Substance Use Disorders: It's a Tough Row to Hoe

NARTC Webinar

January 25, 2017

David Kan, M.D., D.F.A.S.A.M.

Diplomate Am. Bd. Psychiatry & Neurology in Psychiatry & Forensic Psychiatry
Asst. Clinical Professor Psychiatry, UCSF School of Medicine
Associate, Forensic Psychiatric Associates Medical Corporation
President-Elect, California Society of Addiction Medicine
655 Redwood Hwy., Suite 271,Mill Valley, CA 94941
415 812 1092 dkan@fpamed.com

Mark I. Levy, M.D., D.L.F.A.P.A

Medical Director, **fpamed**
Asst. Clinical Professor Psychiatry, UCSF School of Medicine
Inquiries Contact: 415 388 8040 mlevy@fpamed.com

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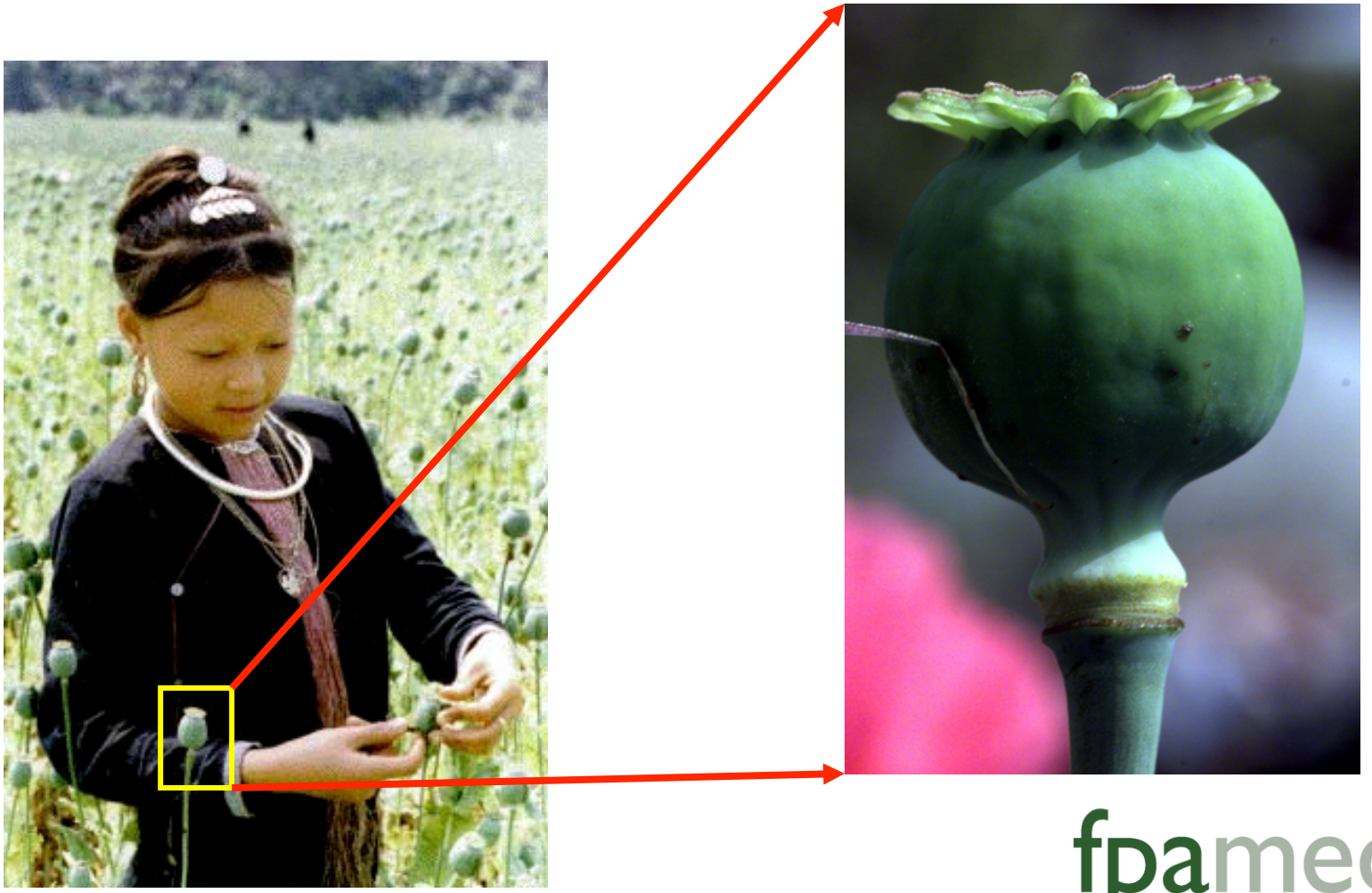
History of Opioids

The “Pod of Pleasure”



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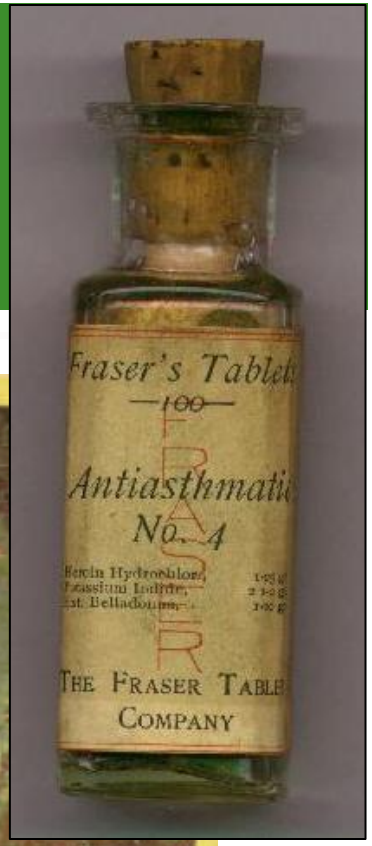
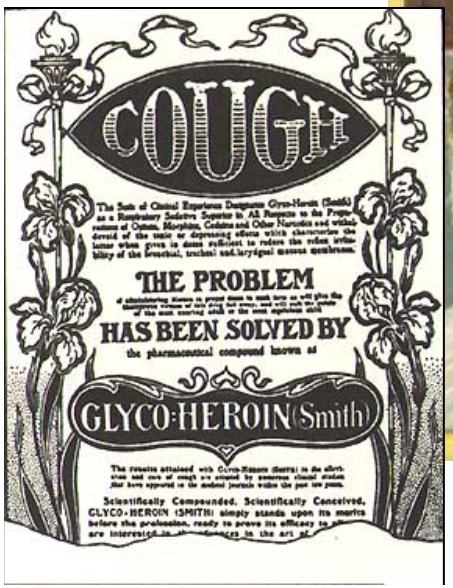
OTC Opiates


AYER'S
AYER'S CHERRY PECTORAL
Cures Colds, Coughs & all Diseases
of the Throat and Lungs


Fraser's Tablet
100
Antiasthmatic
No. 4
FRASER
THE FRASER TABLET
COMPANY


1887
Mrs. Winslow's
SOOTHING
SYRUP
FOR CHILDREN TEETHING


COUGH
THE PROBLEM
HAS BEEN SOLVED BY
the pharmaceutical compound known as
GLYCO-HEROIN (Smith)
Scientifically Compounded. Scientifically Conceived.

