

# Are Abuse Deterrent Formulations Effective?

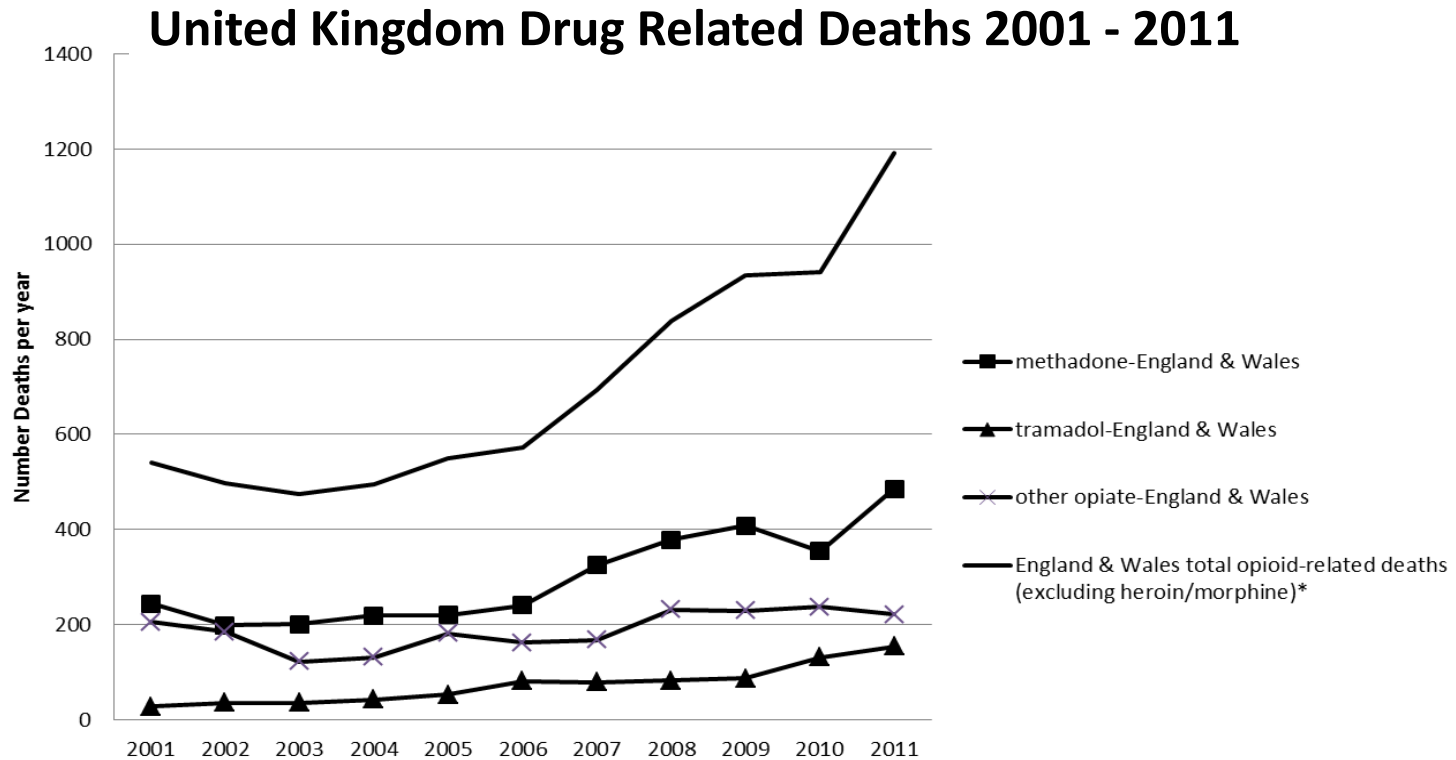
Richard C. Dart, MD, PhD

Director, Rocky Mountain Poison and Drug Center

Professor, University of Colorado

- **Venue:** The Fairfax Embassy Row Hotel, November 18, 2013, **Time:** 0915-1015 (15 min Q&A)
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- **Key objectives:** To understand the current level of misuse and diversion from the national RADARs data and the changing profile dependent on the increasing use of mono-buprenorphine
- 
- **Topics/Evidence to be addressed:**
- 
- Misuse and diversion – is this a common problem worldwide, examples in the OPD population, comparisons?
- Recent FDA decisions on morphine (rejected due to no abuse deterrence) and generic Oxycontin (not approved due to no abuse deterrence)
- Impact of abuse deterrent formulations on misuse and abuse
- Why it is important to favour abuse deterrent formulations and is it important in the OPD population?
- Diversion reflects the treatment system of the particular country/ access to treatment
- Diversion/drug street price = local demand
- Can we identify which patient will divert?
- Abuse deterrent formulations (in relation to overdose/mortality) – risk of different treatment

# Prescription Opioid Deaths are Rising Internationally



\*Note: heroin and morphine are reported as one category in the data from England, Wales and Scotland; since the focus of this analysis is on prescription opioids, that category was not included in this analysis.

# What is the RADARS<sup>®</sup> System?

- History
  - 2006, Denver Health and Hospital Authority (DHHA)
  - Multiple pharmaceutical subscribers
  - Independent program
  - Denver Public Safety Net Hospital for 150 years
  - State sanctioned independent authority
- Conflict of Interest Statement
  - None, other than running system for DHHA as noted above.



