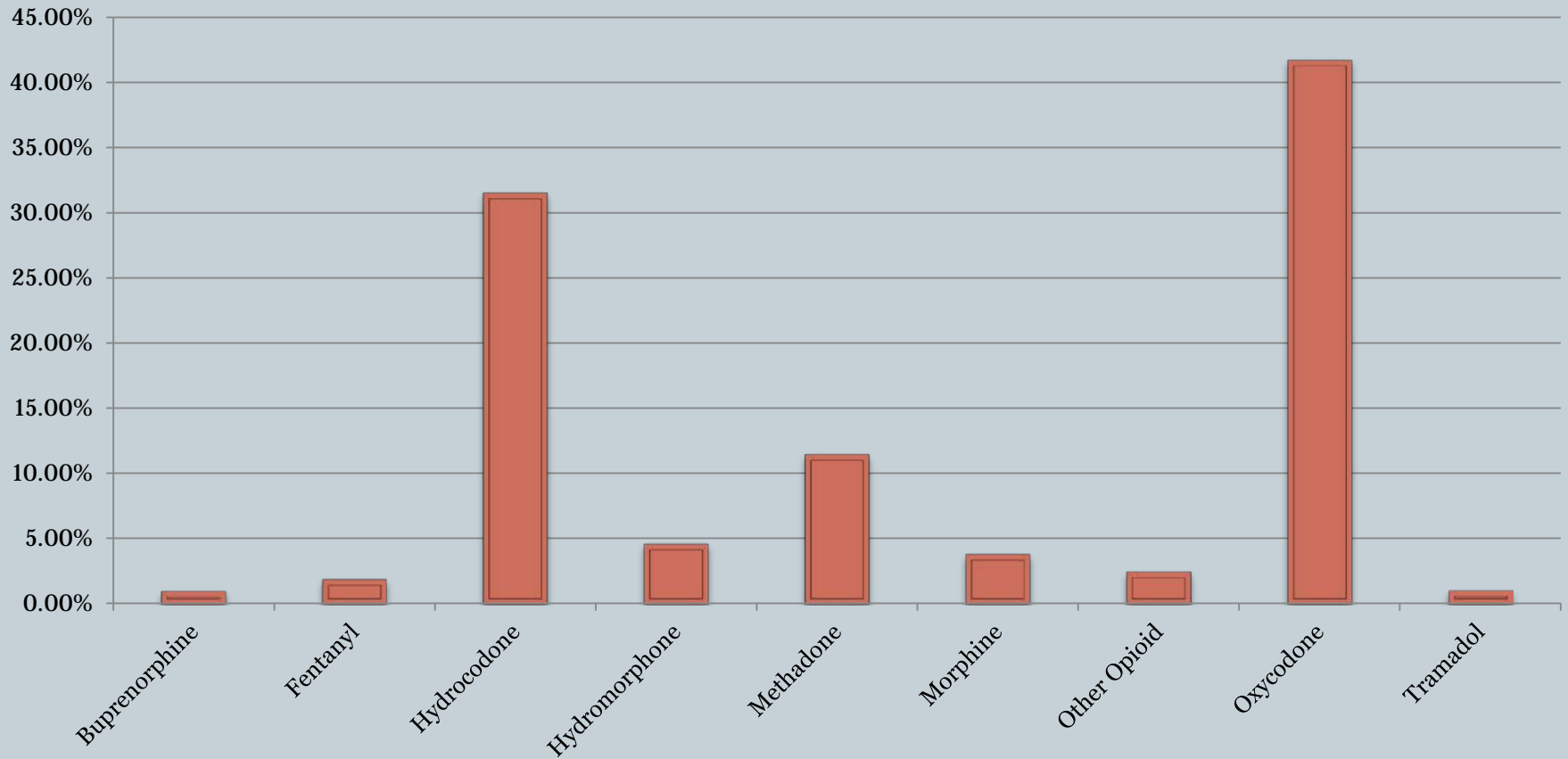




# What Drugs are Used Most Frequently?



