

# Spotlight: New Prescription Drugs of Abuse and Their Opioid Interaction Risks

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**4th Human Abuse Liability & Abuse-Deterrent Formulations**

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# Conflict of Interest Statement

- Most manufacturers of prescription opioids or stimulants subscribe to RADARS System.
- RADARS System is the property of Denver Health and Hospital Authority, a political subdivision of the State of Colorado.
- Subscribers receive information, but do not participate in developing the System, data collection, or analysis. They do not have access to the raw data.
- Employees are prohibited from personal financial relationships with any company.

# Roadmap

- **Why nonopioid prescription drug misuse and abuse is increasingly common**
- **Framework for identifying nonopioid drug misuse and abuse**
- **Highlights of drug classes**

**Why is nonopioid  
prescription drug  
misuse and abuse  
increasingly common?**

# Nonopioid Prescription Drugs

- Potentiate effects of opioids
- “Smooth out” effects of other drugs
- Used as substitution or replacement when drug of choice not available

# **Framework for identifying nonopioid drug misuse and abuse**

# Surveillance Data

- **National Poison Data System**

# NPDS 2006-2014

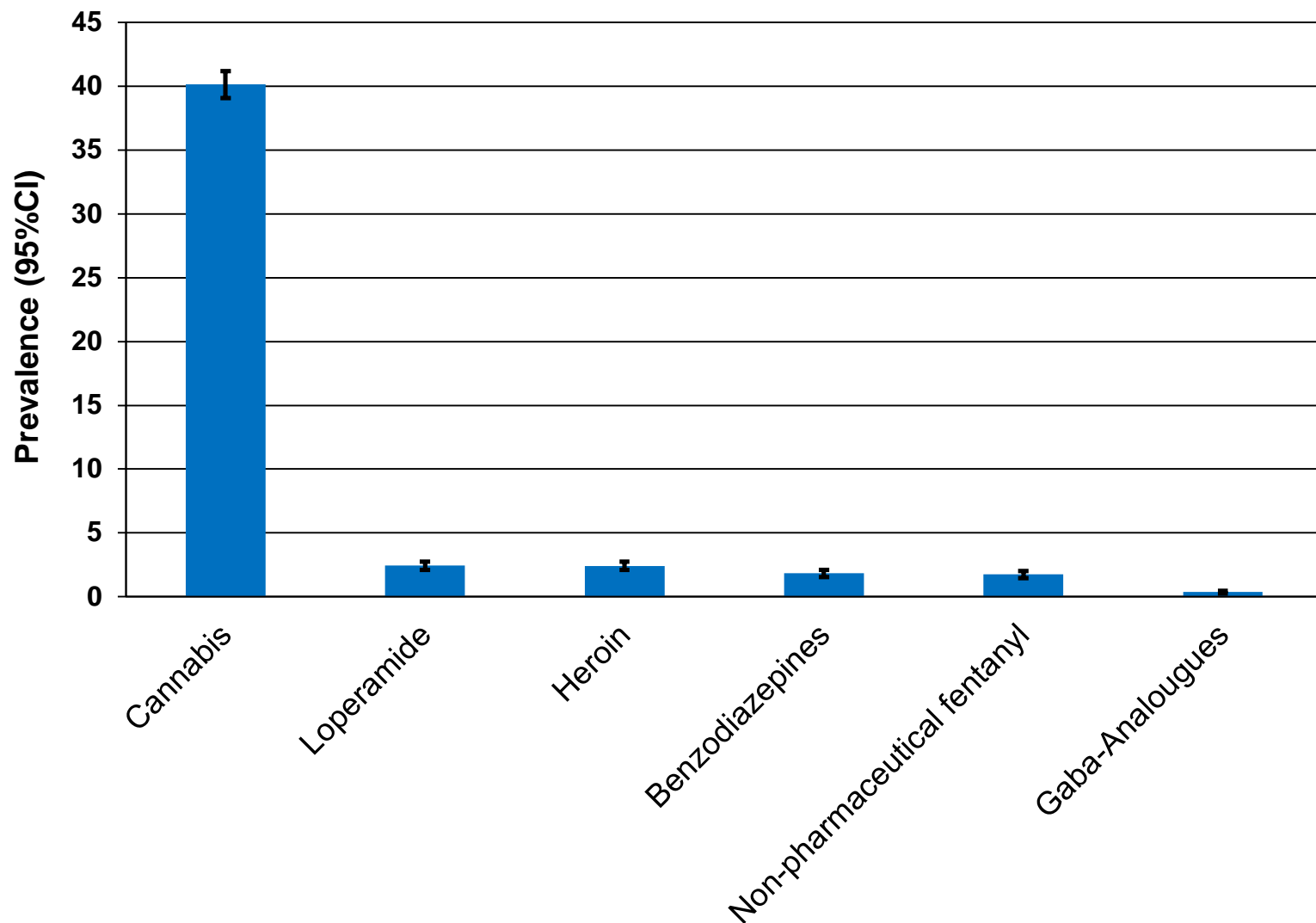
Generic Code	Intentional Abuse	Single Substance
Benzodiazepines	51275	15895
Dextromethorphan	18182	12852
Amphetamines	13833	7402
Carisoprodol	8633	3375
Atypical Antipsychotics	8556	2982
Other Sedative/Hypnotic/Anti-Anxiety or Anti-Psychotic	8150	3700
Diphenhydramine	5927	3163
Other SSRI	5185	1329
Other Antihistamines	5155	2208
Other Anticonvulsant (Excluding Barbiturates)	3931	1371
Methylphenidate	3662	2116
Other Antidepressant	3173	1133
Trazodone	3124	868
Ibuprofen	3017	1057
Other Muscle Relaxant	2989	1257
Cyclobenzaprine	2948	853
Gabapentin	1373	379
Phenothiazines	1288	642
Amitriptyline	1271	365
Clonidine	1159	389