Opioids

- Naturally Occurring
  - Opium, Tincture of Opium (Laudanum), Camphorated Tincture of Opium (Paregoric), Morphine, Codeine
- Semi-Synthetic
  - Hydromophone (Dilaudid), Oxycodone (Percocet, Oxycontin), diacetylmorphine (heroin), Hydrocodone (Vicodin, Zohydro)
- Synthetic
  - Meperidine (Demerol), pentazocine (Talwin), methadone (Dolophine), propoxyphene (Darvon)

Opioids

- Opioids
  - Narcotic pain reliever
  - Side effects: sedation, constipation, itching, nausea, respiratory suppression, dependence, addiction, death
  - Indicated for:
    - Short-term acute pain
      - Postsurgical
      - Acute injury
  - Very limited evidence for
    - Chronic non-cancer pain

America Loves Opioids

- Americans are 4.6% of the world's population, but we consume:
  - 80% of the global opioid supply
  - 99% of the global hydrocodone supply
  - 2/3 of the world's illegal drugs

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Size of the Problem

- Between 1999 and 2010,
  - # of rx of controlled prescription drugs jumped 400%
  - # of overdose deaths increase 400%
  - Between 2010-2013 heroin OD deaths doubled
  - In 2012 OD exceeded car accidents in preventable cause of death
  - In 2015 Heroin OD exceeded gun homicide in preventable cause of death

- Controlled prescription drugs (i.e. - opiates, stimulants, sedatives, and tranquilizers) are now the 4th most abused substances in America
  - Behind marijuana, alcohol, and tobacco
  - 2012 NSDUH survey showed lifetime non-medical use of psychotherapeutics = 20% of the US population (48 million adults)
  - Opiates are the most common prescription drugs of abuse

Who Prescribes Opioids

- According to 2013-2014 CDC data:
  - 40% of opioid prescriptions come from primary care physicians
  - 39% come from emergency department physicians

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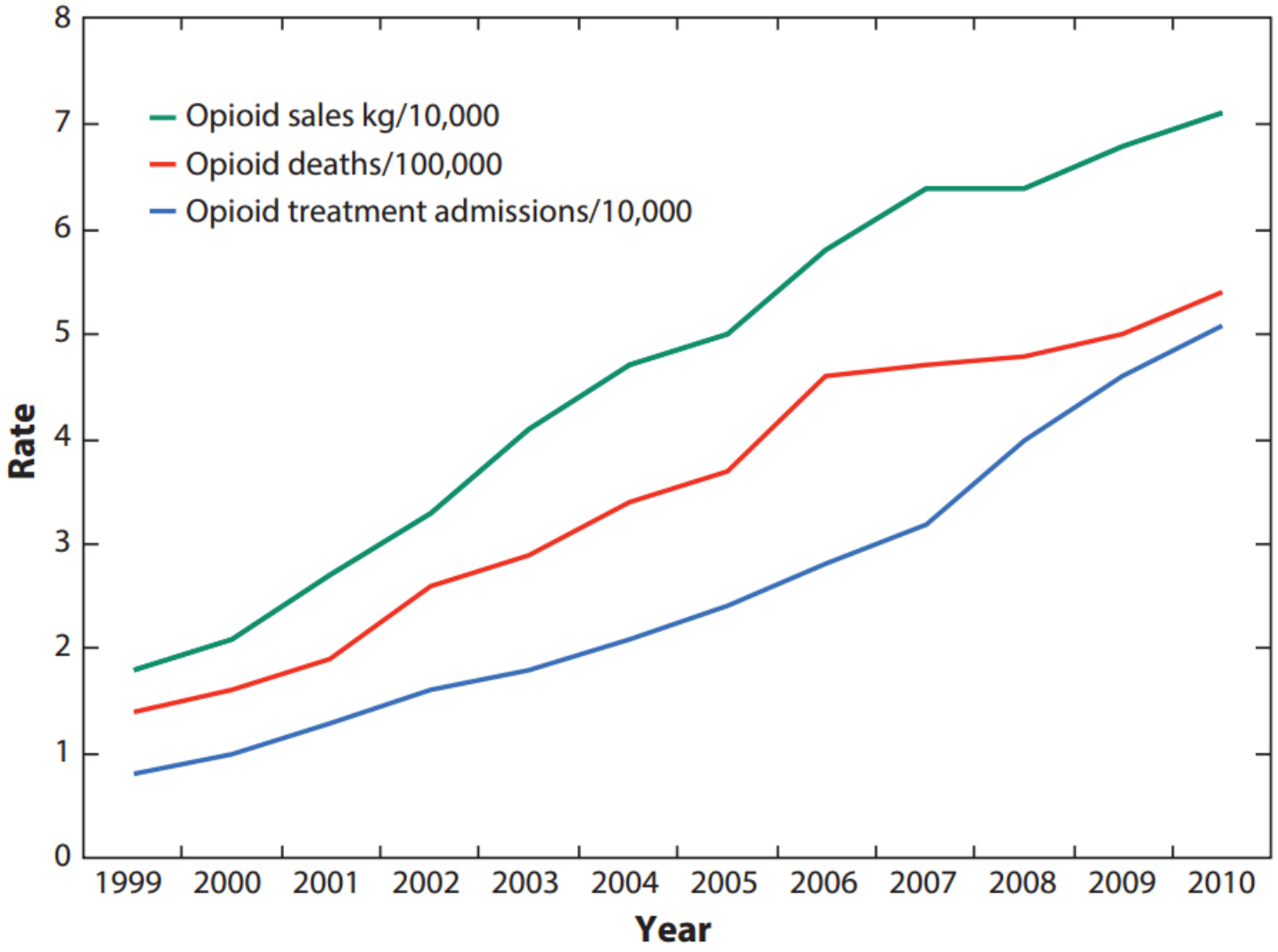
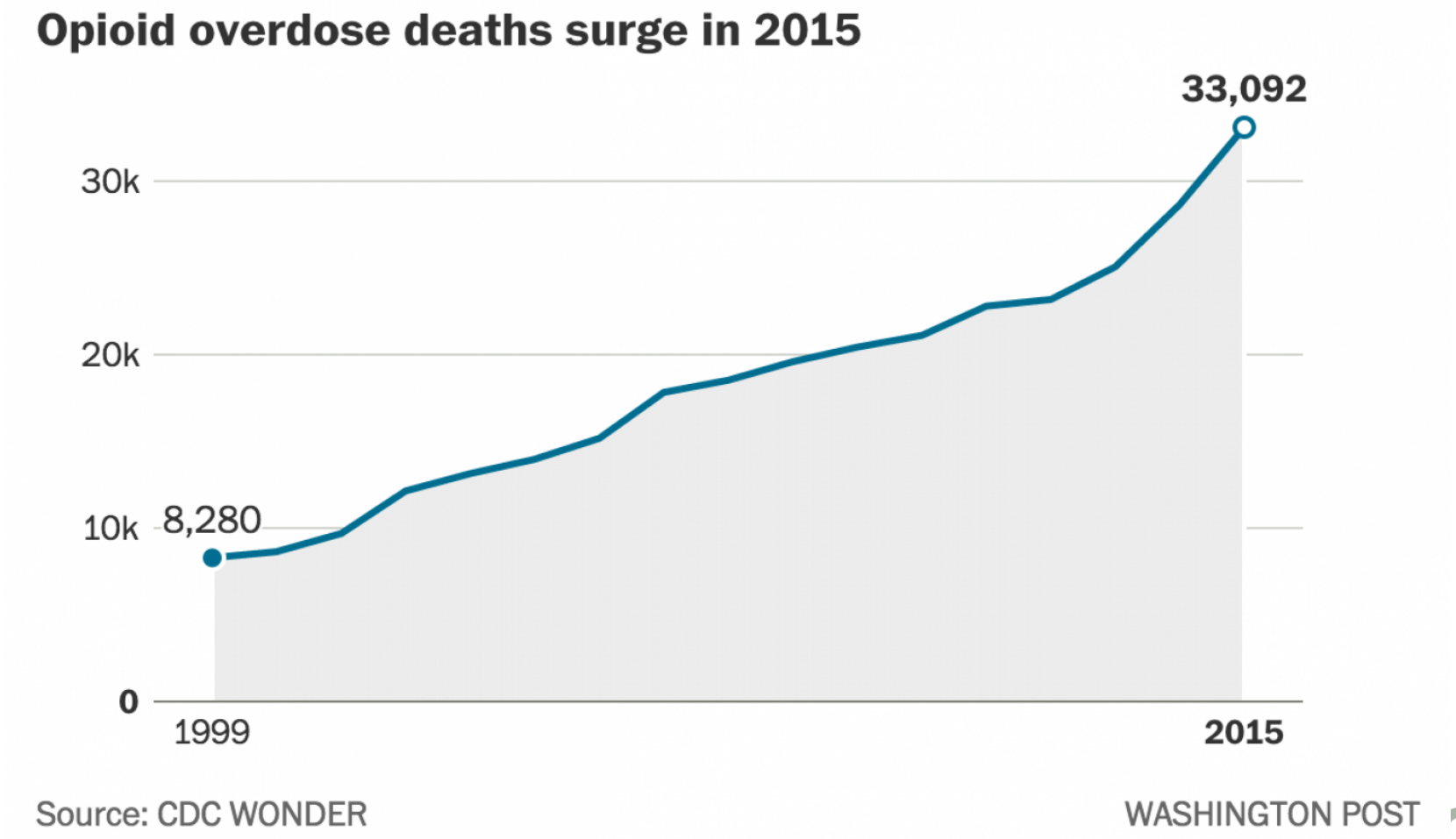
Opioid Sales 2001-2012