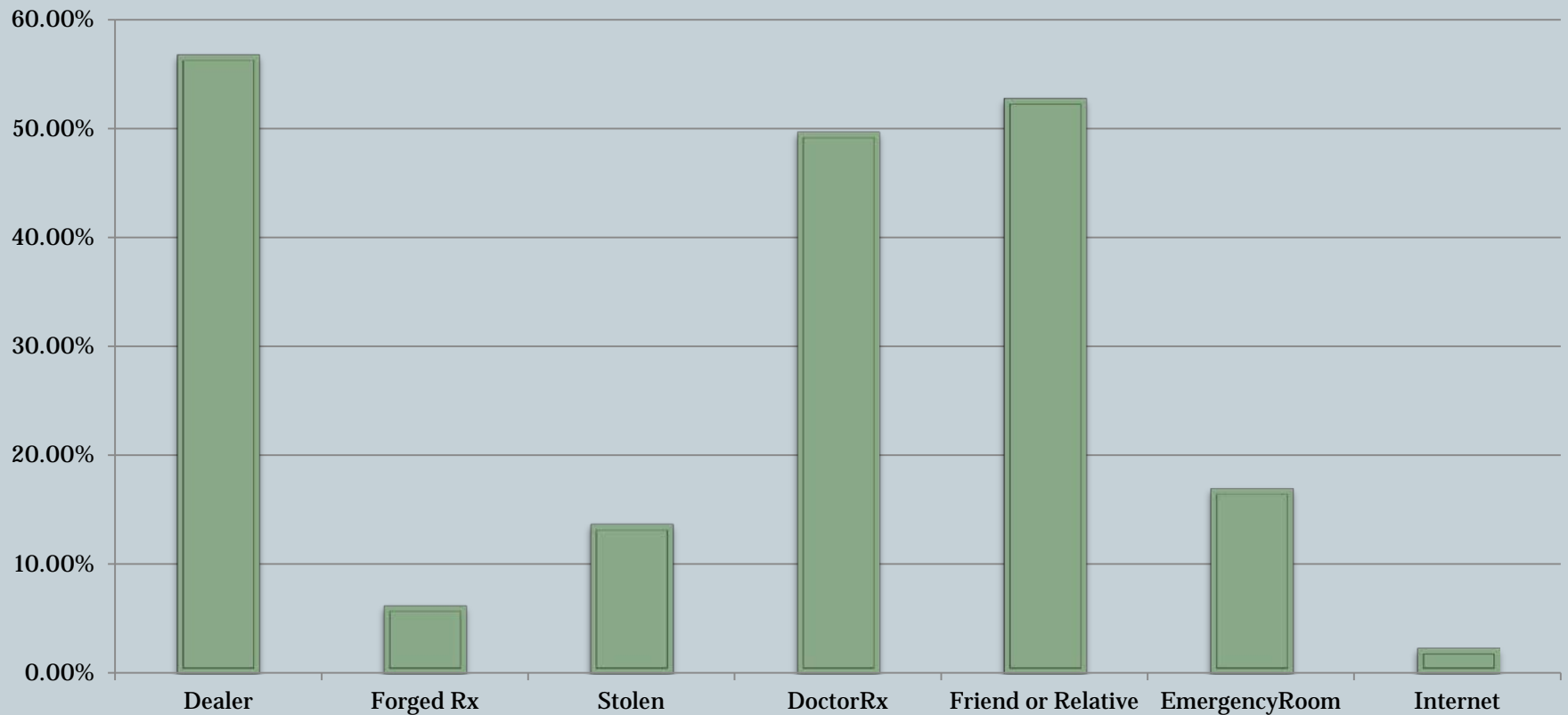
## Primary Drugs Among Rx Abusers, 2007-2009