# Surveillance Data

- **National Poison Data System**
- **General population surveys**

# Lifetime Nonmedical Use



# Surveillance Data

- **High risk groups**
  - **Department of Corrections, Jails**
  - **Teenagers and young adults**
  - **Substance abuse treatment programs**
  - **Diversion**

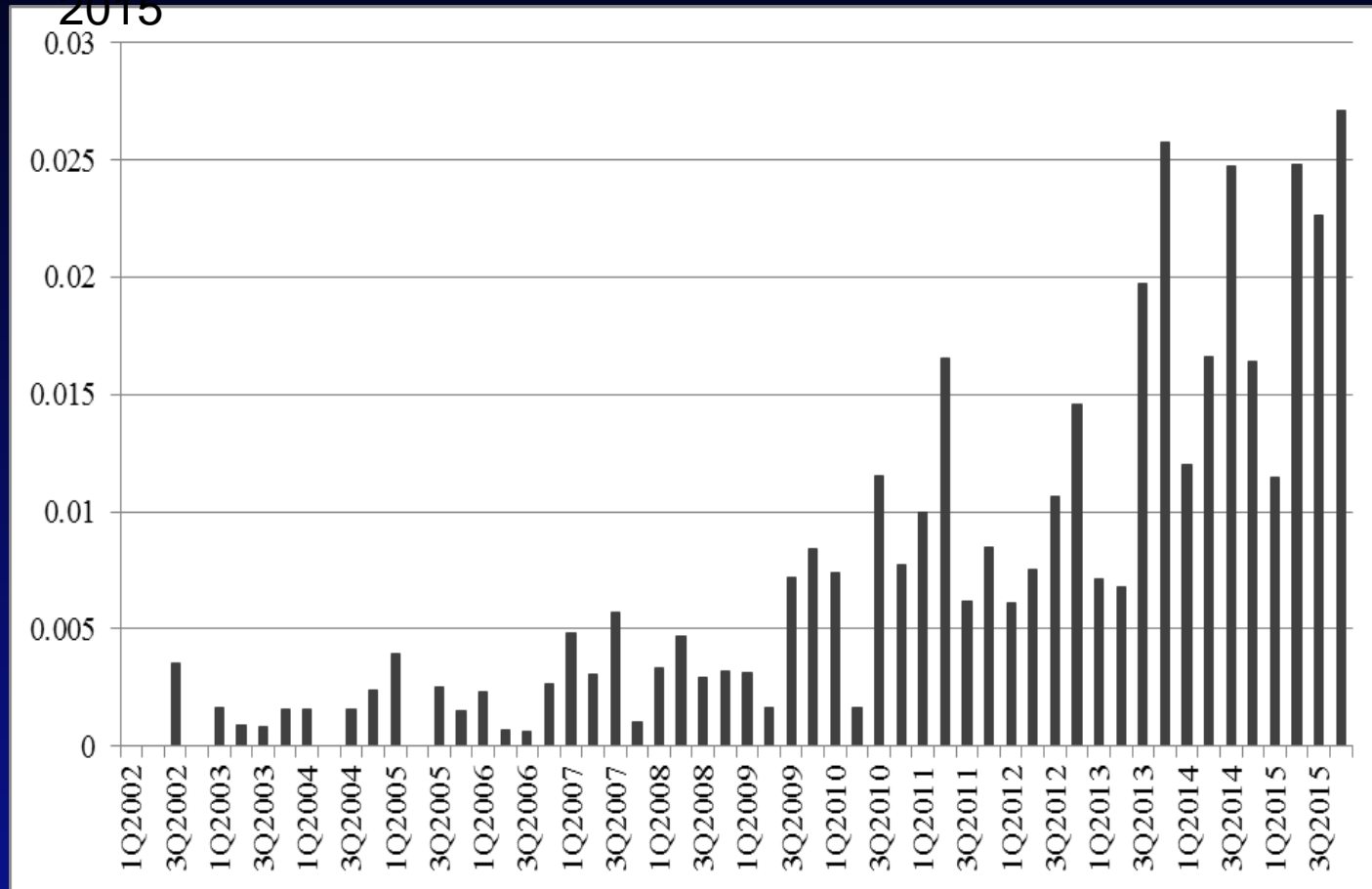
# **Highlights of Commonly Abused Nonopioid Pharmaceuticals**