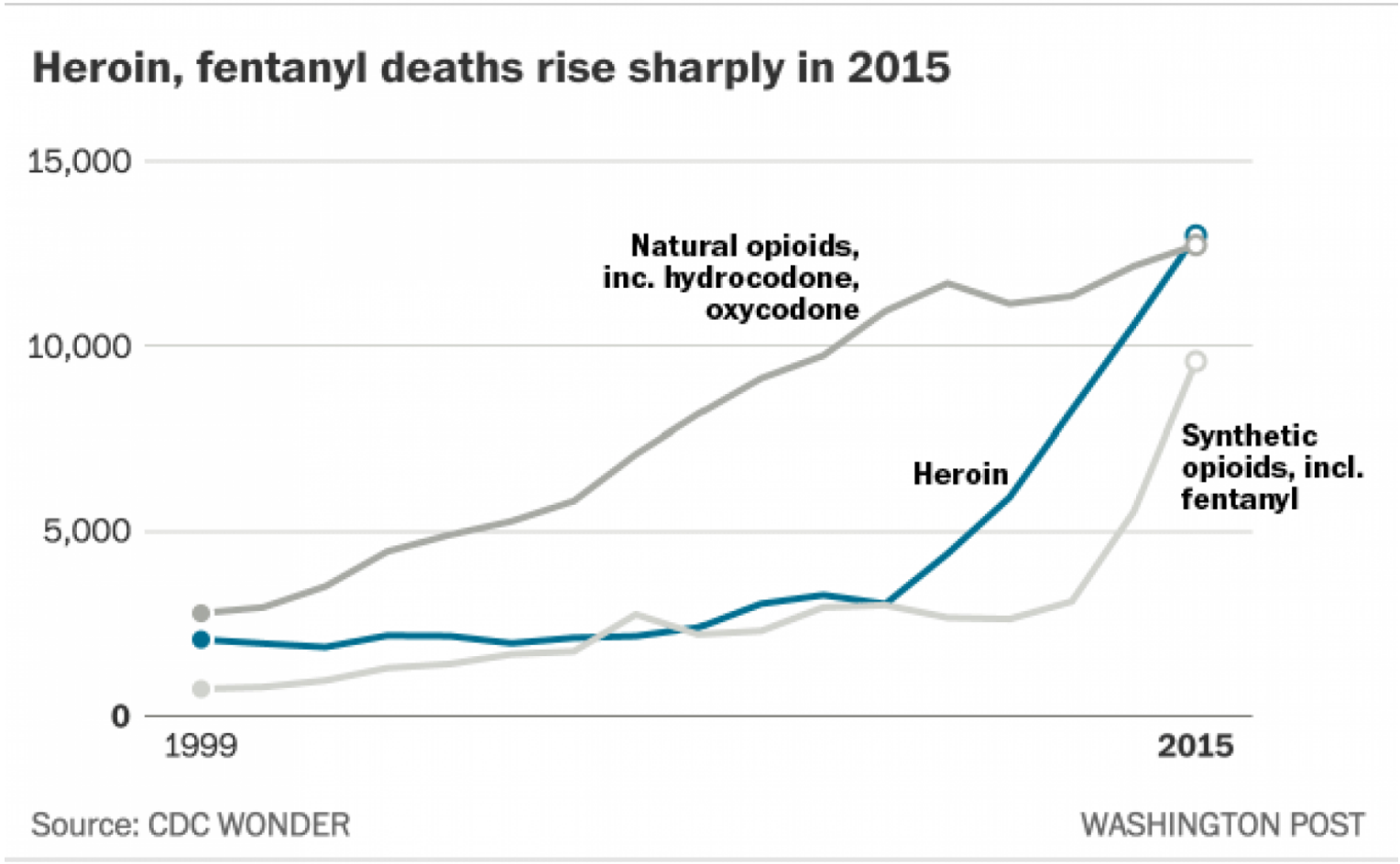
Increasing use of opioid meds



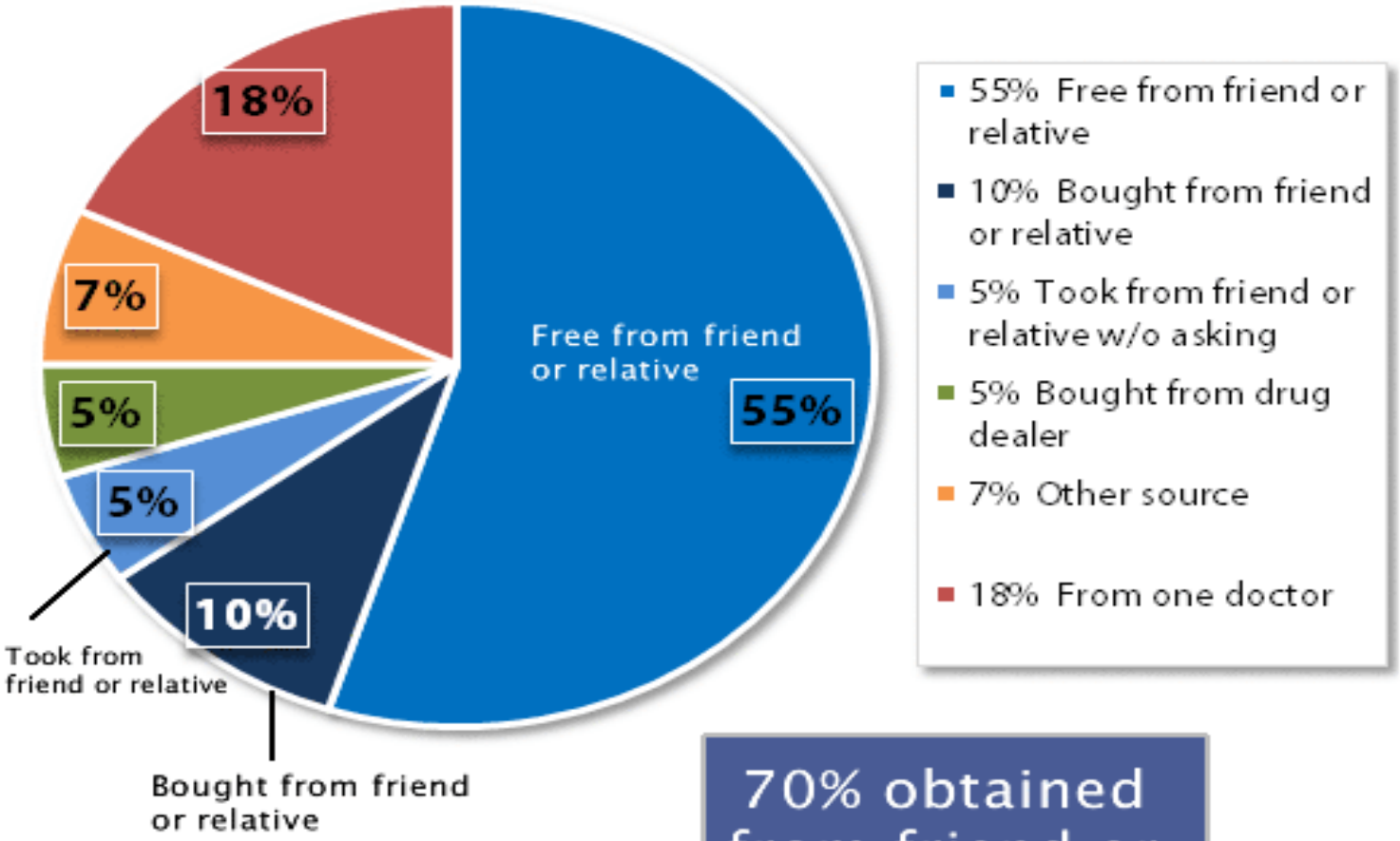
Overdose Deaths



Opioid Overdose



Source of Pain Relievers by Non-medical Users



70% obtained from friend or relative

Past Year Non-medical Users of Pain Relievers = 12.4 million

Source: SAMHSA, 2009 National Survey on Drug Use and Health (September 2010)

A Brief History of Pain Guidelines

- 1992 - Agency for Health Care Policy and Research (AHCPR)
  - *Acute Pain Management Guidelines*
- 1997 - American Society of Anesthesiologists and American Academy of Pain Medicine
  - Clinical guidelines for management of chronic pain
- 1998 - Federation of State Medical Boards
  - *Model Policy for the Use of Controlled Substances for the Treatment of Pain.*
- *Each of these guidelines emphasizes that doctors should be free to prescribe opiates <u>without worrying about sanctions.</u>*

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The Infamous Article

Cited by 900+ scientific articles

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug
Surveillance Program
Boston University Medical Center
Waltham, MA 02154

Opioid
Beliefs vs. Reality

Belief

- Sedating
- Good for all pain conditions
- Non-addicting if prescribed and monitored
- Pain is the 5th vital sign

Reality

- Activating after some period of time
- Indicated for acute but not chronic pain in most
- Rates of aberrant use in chronic prescribing 15-45%
- Pain is subjective and cannot be tested. However, functional restoration can be measured

Opioid
Beliefs vs. Reality

Belief

- Improve Sleep Quality
- Impossible to stop once started
- Will get people back to work
- Nobody should take opioids because of risks

Reality

- Decrease sleep quality
- Majority of patients taper off opioids without problem
- Early use is associated with increased disability