# What Drugs are Used Most Frequently?



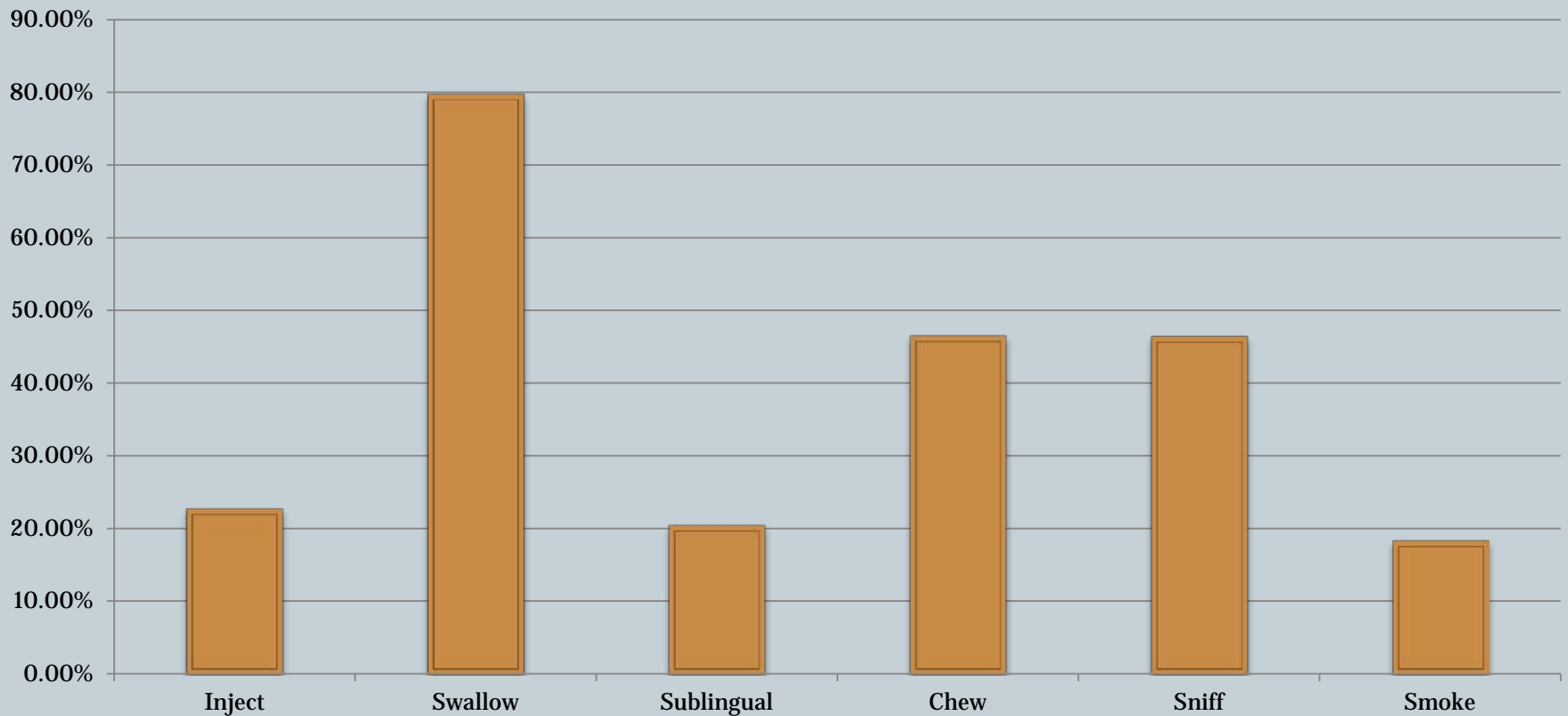
## Source of Primary Drug in the Past 30 Days Among Rx Abusers, 2007 - 2009