# GABA Analogs

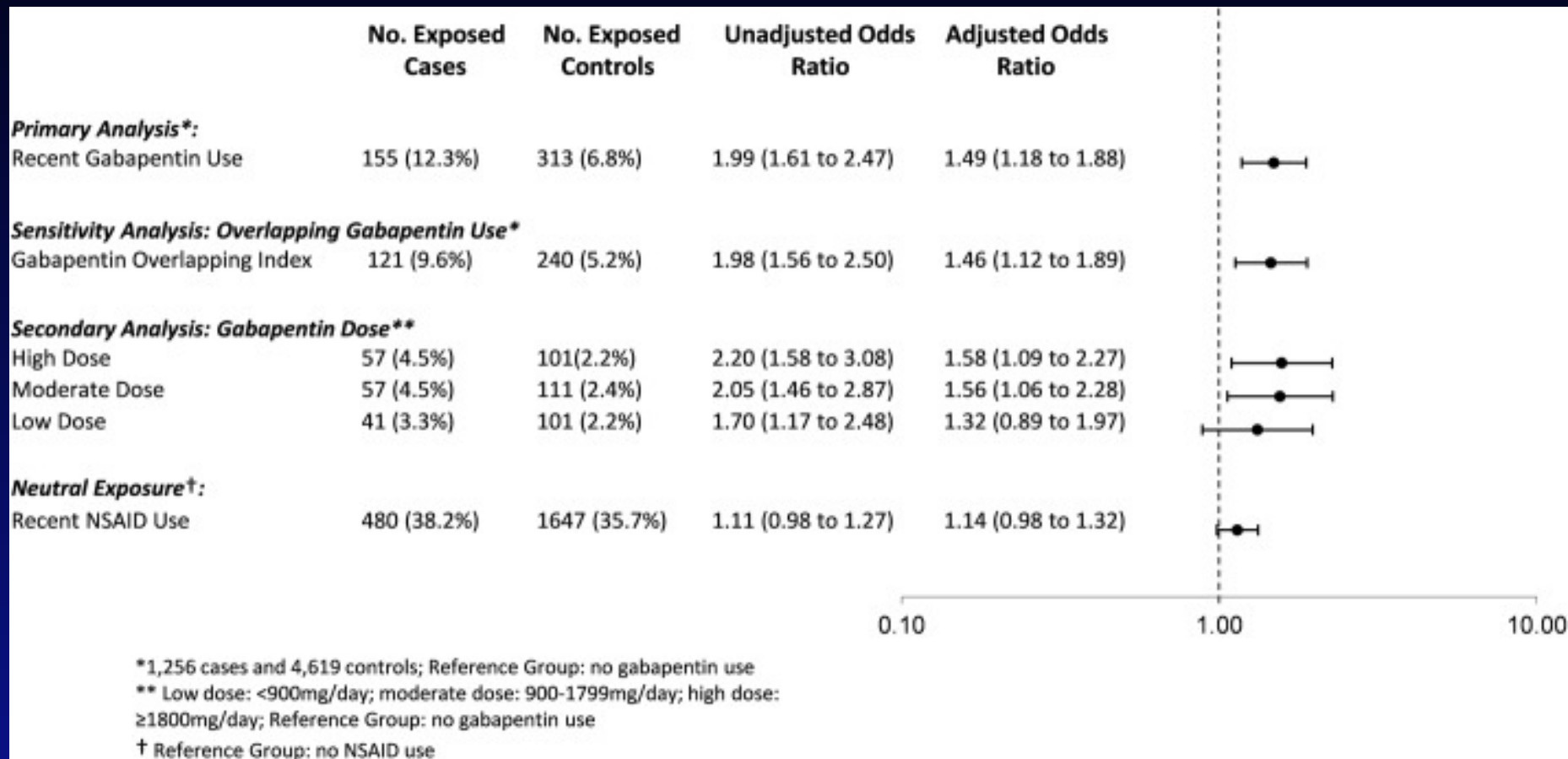
- Gabapentin, pregabalin
- 10-15% prescribed opioids also prescribed gabapentin
- Misuse common in opioid use disorders (15-28%)
- Increased mortality when combined with opioids
  - Likely synergistic respiratory depression

