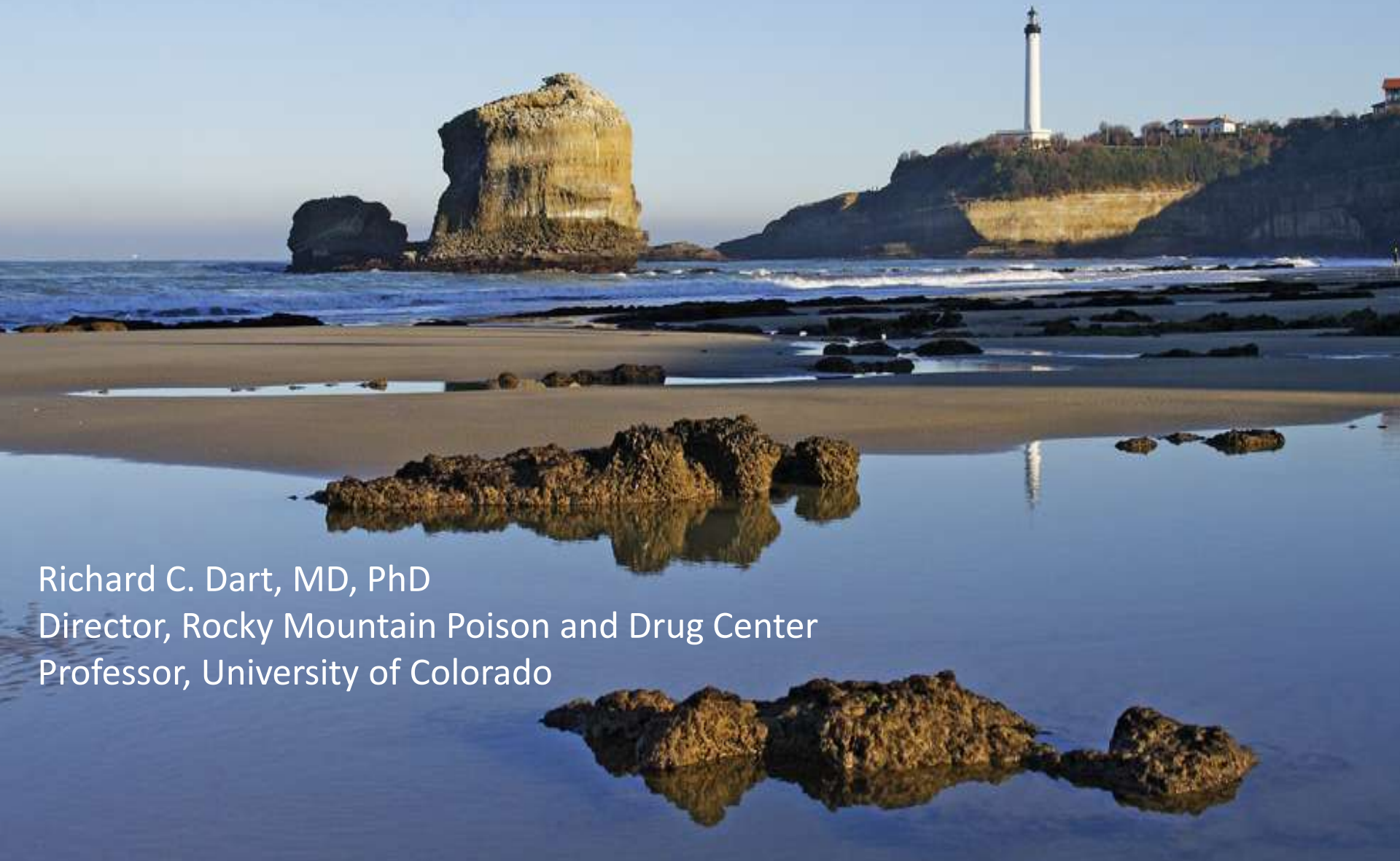
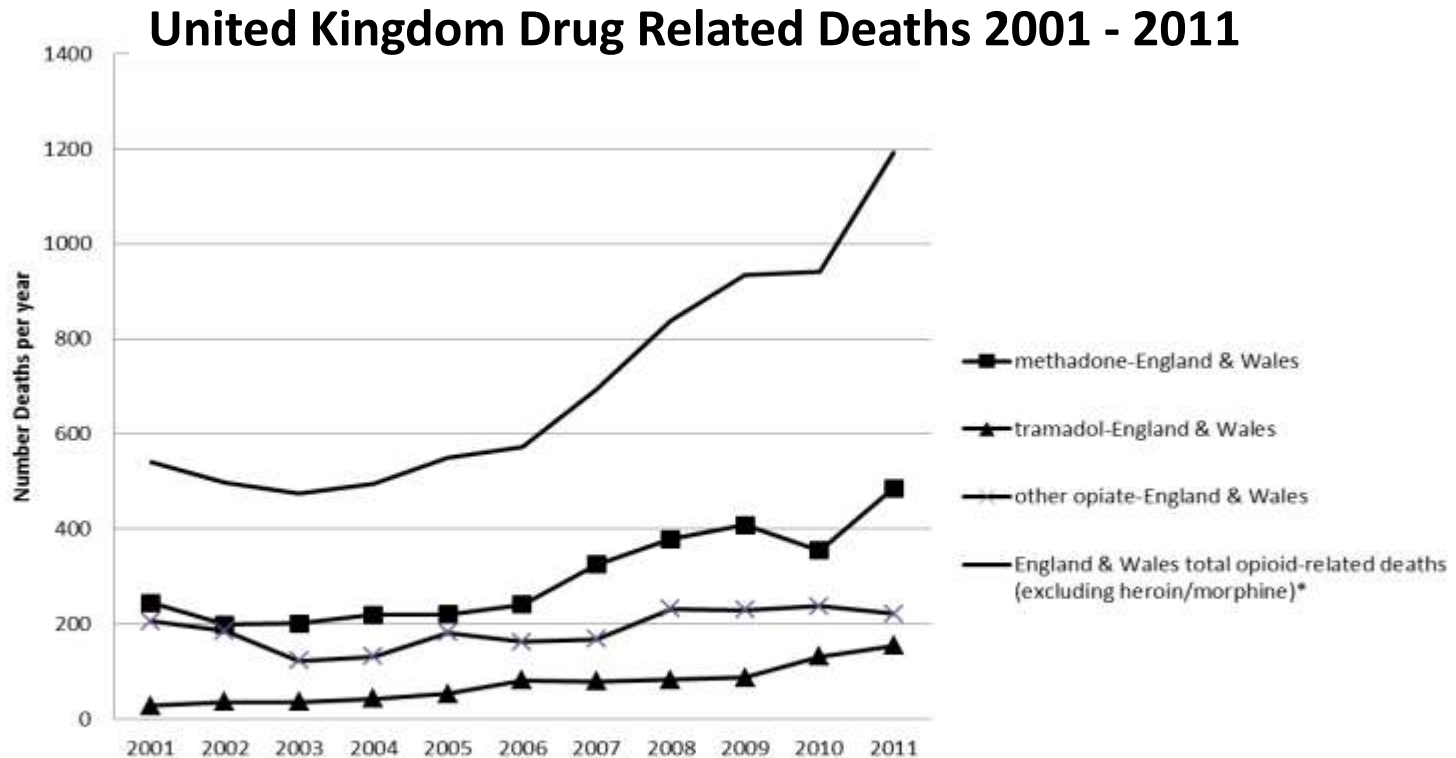