# What Drugs are Used Most Frequently?



## Route of Primary Drug Administration in the Past 30 Days Among Rx Abusers, 2007 - 2009



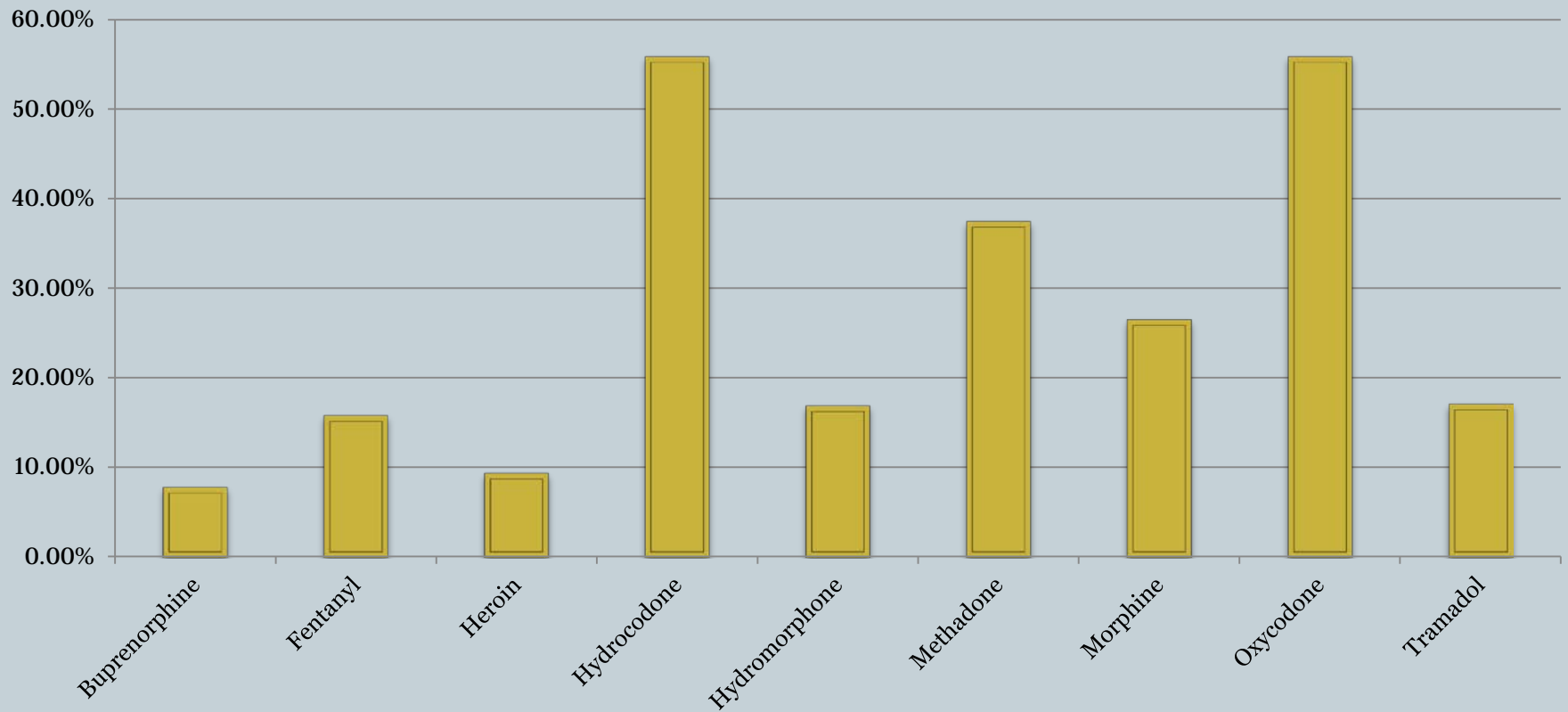


**But abuse is a little more  
complicated than that...**

# But abuse is a little more complicated...



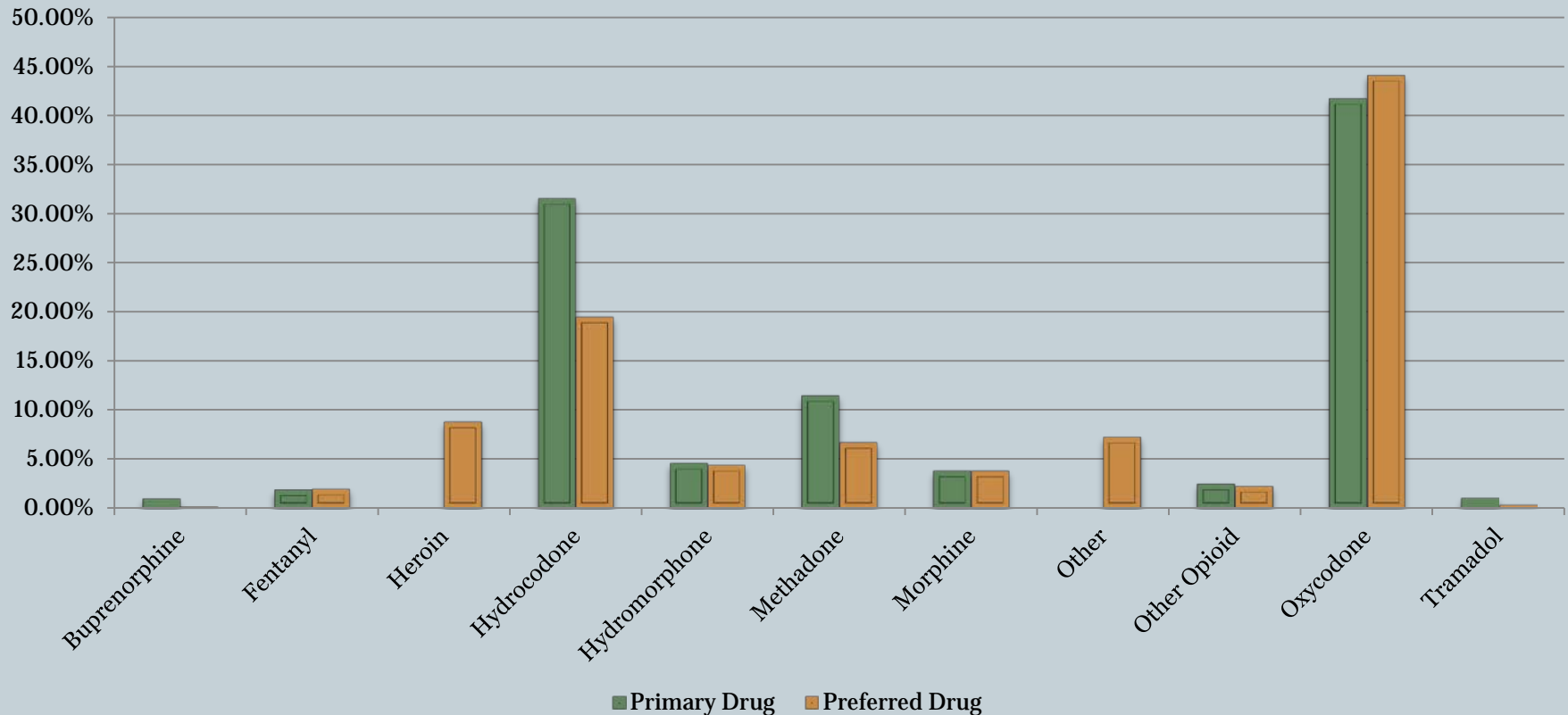
## Drugs Used in the Past 30 Days Among Rx Abusers 2007 - 2009



# But abuse is a little more complicated...



## Primary Drug vs. Preferred Drug Among Rx Abusers if Price and Availability Were Not Factors, 2007- 2009





**Is the recent surge in Rx abuse  
a new problem in otherwise  
healthy individuals?**

# SKIP: Rx Abusers (N=2020)



- **Gender**

- Males (49.9%)
- Females (50.1%)

- **Education**

- None (10.79%)
- High School/GED (42.75%)
- Some College (46.46%)

- **Average Age: 35.03**

- **Ethnicity**

- White (82.48%)
- African-American (5.29%)
- Latino/a (4.29%)
- Other (7.94%)



# SKIP: Rx Abusers (N=2020)



- Avg. # of times entered drug treatment: **3.5**
- Reported Chronic Pain: **59.8%**
- Avg. 1-10 Pain Score: **4.9**
- Treated for Psychiatric Condition: **44.3%**