# RADARS System

## Scientific Advisory Board

### Principal Investigators

- Theodore J. Cicero, PhD  
*Washington University at St. Louis*
- Richard C. Dart, MD, PhD  
*Denver Health and Hospital Authority*
- Hilary Surratt, PhD  
*Nova Southeastern University*
- Mark W. Parrino, MPA  
*American Association for the Treatment of Opioid Dependence*



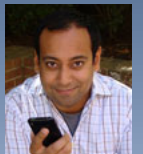
### Substance Abuse Experts

- Herbert D. Kleber, MD  
*Columbia University*
- Sidney Schnoll, MD, PhD  
*Pinney Associates*
- George E. Woody, MD  
*University of Pennsylvania*



### Epidemiology/Biostatistics

- Edgar Adams, ScD  
*Covance*
- Nabarun Dasgupta, MPH  
*Founder – Epidemico*
- Alvaro Muñoz, PhD  
*Johns Hopkins University*



### Law Enforcement

- John Burke  
*National Association of Drug Diversion Investigators*

# Challenges of Prescription Drug Abuse Surveillance

- Clandestine behavior
- Geographical variability
- Changes rapidly
- Multiple age groups
- Product specificity



– 15 active pharmaceutical ingredients (API)

- Opioids: Hydrocodone, oxycodone, hydromorphone, oxymorphone, morphine, fentanyl, tapentadol, tramadol, buprenorphine, methadone
- Stimulants

– Dozens of specific products (Vicodin, OxyContin, Opana ER, Suboxone, Subutex, etc.)

# RADARS System Mosaic

Acute Events

53 Poison  
Centers  
46 States

Drug  
Transactions

Criminal Justice  
280 investigator  
50 states

Entering  
Treatment

OTP  
73 programs  
33 states

Entering  
Treatment

SKIP  
125 practices  
50 states

New  
Initiates

College Survey  
2000 students  
50 States

Illicit Market  
Price

StreetRx.com  
Users/Buyers  
50 states

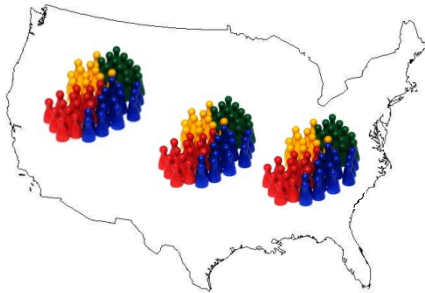


# RADARS<sup>®</sup> System Process

## Two Denominators



Numerators compiled by each program



**POPULATION RATE =  $\frac{\text{Event Count by Area}}{\text{Population}}$**

- Disease burden on population
- **Does not account for drug availability**



**UNIQUE RECIPIENTS OF DISPENSED DRUG (URDD) RATE =  $\frac{\text{Event Count by Area}}{\overline{\text{URDD}}}$**

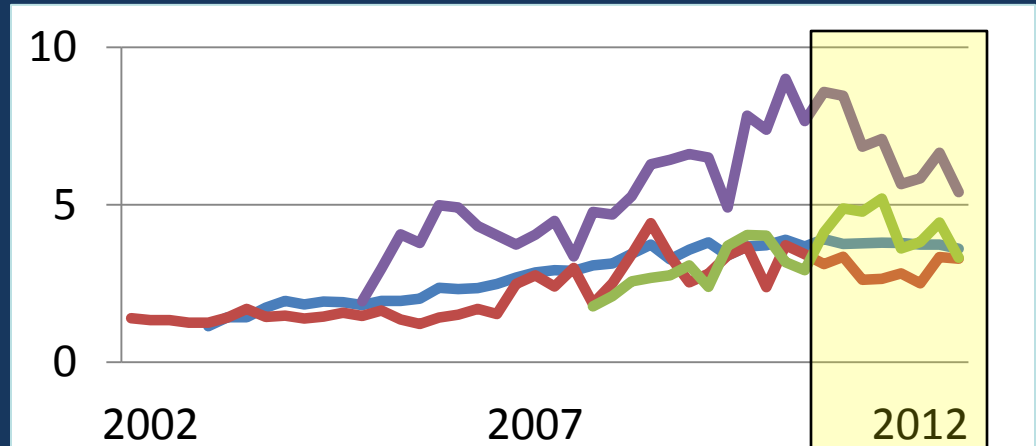
- URDD = Number of unique people filling prescription for drug (refills excluded)



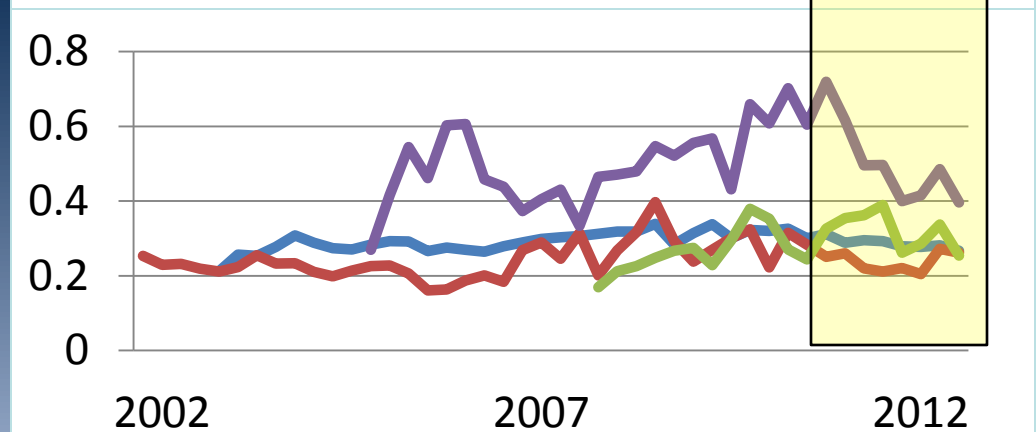
# TRENDS IN PRESCRIPTION OPIOID ABUSE IN THE UNITED STATES

# Overall Opioid Abuse Trends in United States Population Rates, 2002-2012

Population Rate



Availability Rate  
(URDD)