# Diversion of GABA Analog

Rates of gabapentin diversion (per 100,000) by quarter, 2002-2015



# Gabapentin and Mortality

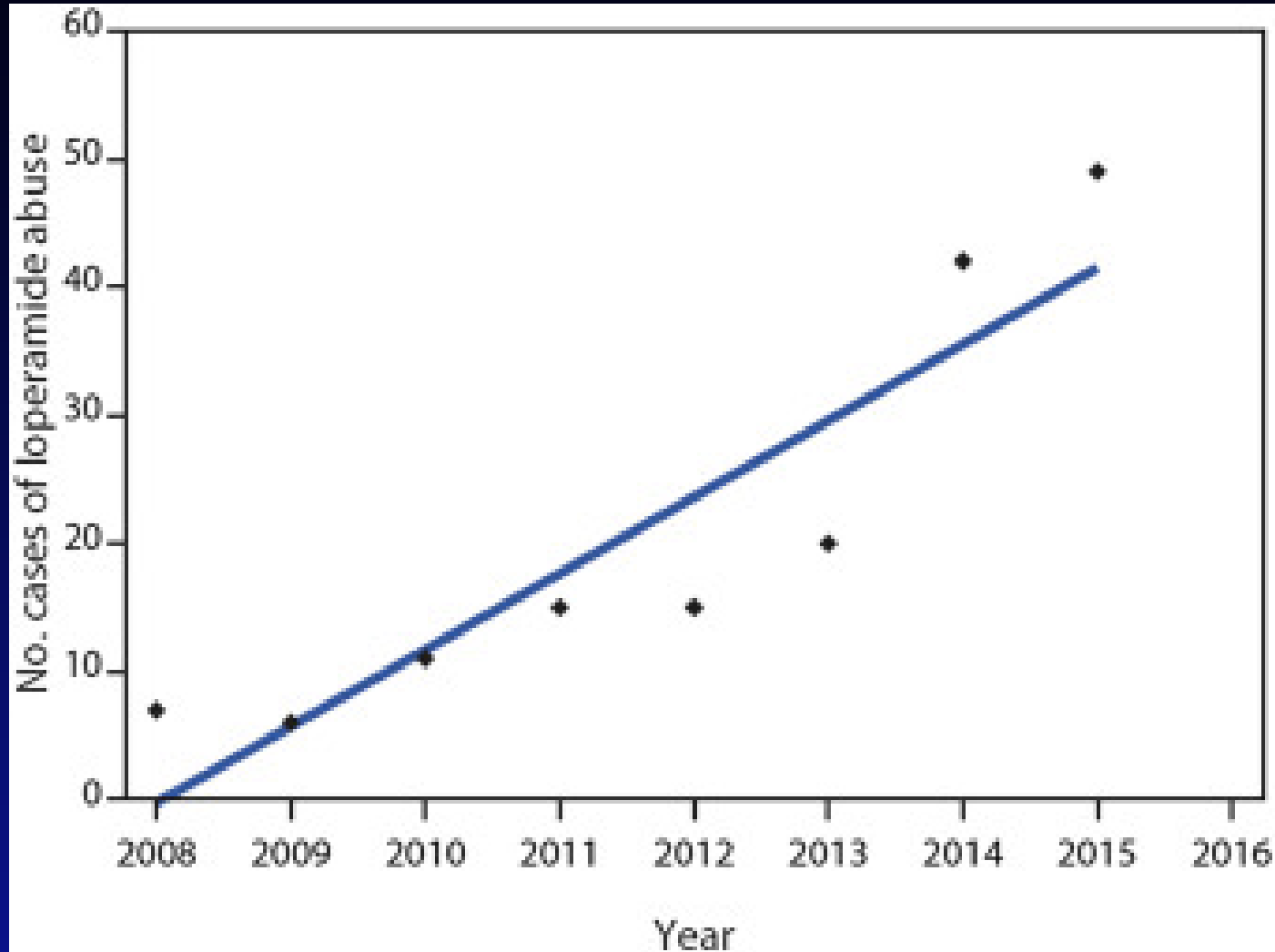


# Loperamide

- Antidiarrheal
- Prescription and OTC
- Intestinal mu agonist
- Poor systemic absorption due to p-glycoprotein
- Abused alone or in combination with opioids



# Loperamide Abuse



# Loperamide Abuse

Reported toxicities categorized by organ

system<sup>13, 17, 18, 19, 23, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38,39, 40</sup>

Organ system	1985-2013 (n = 21)	2014-2016 (n = 33)	Total, 1985-2016 (n = 54)
Gastrointestinal <sup>a</sup>	6	1	7
Cardiovascular <sup>b</sup>	4	15	19
Respiratory <sup>c</sup>	2	2	4
Neurological <sup>d</sup>	4	5	9
Death	10	17	27