# SKIP: Rx Abusers (N=2020)

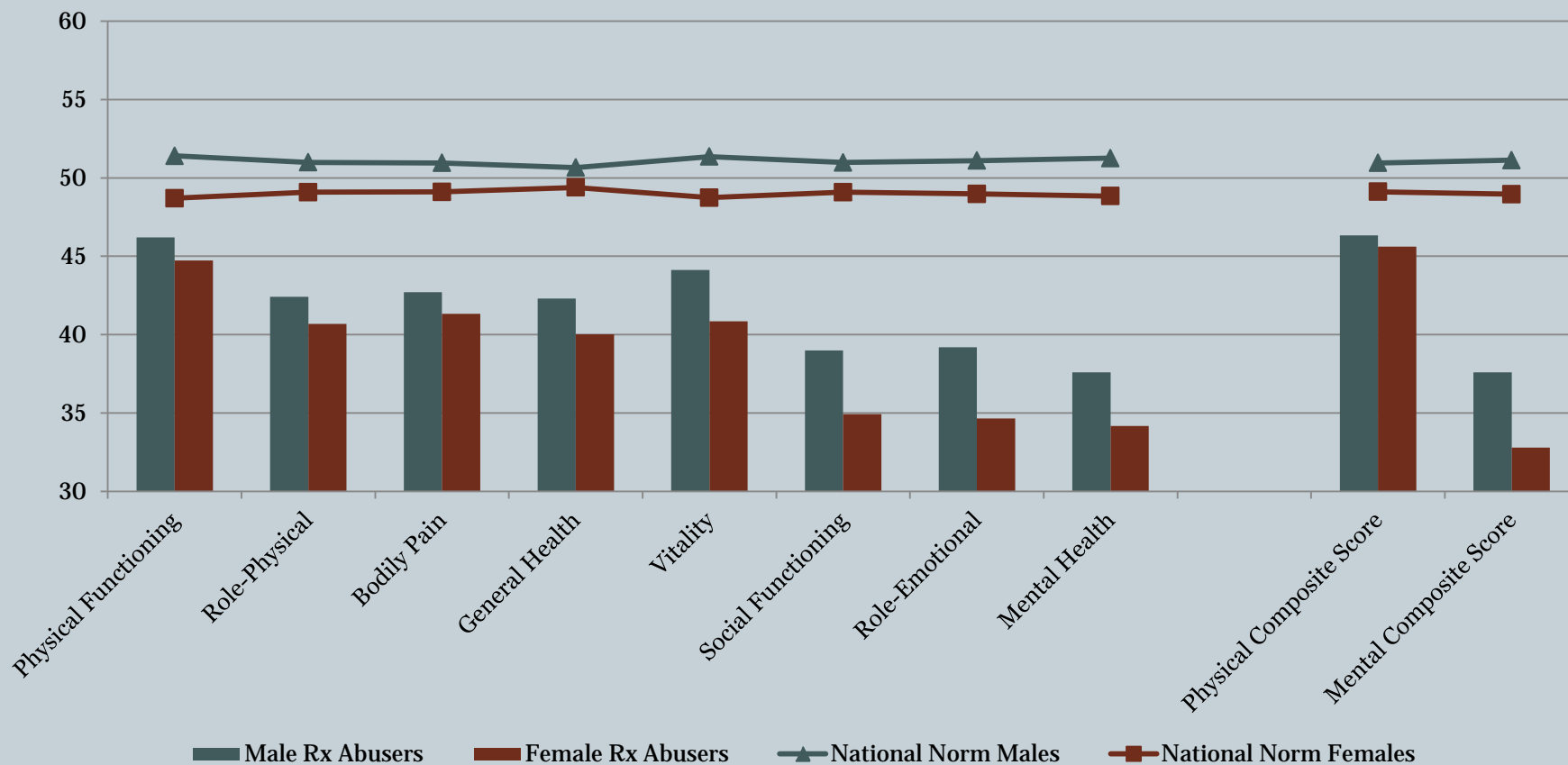


- Nicotine Dependence: **67.3%**
- Alcohol Abuse: **40.3%**
- Meet DSM-IV Criteria for Abuse of Primary Rx: **89.8%**

# SKIP: Rx Abusers (N=2020)



## SF-36v2 Results of Male vs. Female Rx Abusers



# Why is Co-morbidity a Problem?



- **Treatment requires a multi-discipline approach.**
- **Treating Rx abuse in isolation is destined to fail.**

# Why is Co-morbidity a Problem for REMS?



- **What does a REMS target as a mitigation strategy?**

# More Difficulties in Implementing REMS



- Identifying abuse is not a problem.
- Doing something about it is a laudable, but perhaps unattainable goal.
- Why?
  - ✦ Unless you have good data beforehand (i.e., no REMS) how can you assess whether the minimization approach was successful?
  - ✦ Given regional localization of abuse, national databases will not likely be very helpful.

# More Difficulties in Implementing REMS



- **Why?** *(cont'd)*
  - ✦ Abuse in some areas (e.g., Appalachia) has been indigenous for decades. What can be done to eradicate abuse of a new drug within this culture.
  - ✦ Balloon analogy.

# Unintended Consequences



- **Will REMS for a specific drug be so restrictive that patients – not just addicts – will be denied beneficial medications?**