— Poison Center — Drug Diversion  
— SKIP — OTP

# RADARS System Opioid Abuse Trends

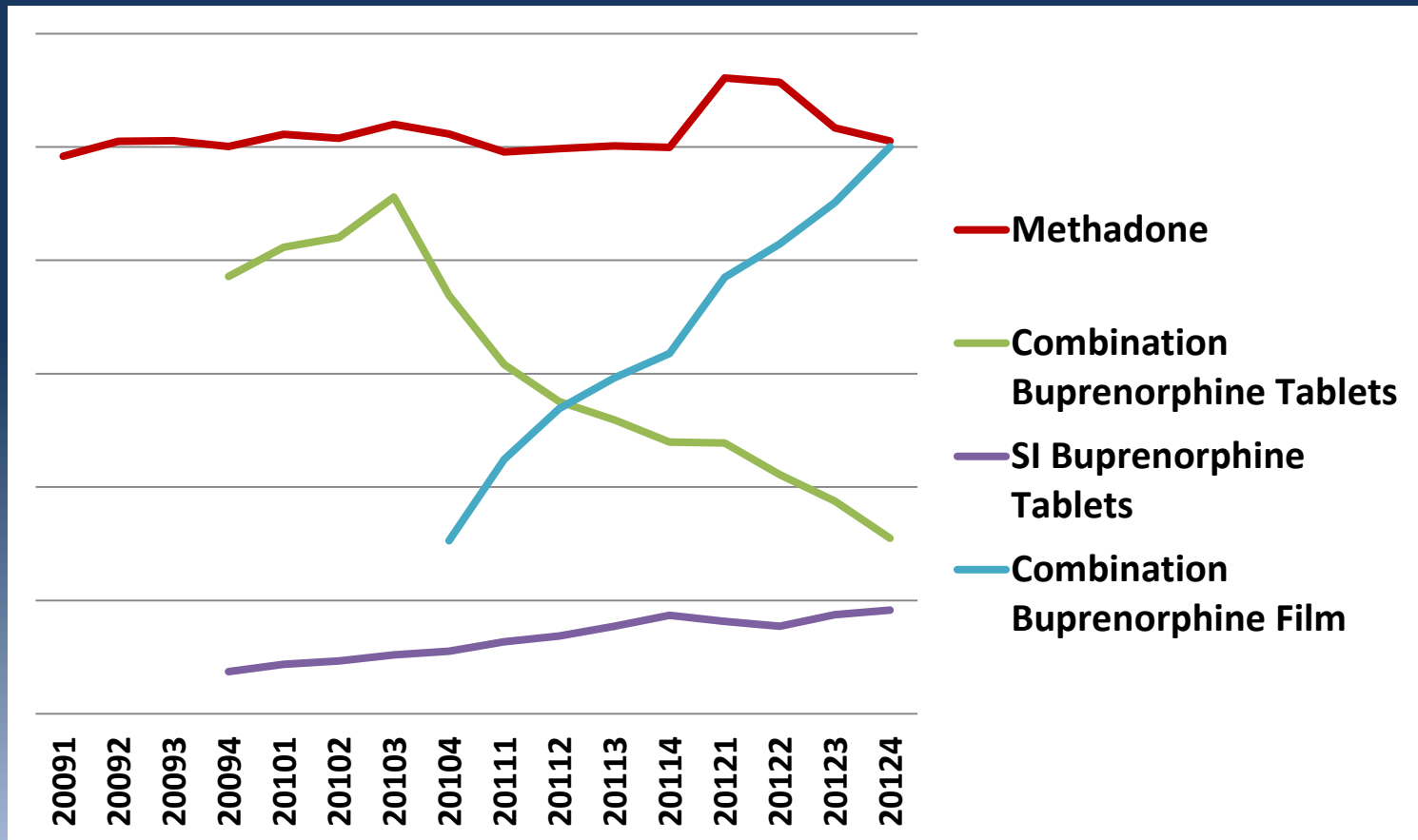
## URDD Rates (Ranked Highest-Lowest)

### 2012

Rank	Poison Center	Opioid Treatment	Survey of Key Informant Pts	Drug Diversion
1	Methadone	Oxymorphone	Oxymorphone	Oxymorphone
2	Oxymorphone	Methadone	Hydromorphone	Hydromorphone
3	Buprenorphine	Hydromorphone	Methadone	Methadone
4	Hydromorphone	Buprenorphine	Buprenorphine	Buprenorphine
5	Morphine	Morphine	Morphine	Morphine
6	Fentanyl	Fentanyl	Fentanyl	Oxycodone
7	Tramadol	Tapentadol	Tapentadol	Fentanyl
8	Oxycodone	Oxycodone	Oxycodone	Hydrocodone
9	Tapentadol	Hydrocodone	Hydrocodone	Tramadol
10	Hydrocodone	Tramadol	Tramadol	Tapentadol

# **BUPRENORPHINE AND METHADONE DATA FOR THE UNITED STATES**

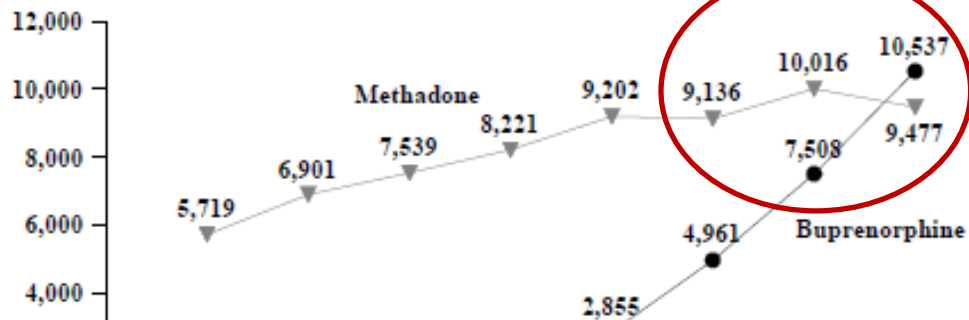
# How Many Patients Fill a Prescription? Unique Recipients of dispensed drug (URDD) 2009Q1 - 2012Q4