- Majority of patients use opioid therapies responsibly and to good effect

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Opioid Receptor Changes

- Chronic opioid exposure (addiction or therapeutic) causes brain changes
  - Opioid receptors increase
  - Brain stops producing enough endorphins and dopamine (manages pain and motivation)
  - Brain chemistry disrupted until chemicals are replaced or brain recovers
  - OUD is much like Type 2 Diabetes

Sleep Apnea

- Sleep Apnea is a dose dependent side effect of opioids
  - Overall prevalence – 24%
  - Methadone Maintenance – 30%
  - MME > 200 - >90%
  - Benzodiazepines and hypnotics increase rate
- Can interrogate CPAP/BiPAP to establish adherence

Opioid-Induced Hyperalgesia

- Associated with long-term use of opioids
- Increasing sensitivity to noxious and benign stimuli
- Tolerance (loss of body's own pain control mechanisms) and opioid-induced hyperalgesia (sensitization of pain pathways) are separate phenomena but clinically similar
- Prevalence rates 15-35% in opioid treated chronic pain

Opioids and Disability

- >40% of people receiving SSDI are taking opioid pain medication
- >20% of people receiving SSDI are on chronic opioid prescriptions
- Depression rates of 38% in chronic opioid users

Morphine Milligram Equivalents

Comparing opioids is like comparing cars. They will all get you from 0-60mph but at very different rates

Calculating morphine milligram equivalents (MME)

OPIOID (doses in mg/day except where noted)	**CONVERSION FACTOR**
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1-20 mg/day	4
21-40 mg/day	8
41-60 mg/day	10
≥ 61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.

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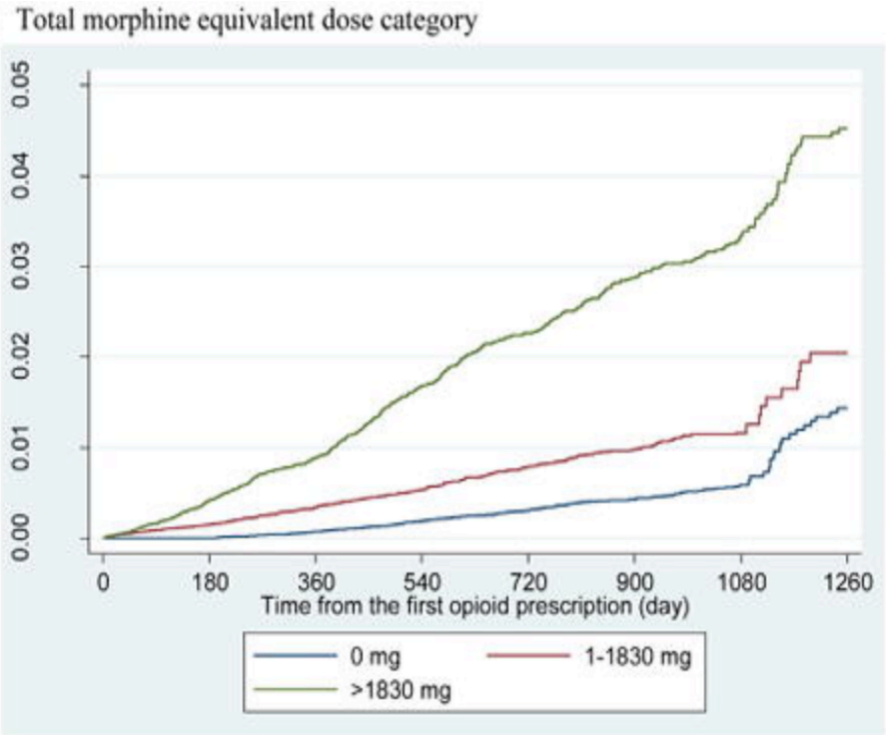
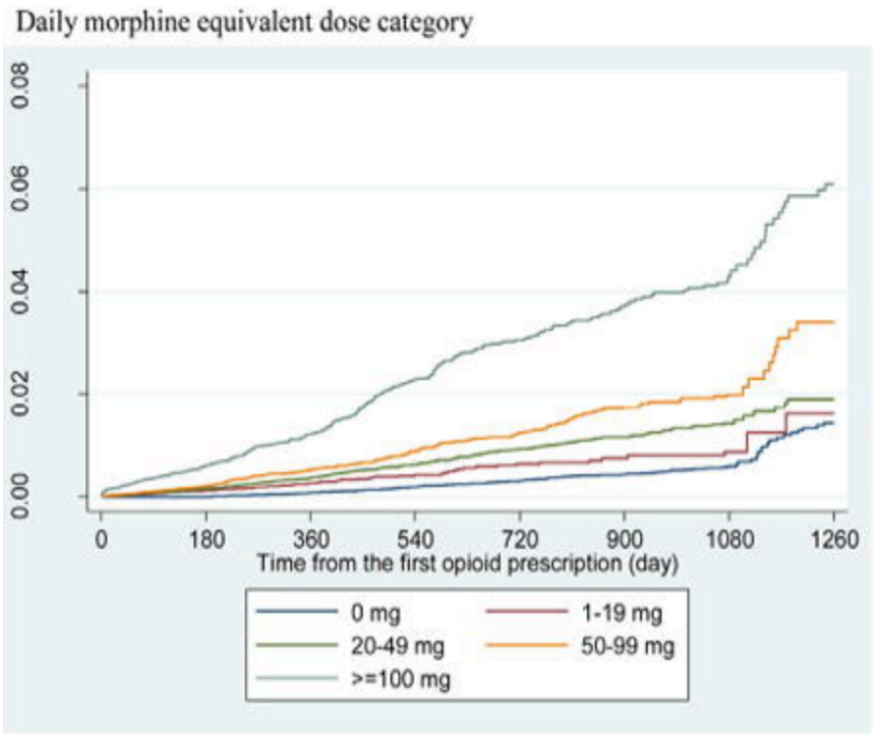
How much is too much?