Diversion, Misuse and Trafficking of Methadone and Buprenorphine in the US and Europe



Richard C. Dart, MD, PhD
Director, Rocky Mountain Poison and Drug Center
Professor, University of Colorado

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[®] 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



Law Enforcement

- John Burke
National Association of Drug Diversion Investigators



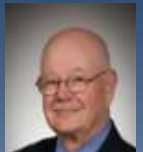
Substance Abuse Experts

- 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



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

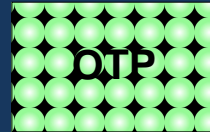
Illicit Market
Price

StreetRx.com
Users/Buyers
50 states

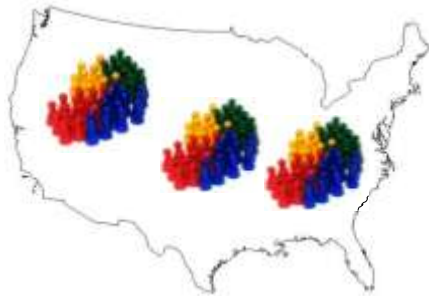


RADARS[®] System Process

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 = $\frac{\text{Event Count by Area}}{\text{URDD}}$

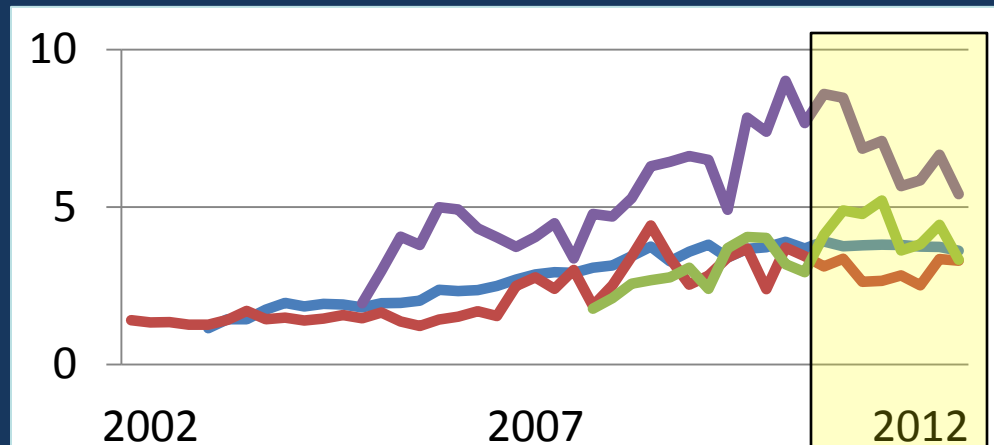
- URDD = Number of unique people filling prescription for drug (refills excluded)