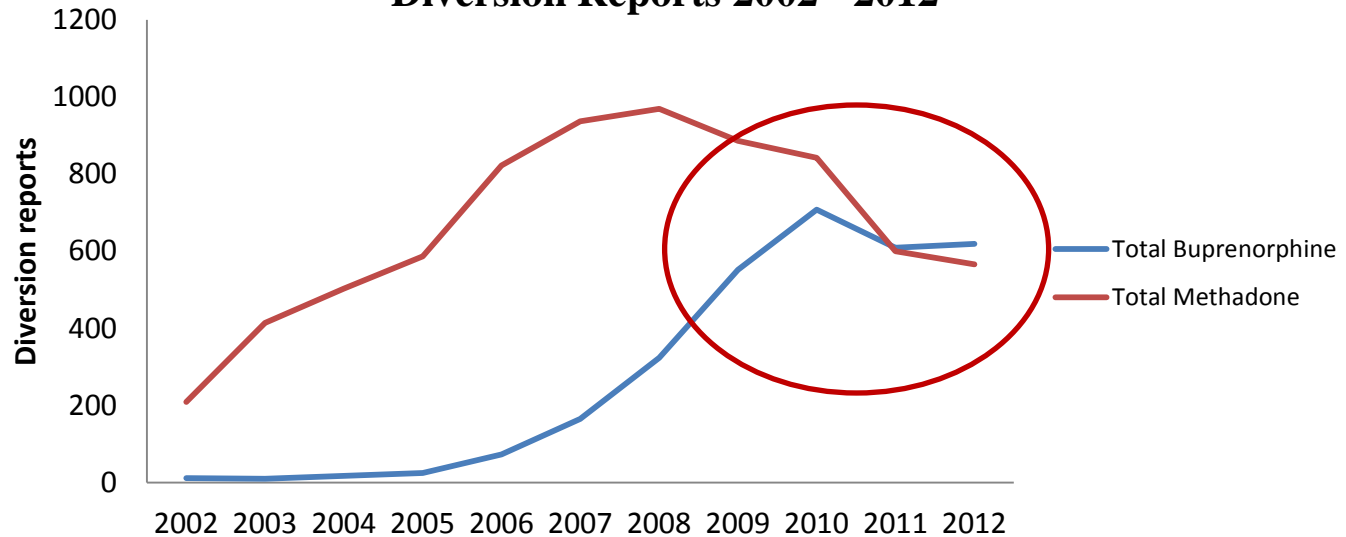
# Buprenorphine Data Comparison

## RADARS System & CESAR Fax

Estimated Number of Total Methadone and Buprenorphine Reports,  
U.S. Law Enforcement-Seized Drug Exhibits Analyzed by Forensic Laboratories, 2003-2010