Low Risk		Moderate Risk		High Risk	
Morphine Milligram Equivalent (MME) < 50 mg/day		Morphine Milligram Equivalent (MME) < 90 mg/day		Morphine Milligram Equivalent (MME) ≥ 90 mg/day	
Morphine	< 50 mg/day	Morphine	< 90 mg/day	Morphine	≥ 90 mg/day
Hydrocodone	< 50 mg/day	Hydrocodone	< 90 mg/day	Hydrocodone	≥ 90 mg/day
Oxycodone	< 30 mg/day	Oxycodone	< 60 mg/day	Oxycodone	≥ 60 mg/day
Hydromorphone	< 12.5 mg/day	Hydromorphone	< 22.5 mg/day	Hydromorphone	≥ 22.5 mg/day
Oxymorphone	< 15 mg/day	Oxymorphone	< 30 mg/day	Oxymorphone	≥ 30 mg/day
Fentanyl patch	**≤ 12 mcg/hr**	**Fentanyl patch**	**≤ 37 mcg/hr (25+12)**	**Fentanyl patch**	**≥ 50 mcg/hr**
Methadone	**< 10 mg/day**	**Methadone**	**≤ 20 mg/day**	**Methadone**	**> 20 mg/day**

**This is not intended to be used for dosing conversions from one opioid to another.

How much is too much?





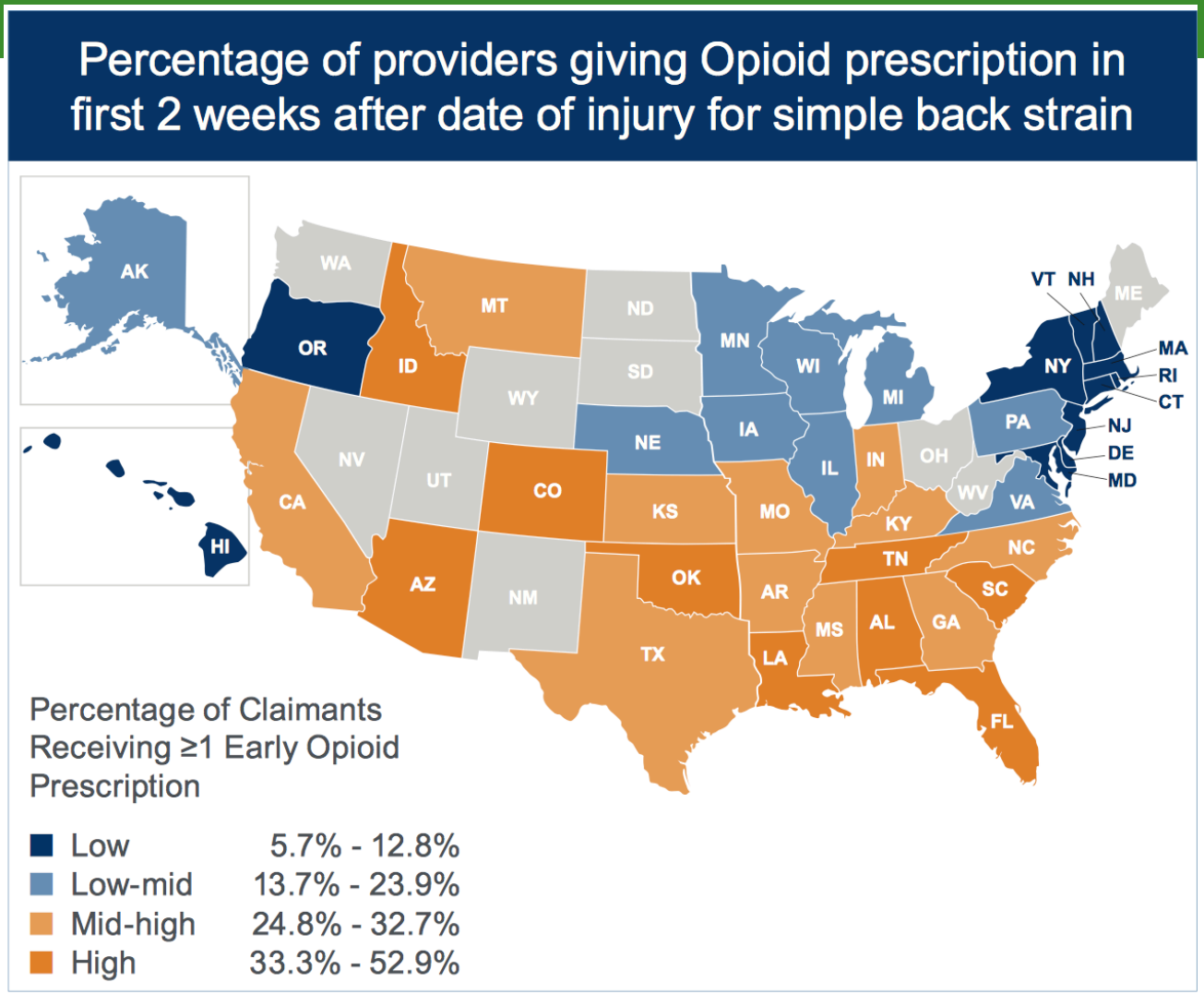
Suffering Relief vs. Functional Restoration

- Suffering
  - State of being
  - Individual mindset
  - "Pain is inevitable, suffering is optional"
  - Easy to treat
    - Keep upping the dose of opioids
- Functional Restoration
  - Should be the goal of pain management
  - Acute pain may be "curable"
  - Chronic pain (lasting longer than 6 months) should be managed
  - Opioids poor choices for chronic non-cancer pain

Suffering Relief vs. Functional Restoration

- Large retrospective worker's comp claims study found:
  - 8443 claimants
  - 21% received at least one early opioid rx
  - Higher doses associated with avg. 69 more days disability
  - Risk for surgery 3x greater in high dose
  - Risk for continuing opioids 6x greater

Opioid Rx Regional Variability



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Opioid Risk Tool

Mark each box that applies	Female	Male
1. Family hx of substance abuse		
Alcohol	☐ 1	☐ 3
Illegal Drugs	☐ 2	☐ 3
Prescription drugs	☐ 4	☐ 4
2. Personal hx of substance abuse		
Alcohol	☐ 3	☐ 3
Illegal Drugs	☐ 4	☐ 4
Prescription drugs	☐ 5	☐ 5
3. Personal hx of substance abuse	☐ 1	☐ 1
4. Hx of preadolescent sexual abuse	☐ 3	☐ 0
5. Psychologic disease		
ADD, OCD, bipolar, schizophrenia	☐ 2	☐ 2
Depression	☐ 1	☐ 1
Scoring totals:		

*0-3 Low Risk *4-7 Moderate Risk *≥ 8 High Risk

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Universal Precautions

- "At Risk" Definition varies
- Therefore:
  - Universal Precautions
  - Like HIV/HCV
- Assume universal risk
- Naloxone with all opioids
  - Don't need rx

Prescription Drug Monitoring Programs (PDMP)