TRENDS IN PRESCRIPTION OPIOID ABUSE IN THE UNITED STATES

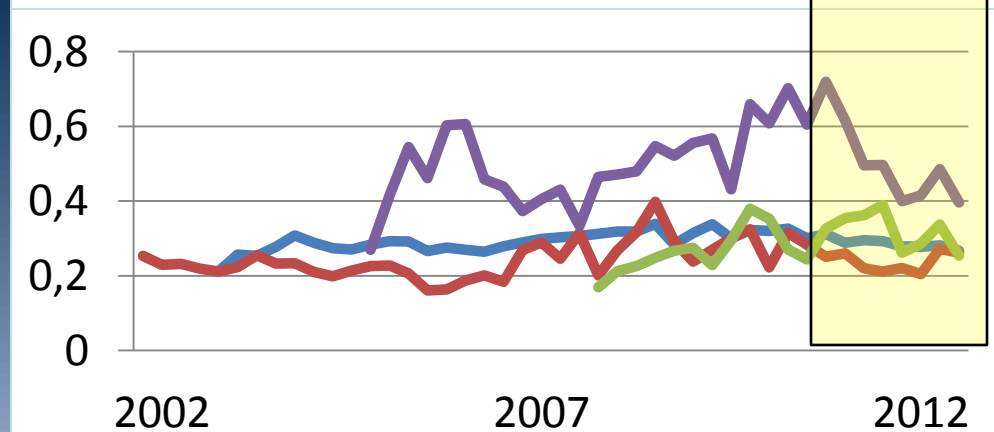
Overall Opioid Abuse Trends in United States

Population Rates, 2002-2012

Population Rate



Availability Rate (URDD)



— Poison Center — Drug Diversion
— SKIP — OTP

RADARS System Opioid Abuse Trends

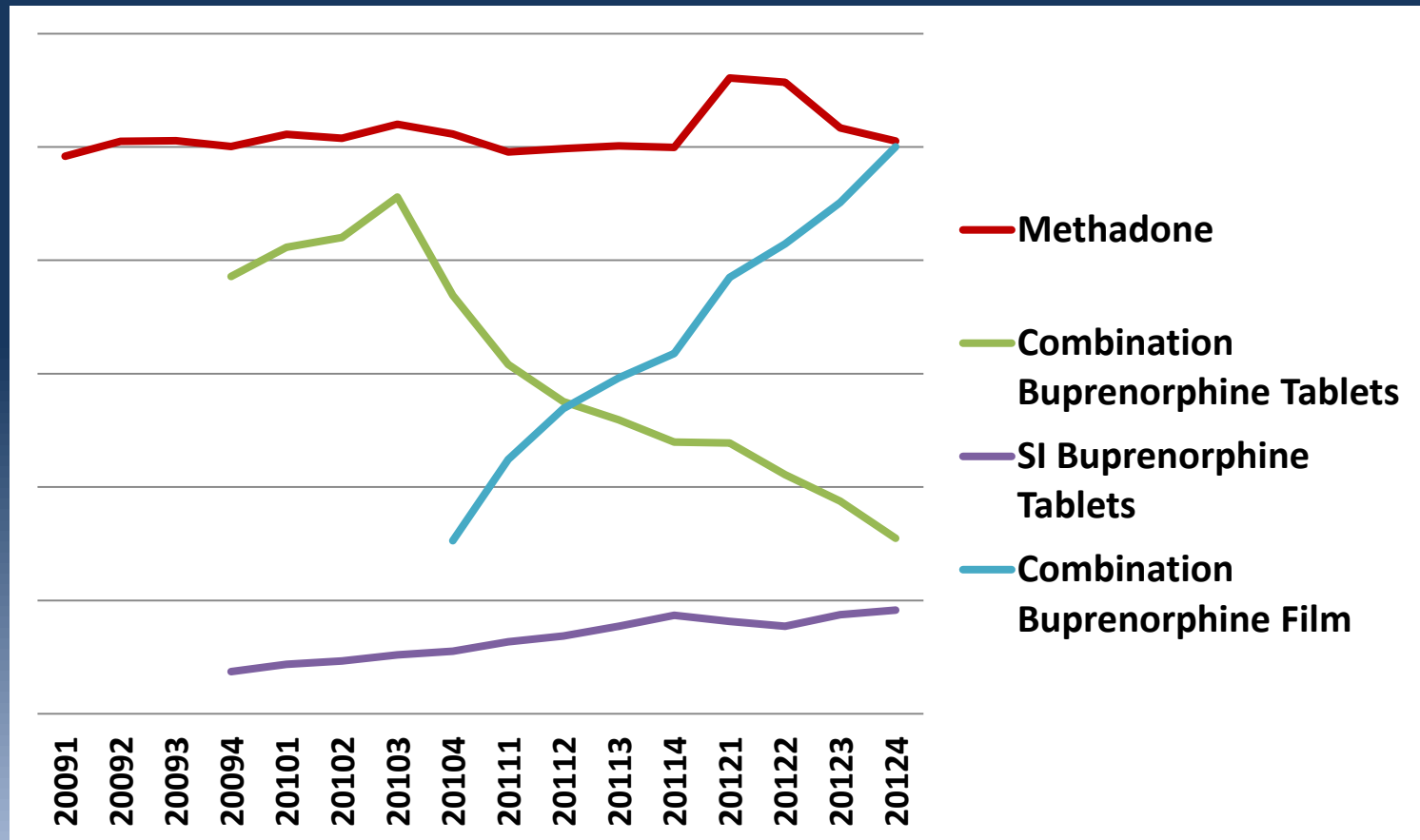
URDD Rates (Ranked Highest-Lowest)