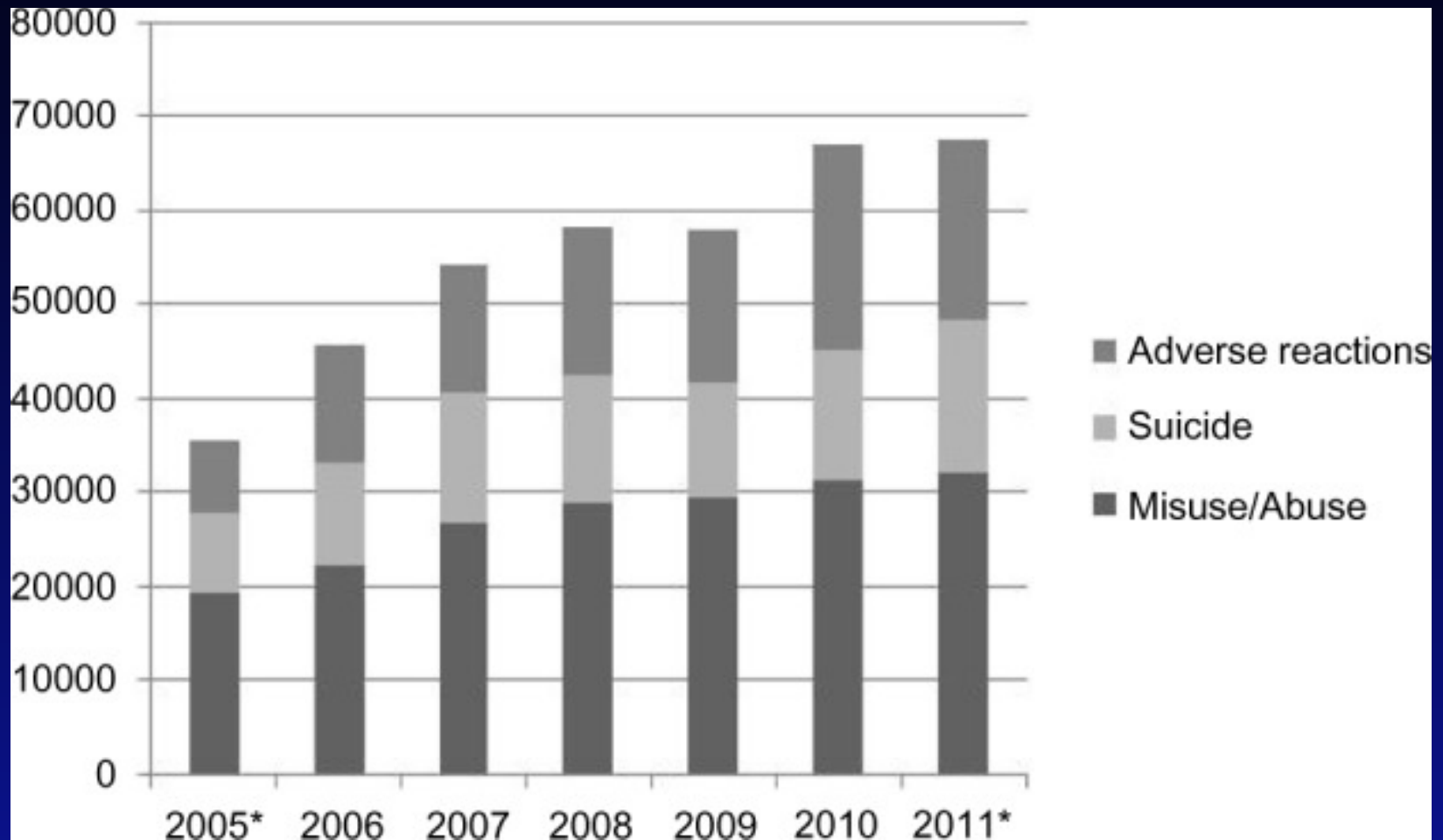
# Antipsychotics

- Atypical antipsychotics commonly abused both alone and in combination with other drugs
- Especially popular in incarcerated population
- Quetiapine often drug of choice

# Antipsychotic Abuse

- 429 patients from detox and rehab units
- 73 (17%) abuse atypical antipsychotics with alcohol, opioids, cocaine/crack, methamphetamine, and/or cannabis
- Quetiapine most common (84.9%)
- Other antipsychotics - olanzapine (17.8%), risperidone (24.7%), aripiprazole (20.5%), ziprasidone (8.1%), and asenapine (2.9%)
- Goals: "getting mellow", "slowing down", or enhancing effects of other drugs

# Quetiapine DAWN ED visits



# Antidepressants

- Reports of abuse of all classes
- May have higher rates with SNRI
  - Stimulant effects due to norepinephrine reuptake inhibition
  - When used with opioids, pharmaceutical “speedball” effect
  - Adverse effects include seizures and dysrhythmias

# Cyclobenzaprine

- Reported via NPDS
- Few studies of misuse/abuse
- Anticholinergic effects
- Structural similarity to tricyclic antidepressants
- Anticipate synergistic CNS and respiratory depression with opioids

# Other Antiepileptics

- Nearly all have been reported both in single substance and polysubstance abuse cases
- Levitiracetam may be on the horizon
- Synergistic CNS depression with opioids
- Cardiac effects also possible



# Gaps in Knowledge

- What interventions are needed to decrease polysubstance abuse?
- Is postmarketing surveillance needed for nonopioid drugs?
- What education should be given to prescribers regarding risks?

# Summary

- **Nonopioid pharmaceutical drug abuse is becoming more common**
- **Many likely to be co-abused with opioids**
- **Synergistic CNS and respiratory depression most common interaction**
- **Need methods for surveillance and early warning**

# Questions?

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