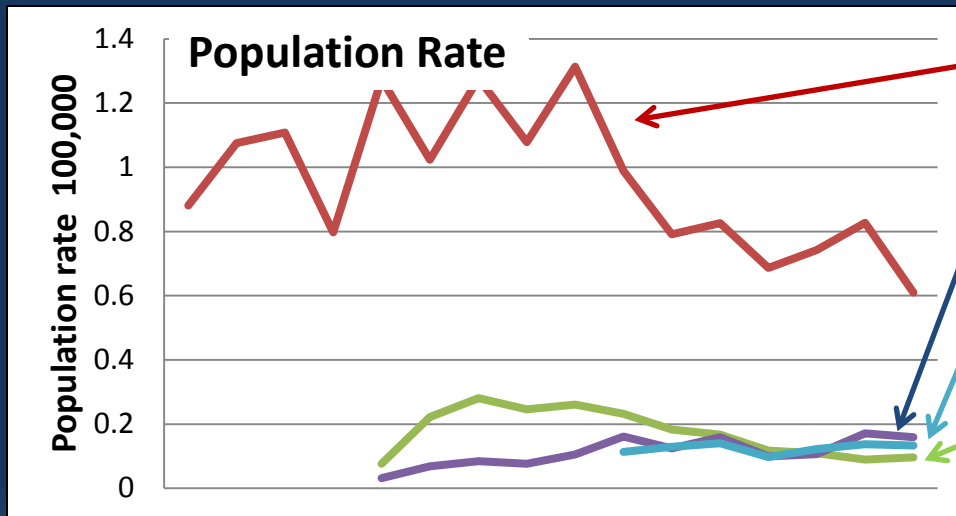


RADARS System Drug Diversion Program  
Diversion Reports 2002 - 2012



CESAR = Center for Substance Abuse Research

# Opioid Treatment Program Past 30 Day Endorsements, 2009-2012

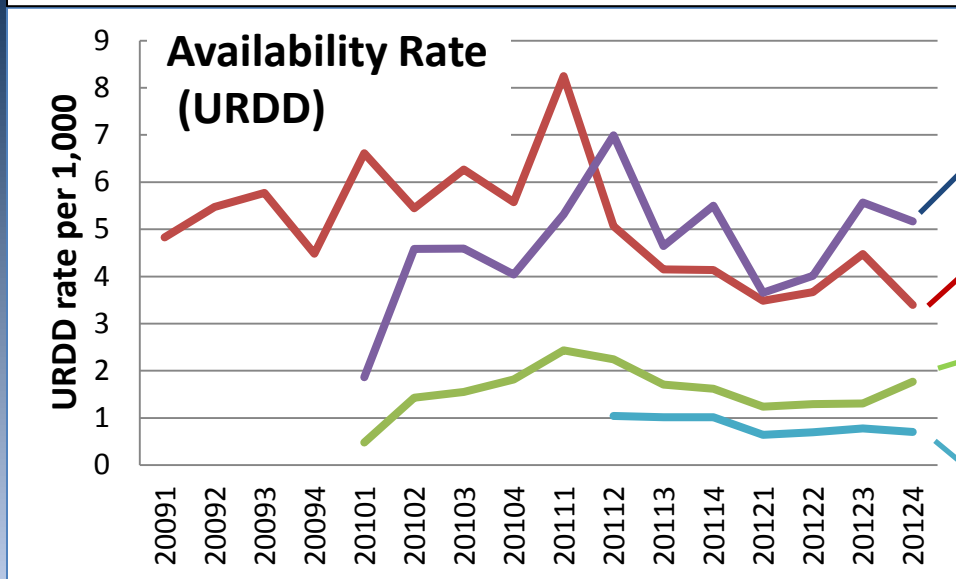


**Methadone high, but decreasing**

**Bup-Single Ingredient**  
Increasing slightly

**Bup-Naloxone Film Strip**  
increasing slightly

**Bup-Naloxone Combination**  
Decreasing Slightly



**Bup-Single Ingredient Highest,**  
Increased, Flat

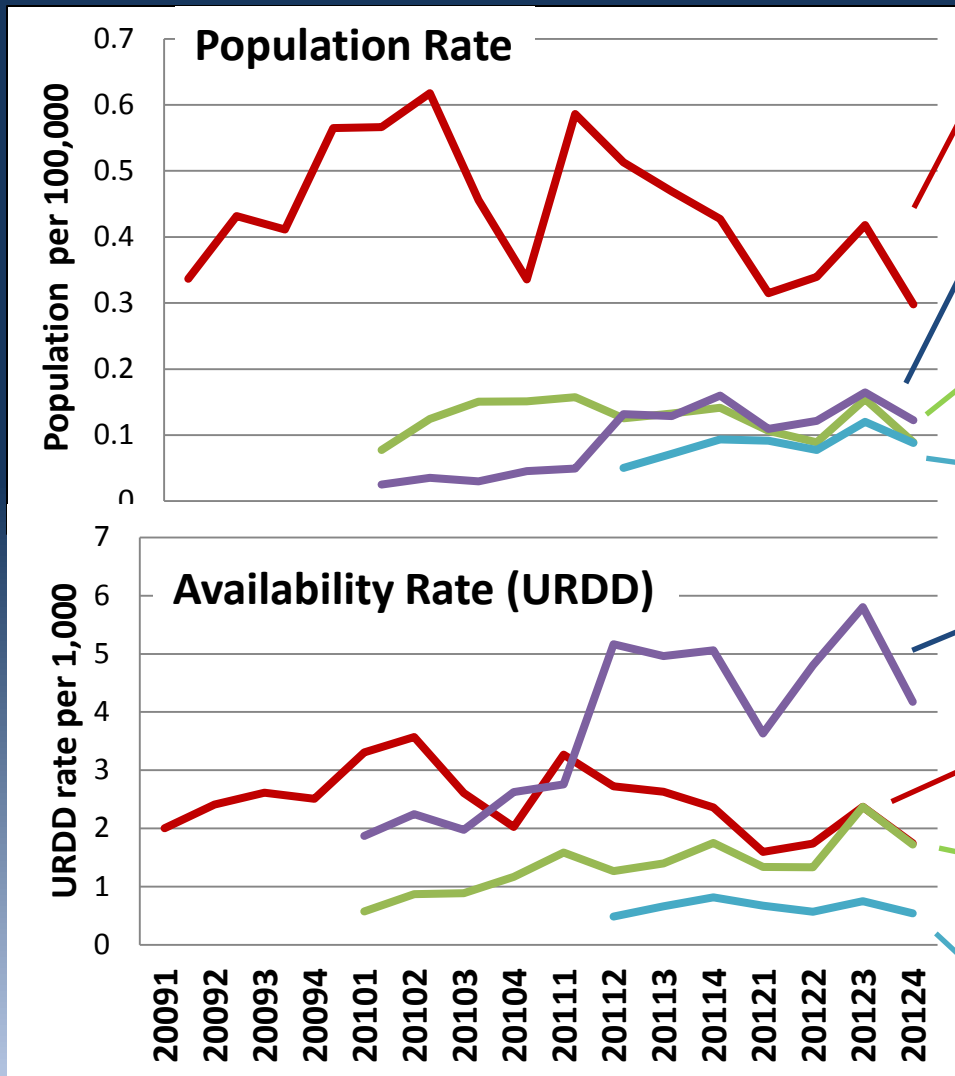
**Methadone Decreasing**

**Bup-Naloxone Combination**  
Lower, Flat

**Bup-Naloxone Film Strip**  
Lowest, Decreasing

# Survey of Key Informant Patients

## Past 30 Day Endorsements, 2009-2012



**Methadone high, but decreasing**

**Bup-*Single Ingredient* Increasing**

**Bup-Naloxone *Combination* Increasing Flat**

**Bup-Naloxone *Film Strip* Increasing slightly**

**Bup-*Single Ingredient* Increasing Dramatically**

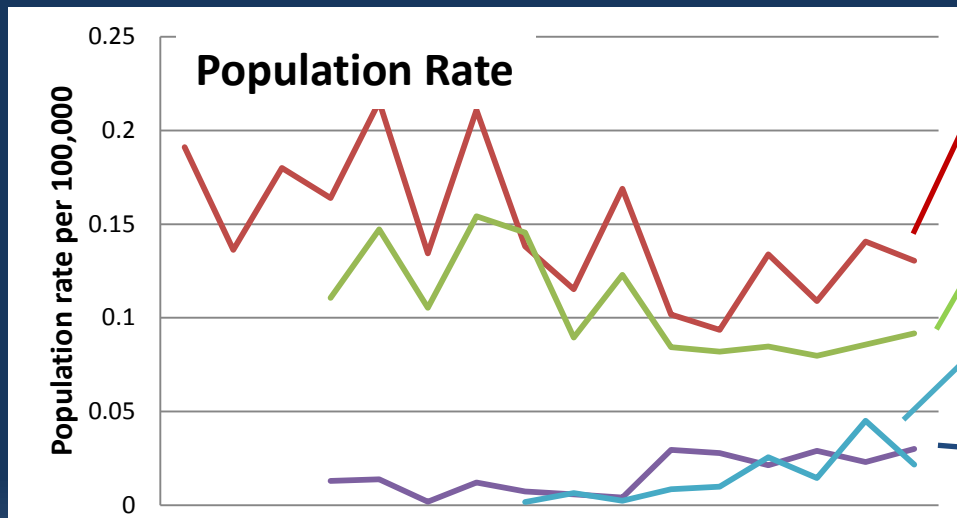