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

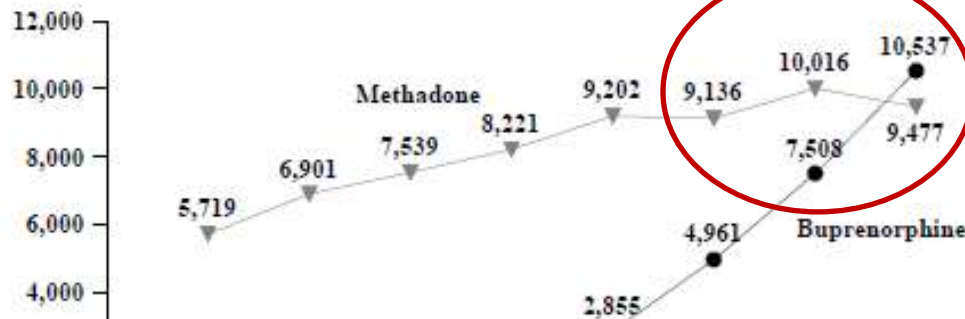
How Many Patients Fill a Prescription? Unique Recipients of dispensed drug (URDD) 2009Q1 - 2012Q4



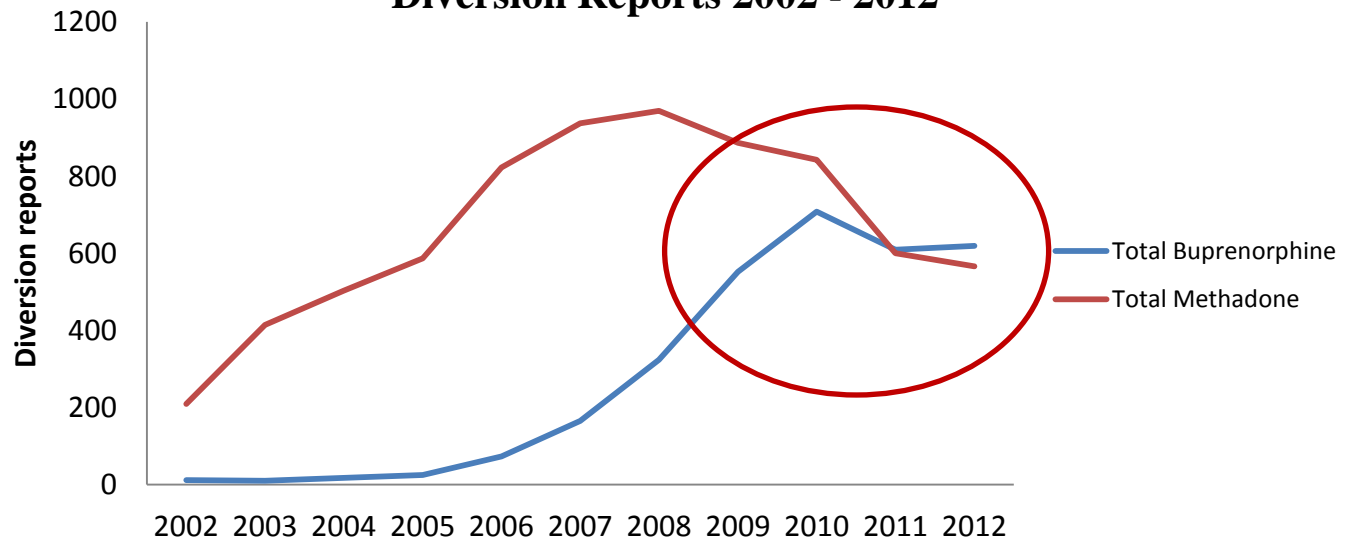
Buprenorphine Data Comparison

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



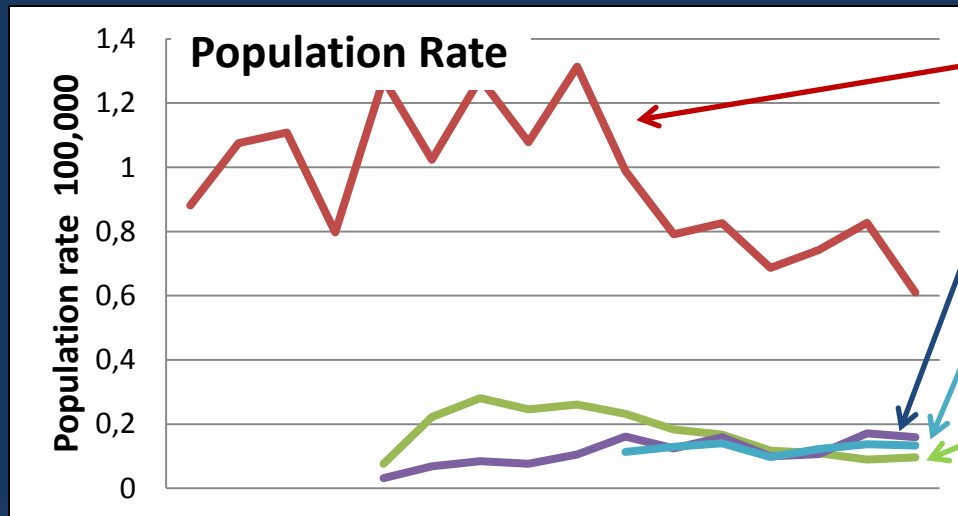
RADARS System Drug Diversion Program
Diversion Reports 2002 - 2012