- The National All Schedules Prescription Electronic Reporting (NASPER) Act, was signed into law on August 11, 2005.
  - Authorized **$60 million** to establish or improve state-run Prescription Drug Monitoring Programs (PDMP) which analyze prescription data
- PDMP can identify individuals, physicians, or pharmacies that have unusual patterns suggesting drug diversion, abuse, or doctor shopping
- Operational in 49 states, Guam, and Washington D.C.
  - Missouri only one without
- California requires PDMP query prior to prescribing controlled substances

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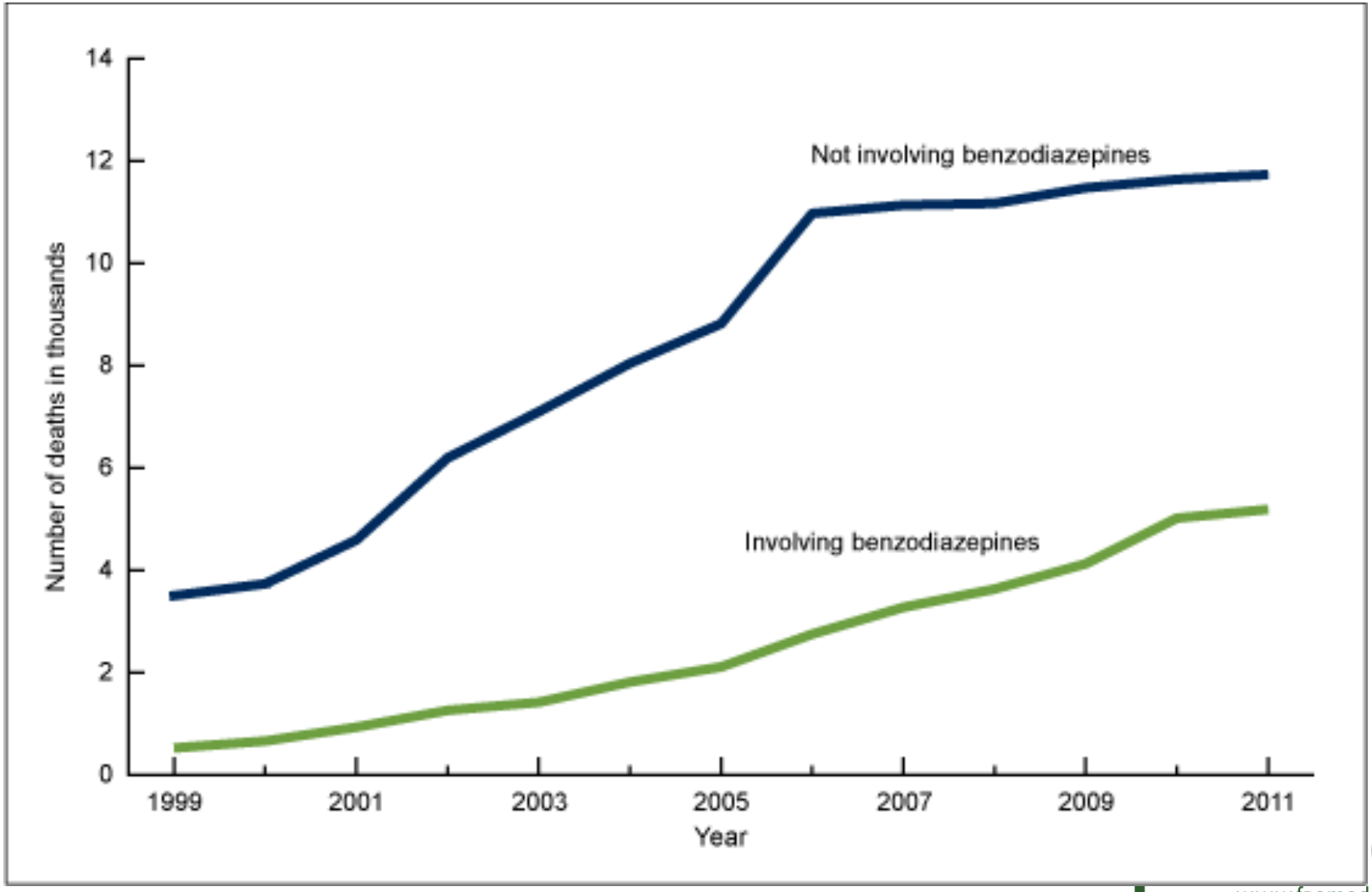
Benzodiazepines

- Benzodiazepines
  - Sedative, anti-anxiety, sleep aid
  - Side effects: sedation, slowed reaction time, confusion, incoordination, dependence, addiction
  - Good evidence for:
    - Panic Disorder
    - Generalized Anxiety Disorder
  - Very limited evidence for
    - Posttraumatic Stress Disorder

Benzodiazepines



49 CFR Part B.II.219.103

- **§219.103 Prescribed and over-the-counter drugs.**

(a) This subpart does not prohibit the use of a controlled substance (on Schedules II through V of the controlled substance list) prescribed or authorized by a medical practitioner, or possession incident to such use, if—

(1) The treating medical practitioner or a physician designated by the railroad has made a good faith judgment, with notice of the employee's assigned duties and on the basis of the available medical history, that use of the substance by the employee at the prescribed or authorized dosage level is consistent with the safe performance of the employee's duties;

(2) The substance is used at the dosage prescribed or authorized; and

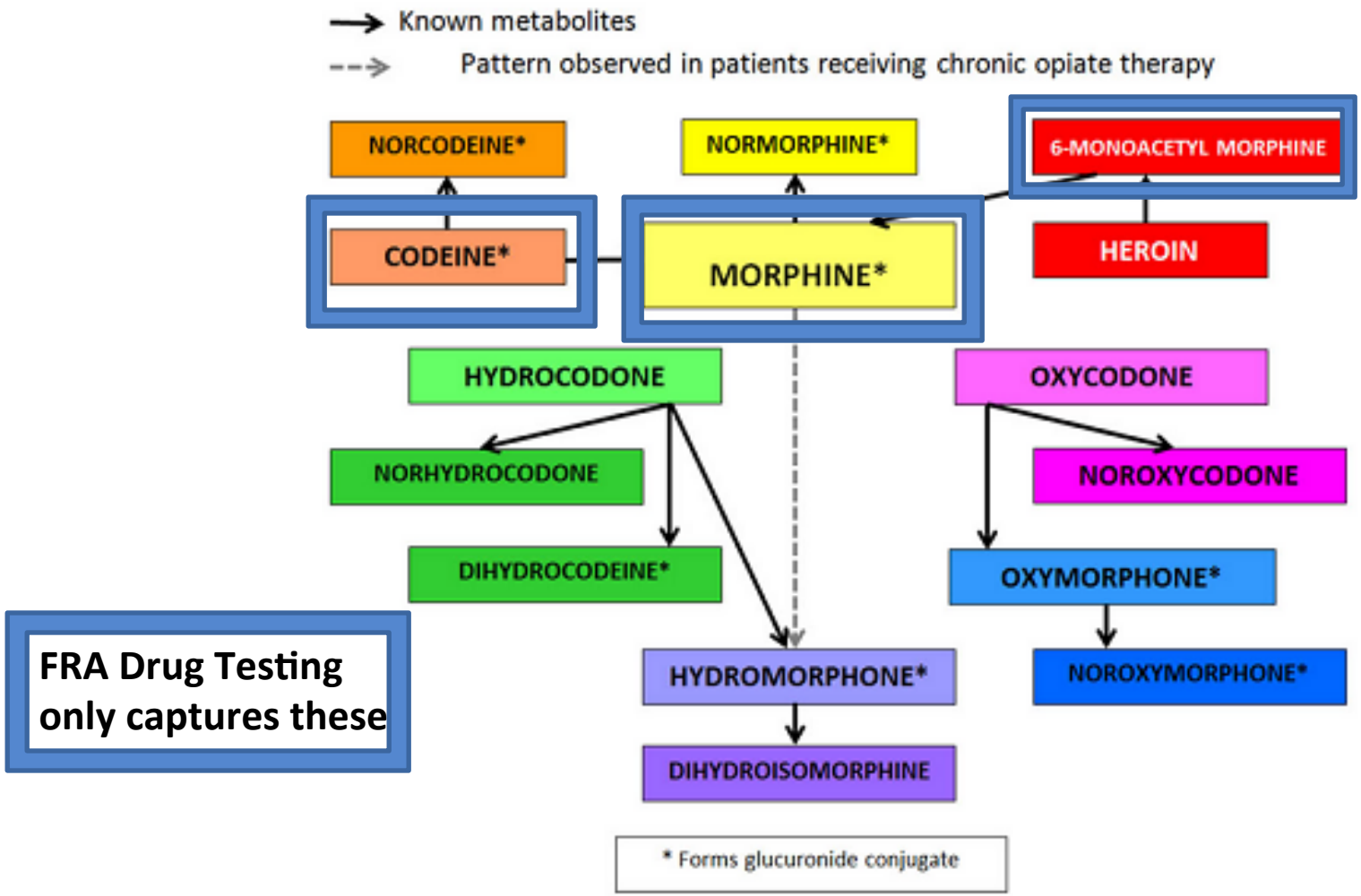
(3) In the event the employee is being treated by more than one medical practitioner, at least one treating medical practitioner has been informed of all medications authorized or prescribed and has determined that use of the medications is consistent with the safe performance of the employee's duties (and the employee has observed any restrictions imposed with respect to use of the medications in combination).