**Methadone Slight Decrease**

**Bup-Naloxone *Combination* Increasing**

**Bup-Naloxone *Film Strip* low, flat**



# RADARS System Drug Diversion Cases 2009-2012

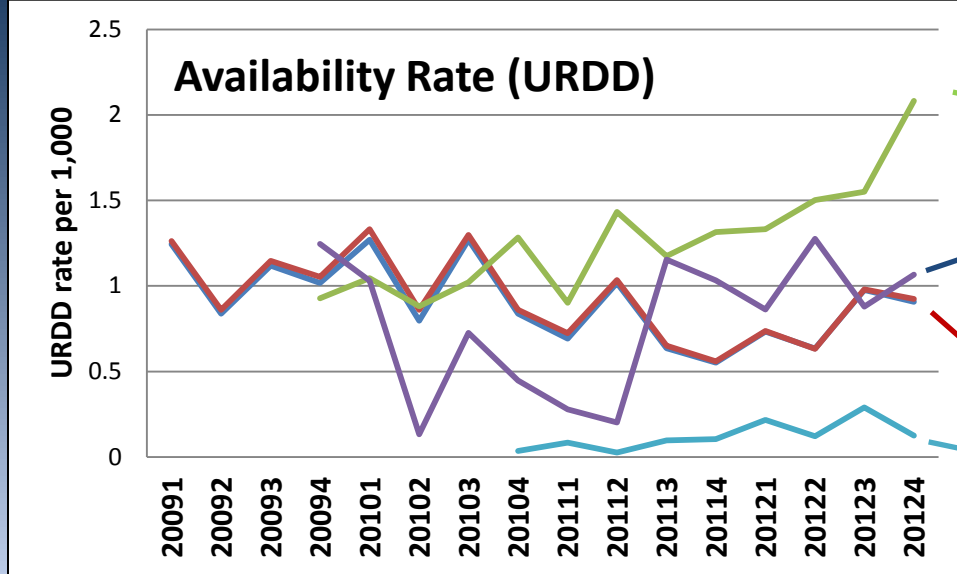


**Methadone high, but decreasing slightly**

**Bup-Naloxone *Combination* Decreasing Slightly**

**Bup-Naloxone *Film Strip* Increasing**

**Bup-*Single Ingredient* Increasing**



**Bup-Naloxone *Combination* Increasing Greatly**

**Bup-*Single Ingredient* Increasing Greatly**

**Methadone Slight Decrease**

**Bup-Naloxone *Film Strip* increasing slightly**

# Why Are Endorsements of Buprenorphine Strip So Low?

- The quickly replaced tablet in United States before generic tablets became available.
- But the rate of abuse endorsement was low
- Potential explanations
  - Misidentification
  - Serial numbers
  - Different packaging (child proof)
  - Others?

# StreetRx

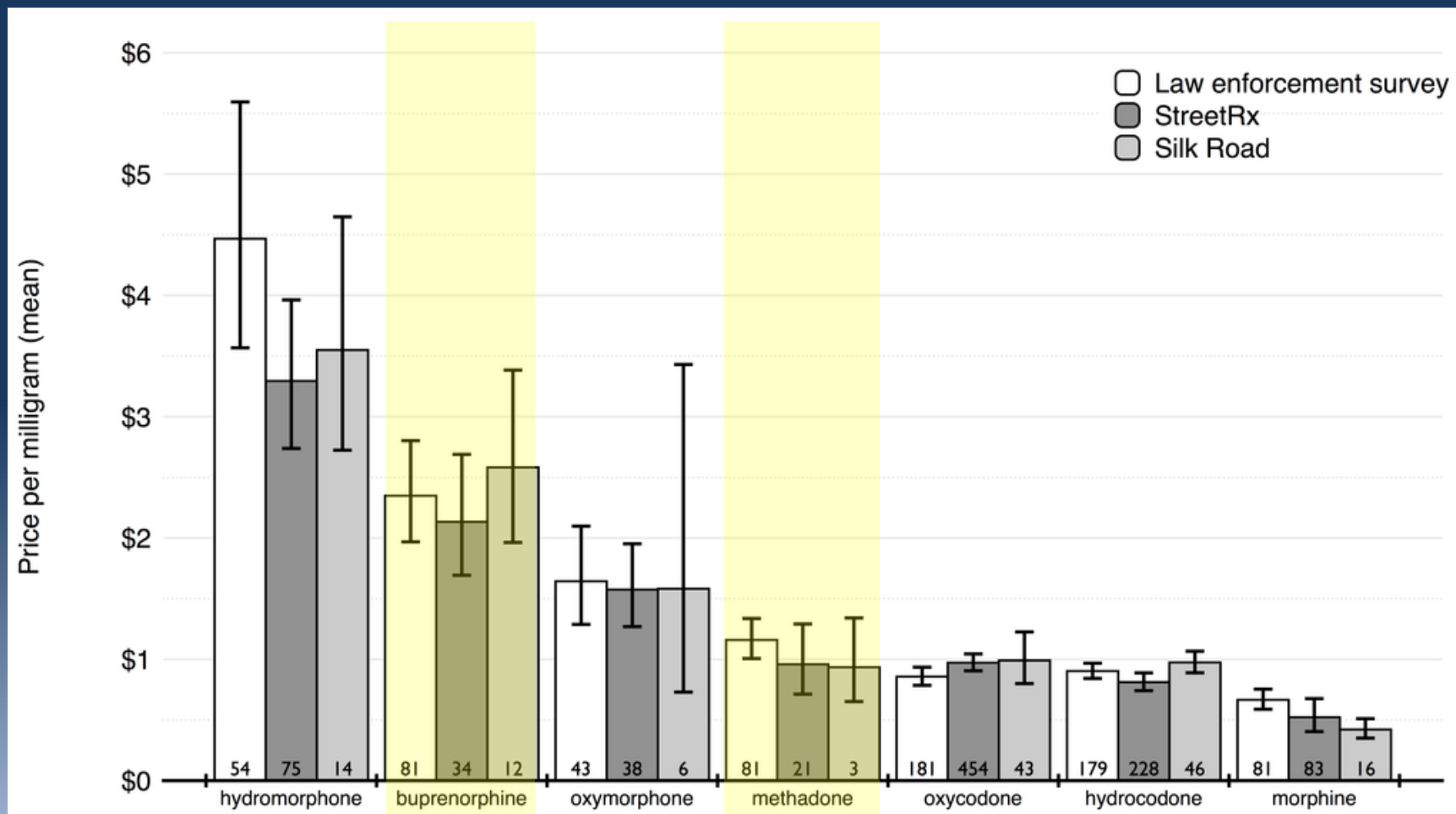
[www.streetrx.com](http://www.streetrx.com)