CESAR = Center for Substance Abuse Research

Opioid Treatment Program

Past 30 Day Endorsements, 2009-2012

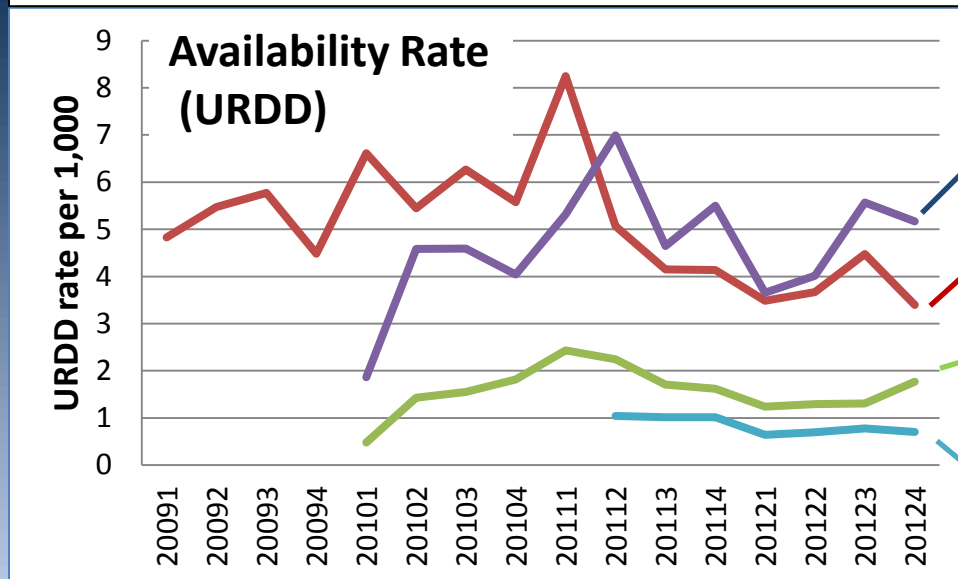


Methadone high, but decreasing

Bup-Single Ingredient
Increasing slightly

Bup-Naloxone Film Strip
increasing slightly

Bup-Naloxone Combination
Decreasing Slightly



Bup-Single Ingredient Highest,
Increased, Flat

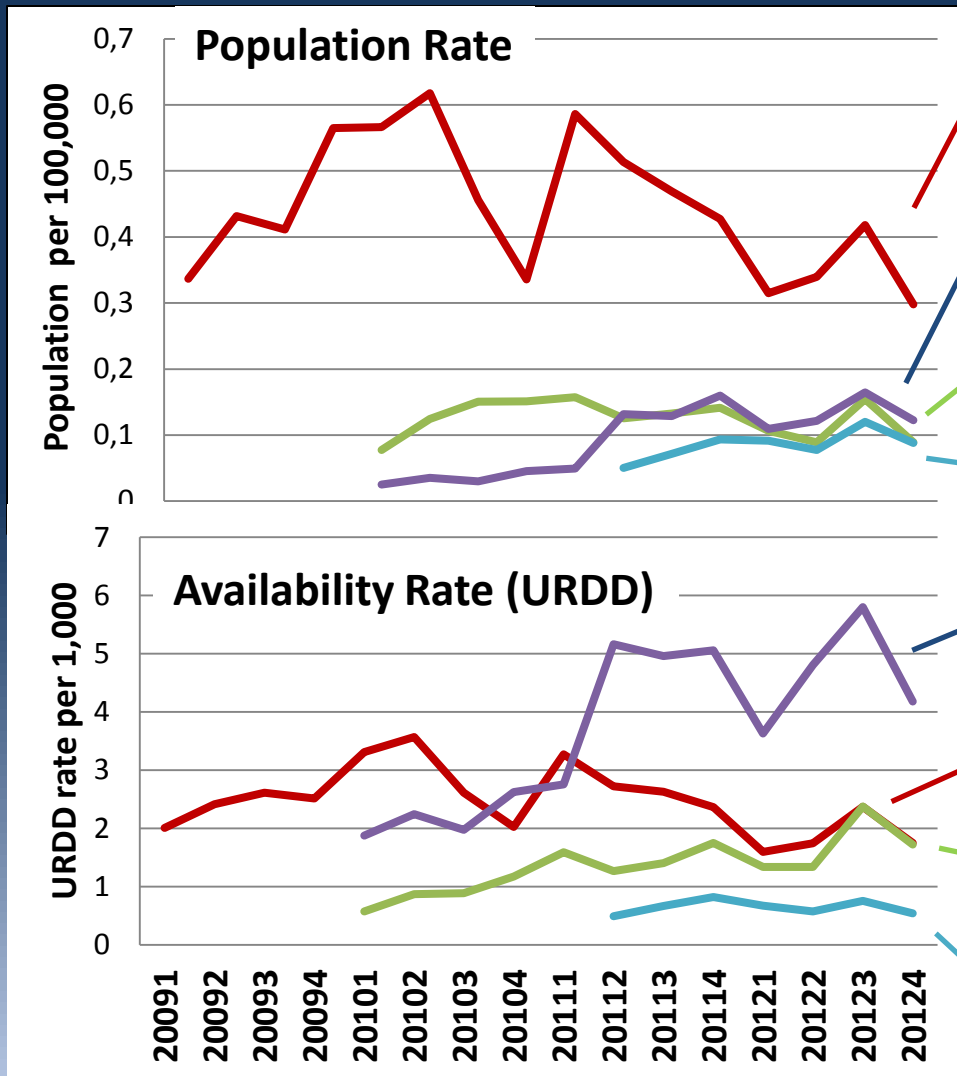
Methadone Decreasing

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

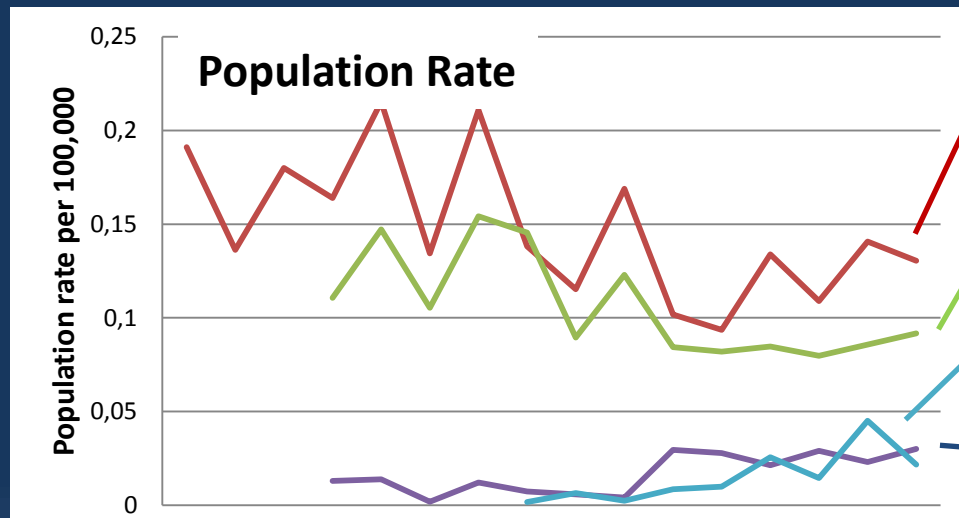
Bup-Single Ingredient Increasing Dramatically

Methadone Slight Decrease

Bup-Naloxone Combination Increasing

Bup-Naloxone Film Strip low, flat

RADARS System Drug Diversion Cases 2009-2012

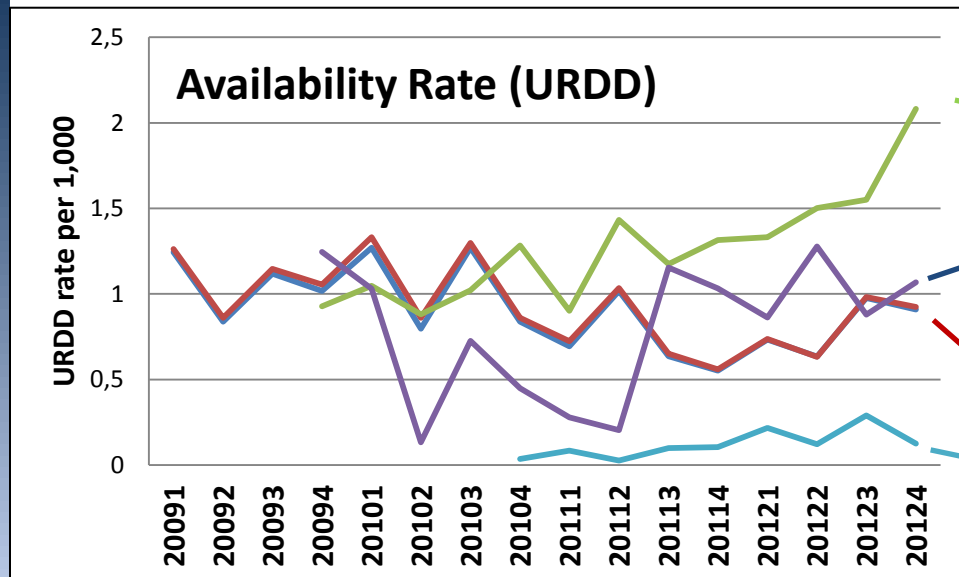


Methadone high, but decreasing slightly

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

- **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, there is a navigation bar with the StreetRx logo and the tagline "latest street prices for prescription drugs". Below the navigation bar, there is a search form with fields for "Name of drug*", "City", "State*", and "\$ Price*", along with a "Continue" button. To the right of the search form is a map of the United States with numerous orange markers indicating drug prices in various locations. Below the map is a table titled "Latest prices in the US" with columns for Drug, Location, Price, Date, and Rating. The table lists several drugs and their prices in different locations, including Chicago, Fort Walton Beach, New York, and Salisbury, Maryland.

Submissions are anonymous
DID YOU GET a good deal?