(b) This subpart does not restrict any discretion available to the railroad to require that employees notify the railroad of therapeutic drug use or obtain prior approval for such use.

FRA Drug Testing

- Cannabis, cocaine, amphetamines, opiates, phencyclidine
- Post-Accident
  - Barbiturates
  - Benzodiazepines
- Companies can test for additional drugs

FRA Drug Testing
Metabolic Pathways



FRA Drug Testing
What's Missing?

- Z-drugs
  - Zolpidem (Ambien), Zaleplon (Sonata)
- Muscle Relaxants
  - SOMA, Baclofen, Flexeril
- Cannabinoid Receptor Analogues
  - Spice, K2
- Other sedating medications
  - Many
  - Antihistamines, gabapentinoids

FRA Drug Testing
What's Missing?

- Opioids
  - Tests for morphine, codeine, and 6-MAM (heroin metabolite)
  - Medical Review Officer
    - Presence of a legitimate prescription will result in positive drug test being negative
- Recommendation
  - Routinely employ expanded drug testing panels

Opioid Use Disorder Treatment

- Medication Assisted Treatment (MAT) is gold standard
- Very good outcomes with:
  - Methadone Maintenance
  - Buprenorphine Maintenance
- Marginal evidence for Naltrexone (opioid blocker) both oral and injected
- Detoxification is of limited-long term efficacy and associated with risks (overdose)

Methadone Maintenance Outcomes

- Gold-Standard for Opioid Treatment
  - One of the most over-proven treatments in entire psychiatry and drug abuse literature
  - Detoxification methods succeed only < 3% of the time.
- Outcomes Measures
  - **Reduction of …**
    - Death rates (8-10X reduction)
    - Drug use
    - Criminal activity
    - HIV spread
  - **Increase in …**
    - Employment
    - Social stability
    - Retention, medication compliance, and monitoring

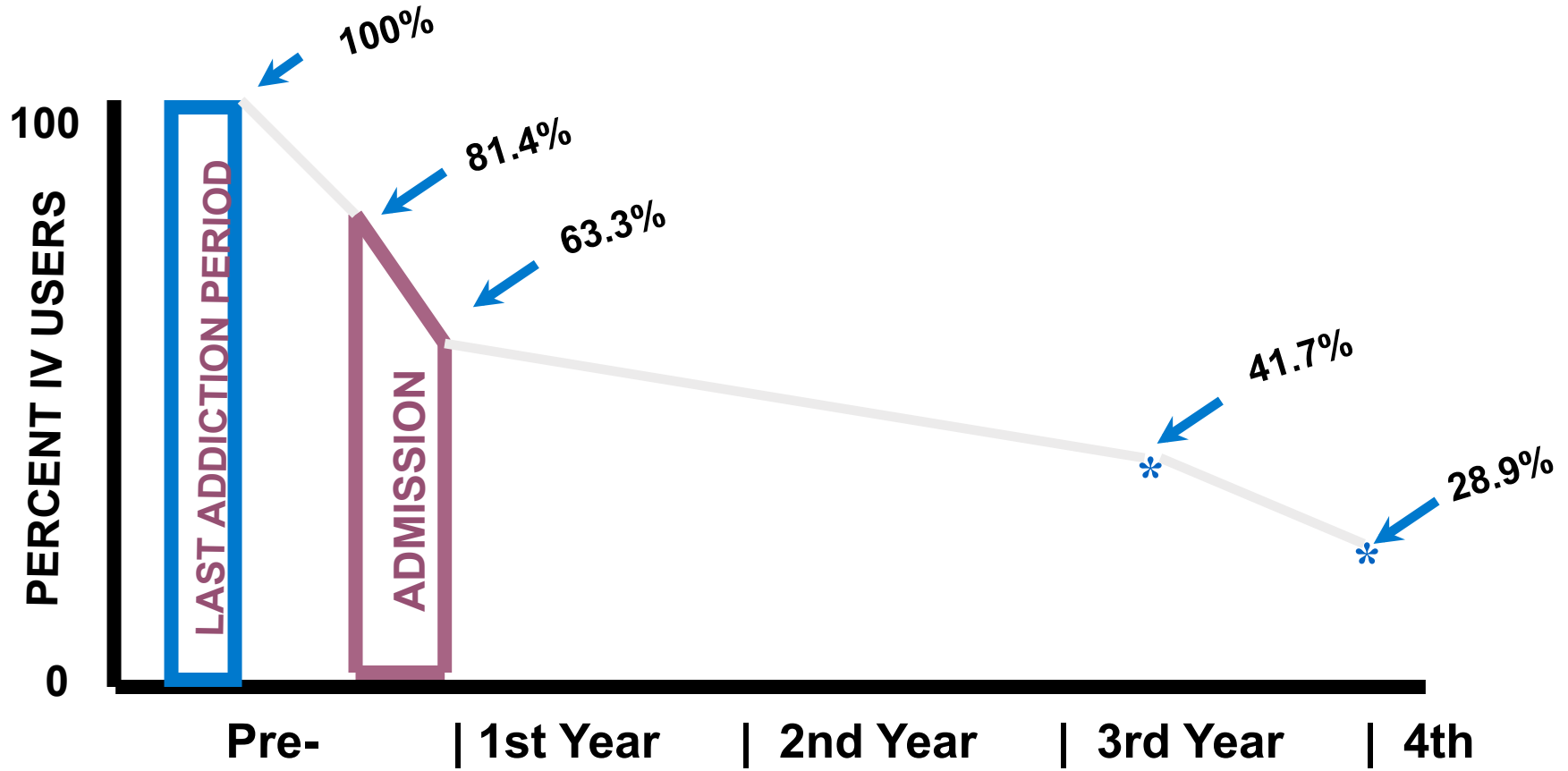
What are Health Plans doing?