- **Population**
  - Any person in US with access to the internet
- **Definition/Type of Cases**
  - Utilize crowdsourcing methodology to calculate average price of specific prescription drug in particular location
  - Validated by DD
- **Coverage**
  - All 50 states

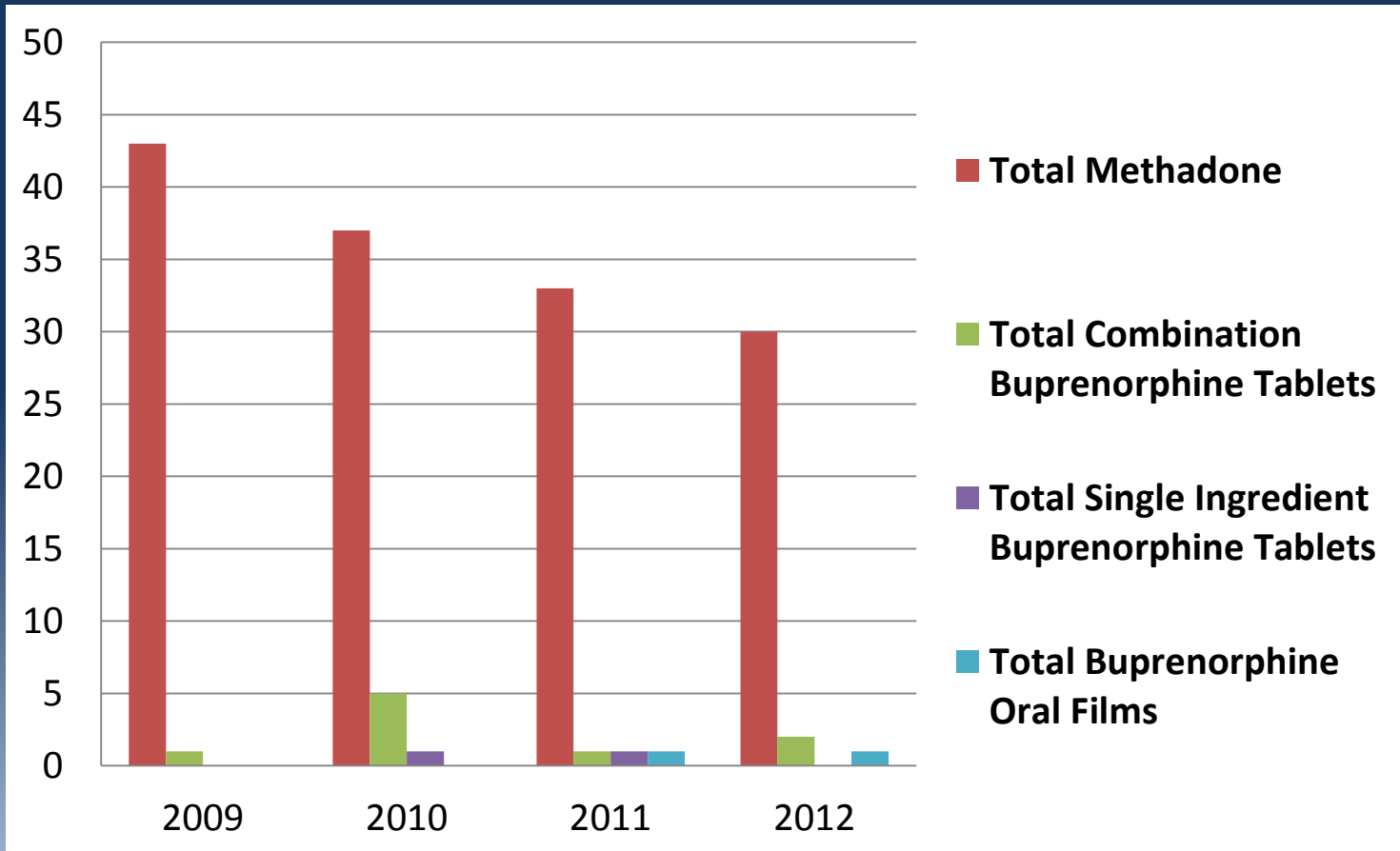
The screenshot shows the StreetRx website interface. At the top, the logo "streetRx" is displayed with the tagline "latest street prices for prescription drugs". Navigation links for "login", "Register", "Blog", and "Contact" are visible. A search bar contains the text "e.g. diauidid california" and a "Search" button. Below the search bar, there are three filter buttons: "All", "Most Popular", and "Best Price". The main content area is split into two sections. On the left, a form titled "Submissions are anonymous" asks "DID YOU GET a good deal?" and includes fields for "Name of drug\*", "City", "State\*", and "\$ Price\*", with a "Continue" button. On the right, a map of the United States is shown with numerous orange pins indicating drug prices across various locations. Below the map, a table titled "Latest prices in the US" displays drug information, location, price, date, and rating.