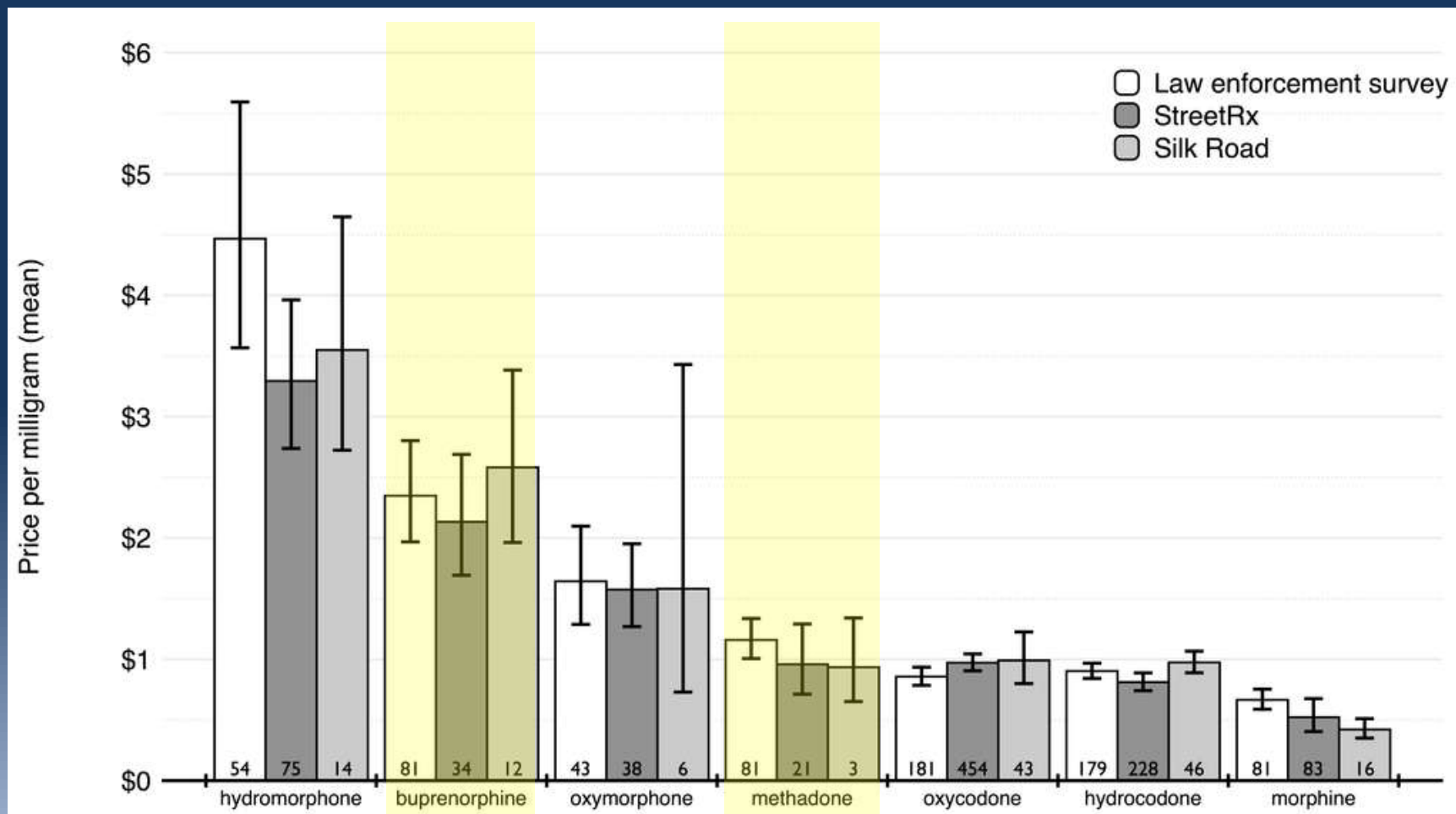
Name of drug*
City State*
\$ Price*
Continue