Drug	Location	Price	Date	Rating
Norco hydrocodone, 7.5/325mg pill	Chicago, Illinois	\$5	Mar 29	Rate: \$\$\$\$\$\$
oxycodone, 30mg pill	Fort Walton Beach, Florida	\$35	Mar 29	Rate: Overpriced \$\$\$\$\$\$
hydrocodone/APAP, 5mg pill	New York	\$2	Mar 28	Rate: \$\$\$\$\$\$
hydrocodone/APAP, 2.5mg pill	Arkansas	\$2	Mar 28	Rate: \$\$\$\$\$\$
MS Contin (generic morphine), 30mg pill	Salisbury, Maryland	\$15	Mar 28	Rate: \$\$\$\$\$\$
MS Contin (generic morphine), 1.5mg pill	Salisbury, Maryland	\$10	Mar 28	Rate: \$\$\$\$\$\$

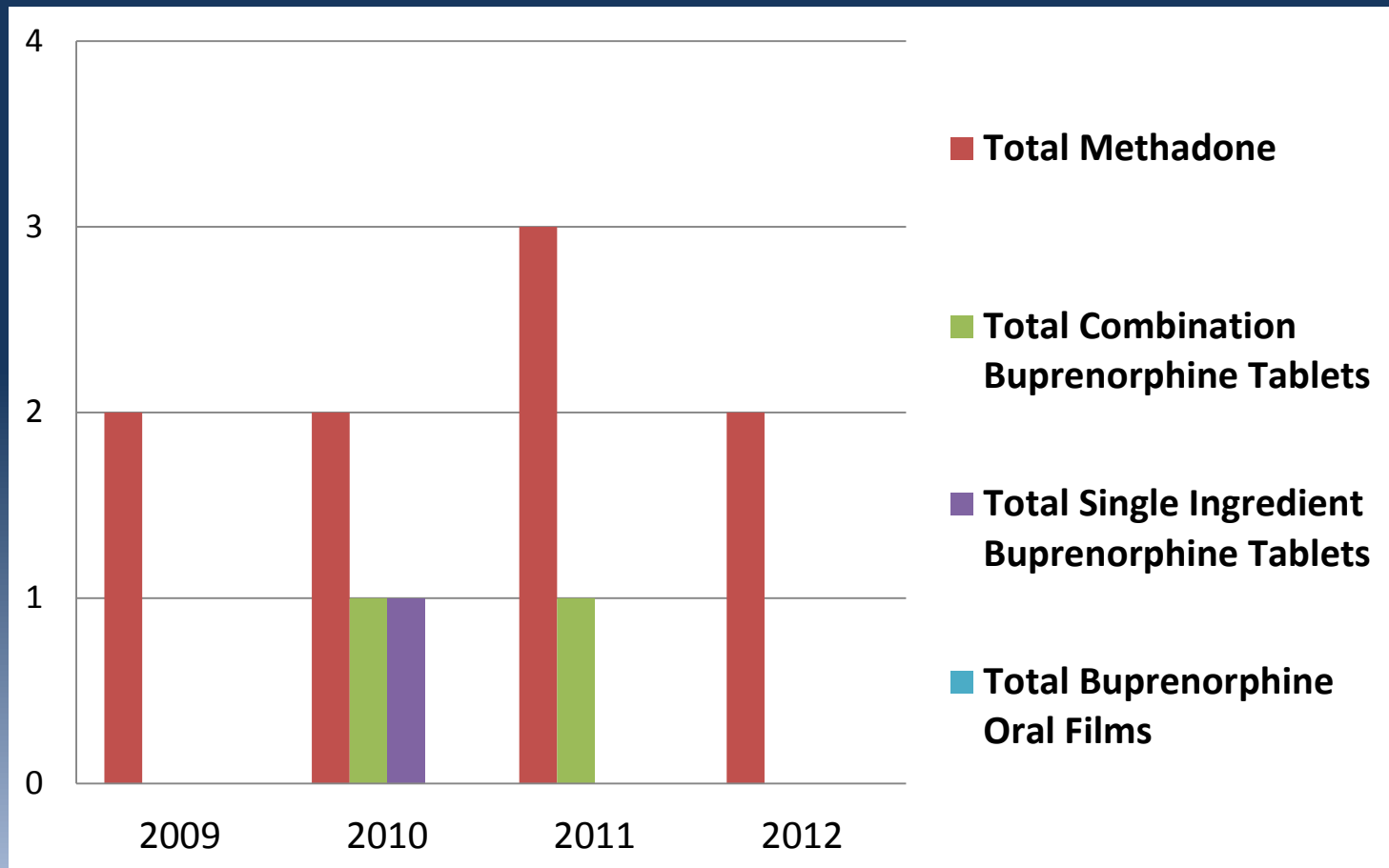
# Comparison of StreetRx, RADARS System Drug Diversion and Silk Road – Price per milligram of drug



# Death Cases in Poison Center Program All Ages, 2009Q1 - 2012Q4



# Death Cases in Poison Center Program Ages under 12 years, 2009Q1 - 2012Q4



# Conclusions

- Prescription opioid abuse in the US may be plateauing, but still causes 16,000 deaths per year
- Methadone
  - Endorsements in treatment programs decreasing
  - **More deaths than any other opioid**
  - But many deaths involve pills (treatment of pain)
- Buprenorphine
  - Endorsements are relatively flat, but there is dramatic shift of products involved
  - **Abuse is increasing quickly perhaps due to generic availability**
    - Single-ingredient “Subutex”
    - Combination tablet (Bup-naloxone; “Suboxone”)
  - **Exceptional safety in all groups**
  - Endorsement of buprenorphine strip has been very low. Diversion has also been low.
  - Why is the price of buprenorphine so high

Thank you!