See what **OTHERS** paid
e.g. diazepam california Search

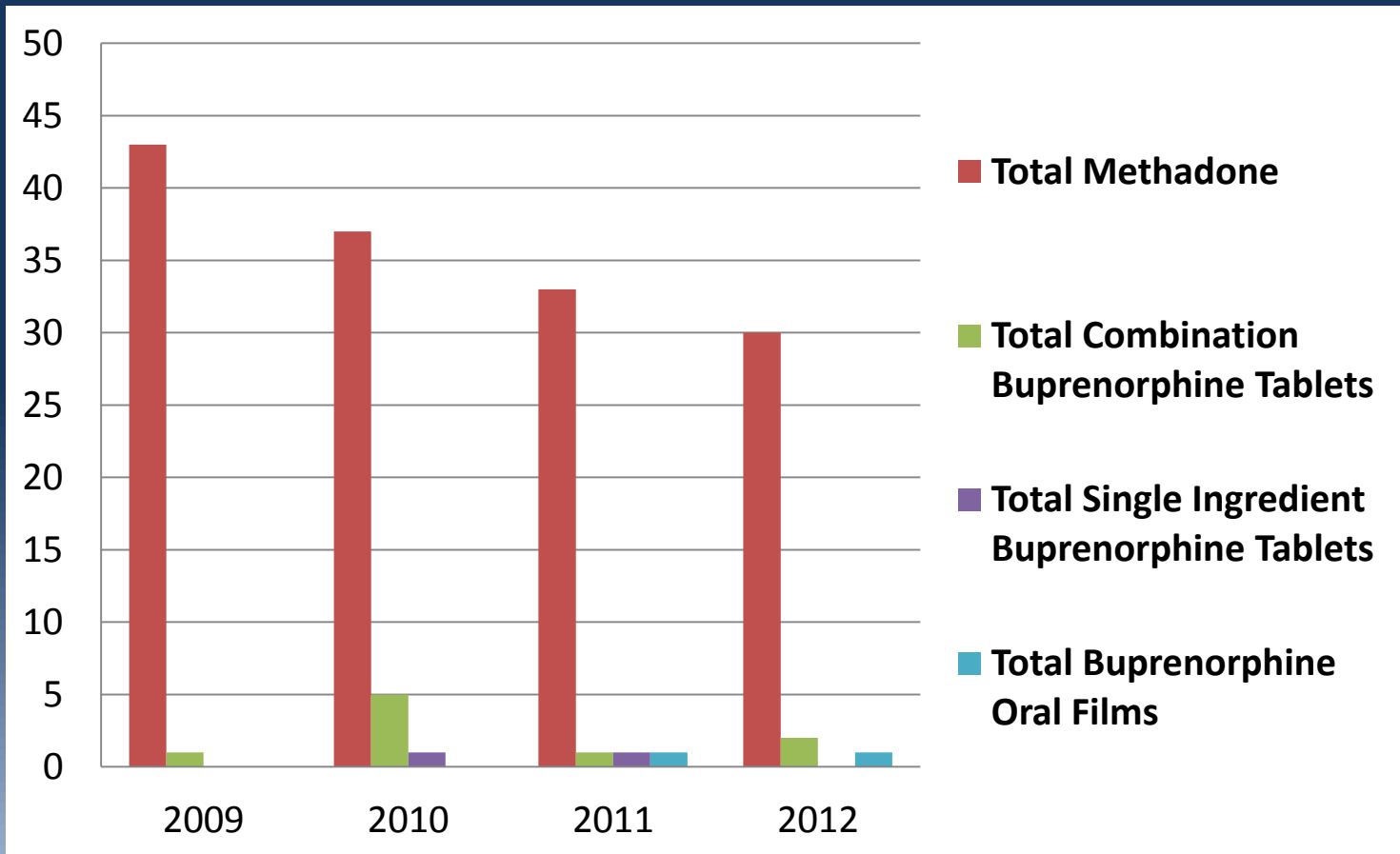
Show me:
All
Most Popular
Best Price

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), 15mg pill	Salisbury, Maryland	\$10	Mar 28	Rate: \$ \$ \$ \$ \$ \$

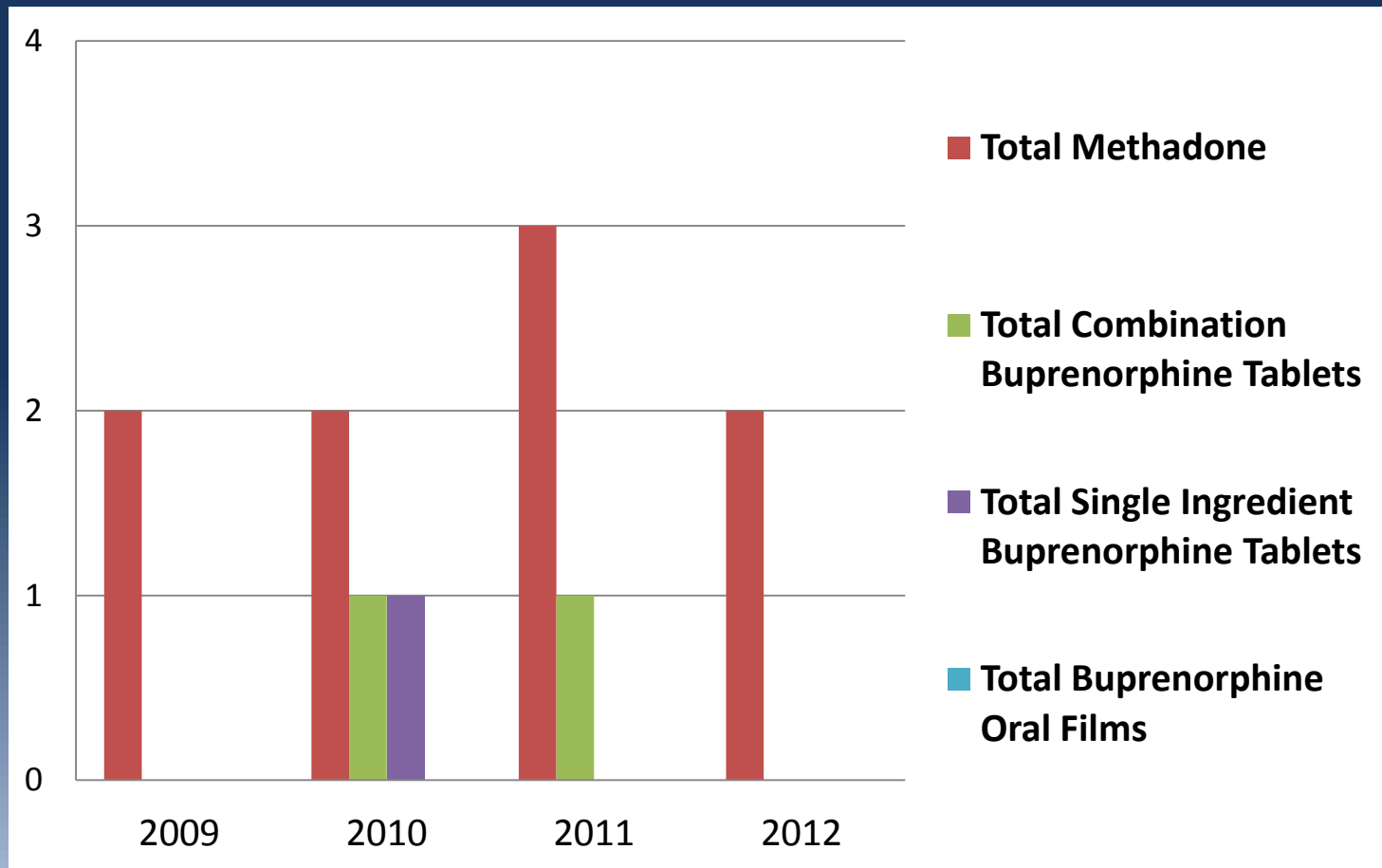
Comparison of StreetRx, RADARS System Drug Diversion and Silk Road – Price per milligram of drug



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!