- Blue Shield – has set goal 50% reduction in opioids by 2019
- Aligning Formulary and Authorization Practices
  - Remove high dose formulations (Oxycontin 80mg)
  - Remove non-opioids with abuse potential (SOMA)
  - Limiting prescription quantity
  - Limiting early refills
  - Limit total daily dose (Morphine mg Equivalents)

Authorization Review

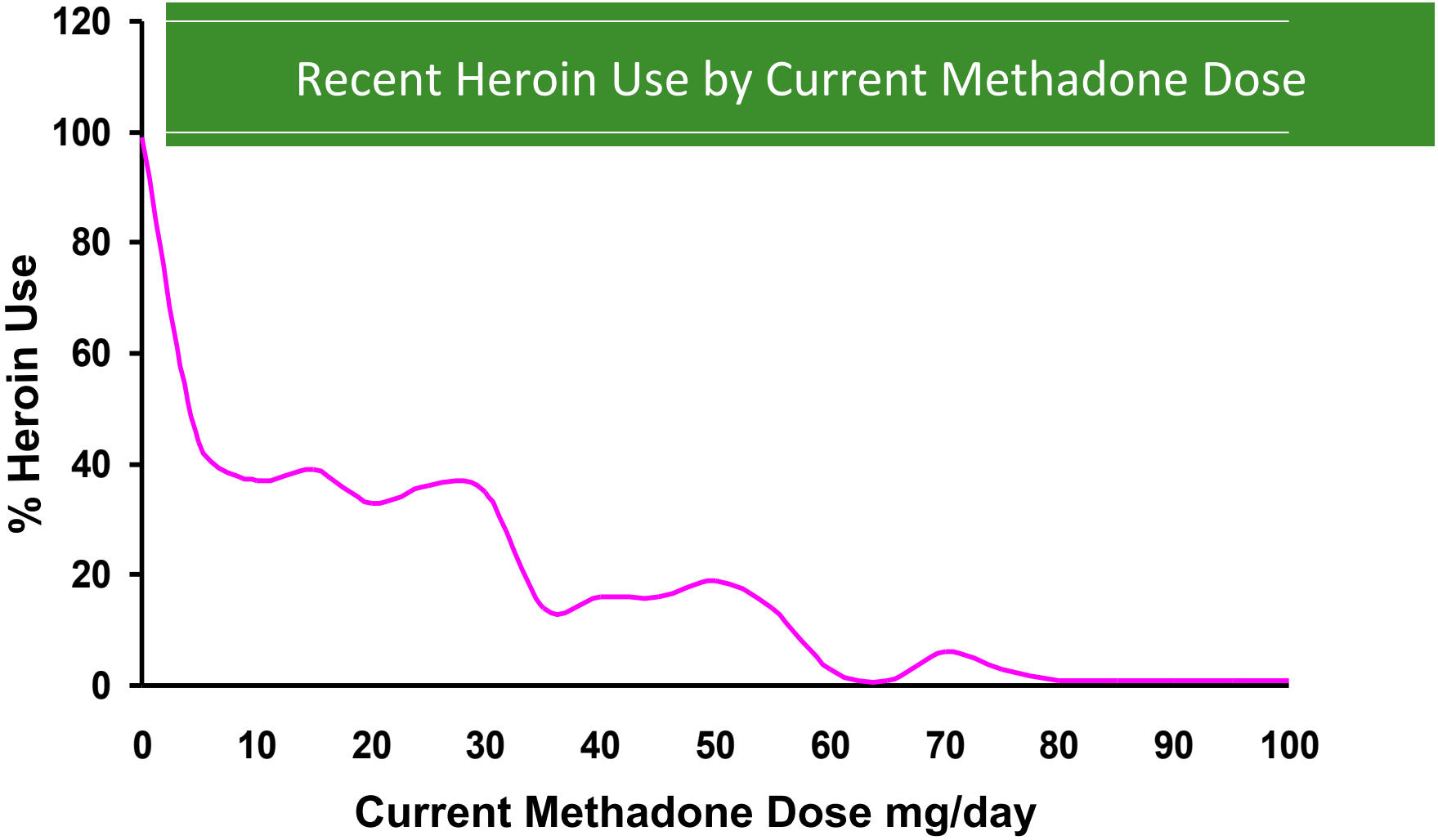
- High dose opioids
  - Morphine Milligram Equivalents (MME)
  - >100 MME increases overdose deaths **ninefold**
  - 67% of patients using opioids for 90 days continue to use them long-term (>2 years)

Impact of MMT on IV Drug Use for 388 Male MMT Patients in 6 Programs



Adapted from Ball & Ross - The Effectiveness of Methadone Maintenance Treatment, 1991

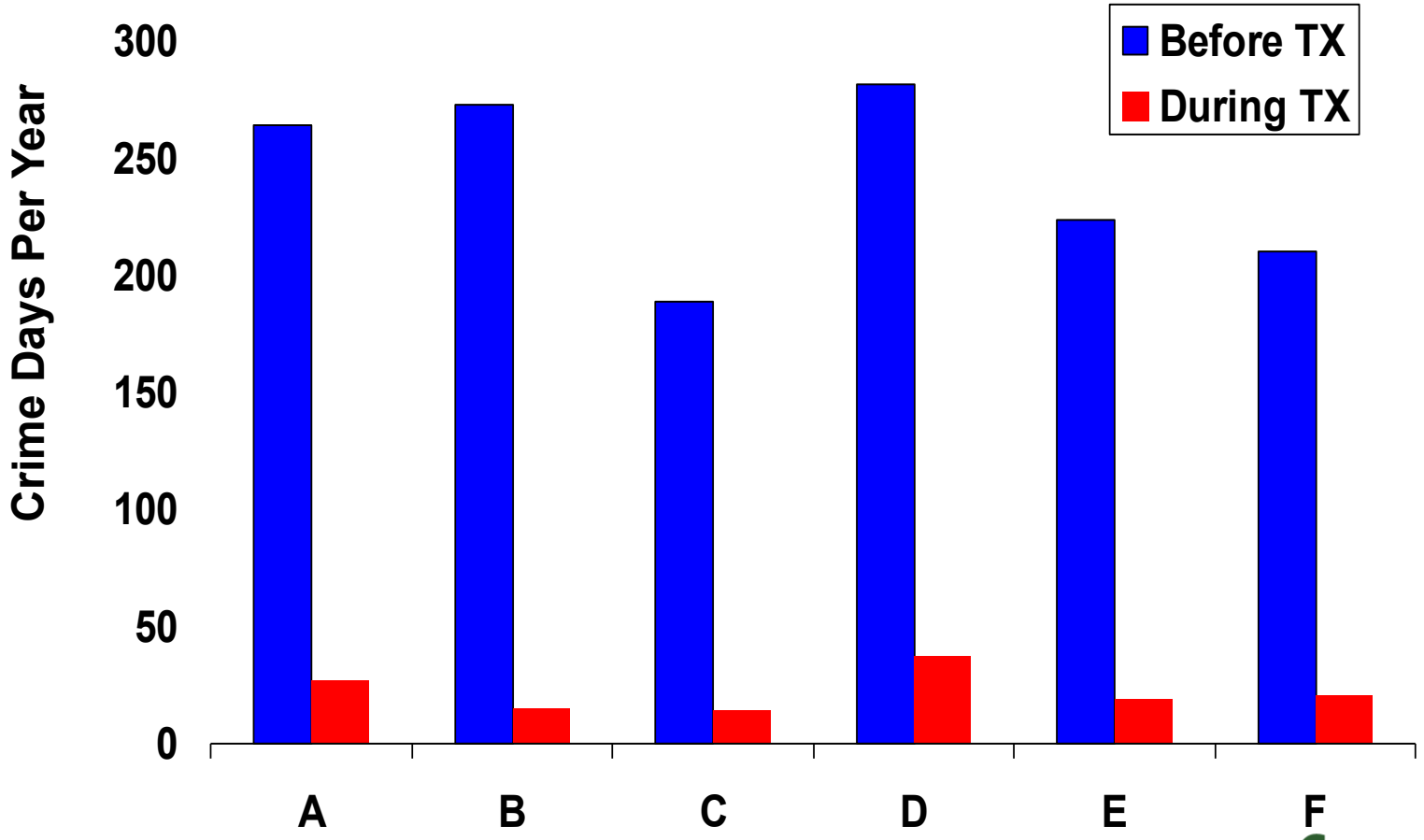
Recent Heroin Use by Current Methadone Dose



Opioid Agonist Treatment of Addiction - Payte - 1998

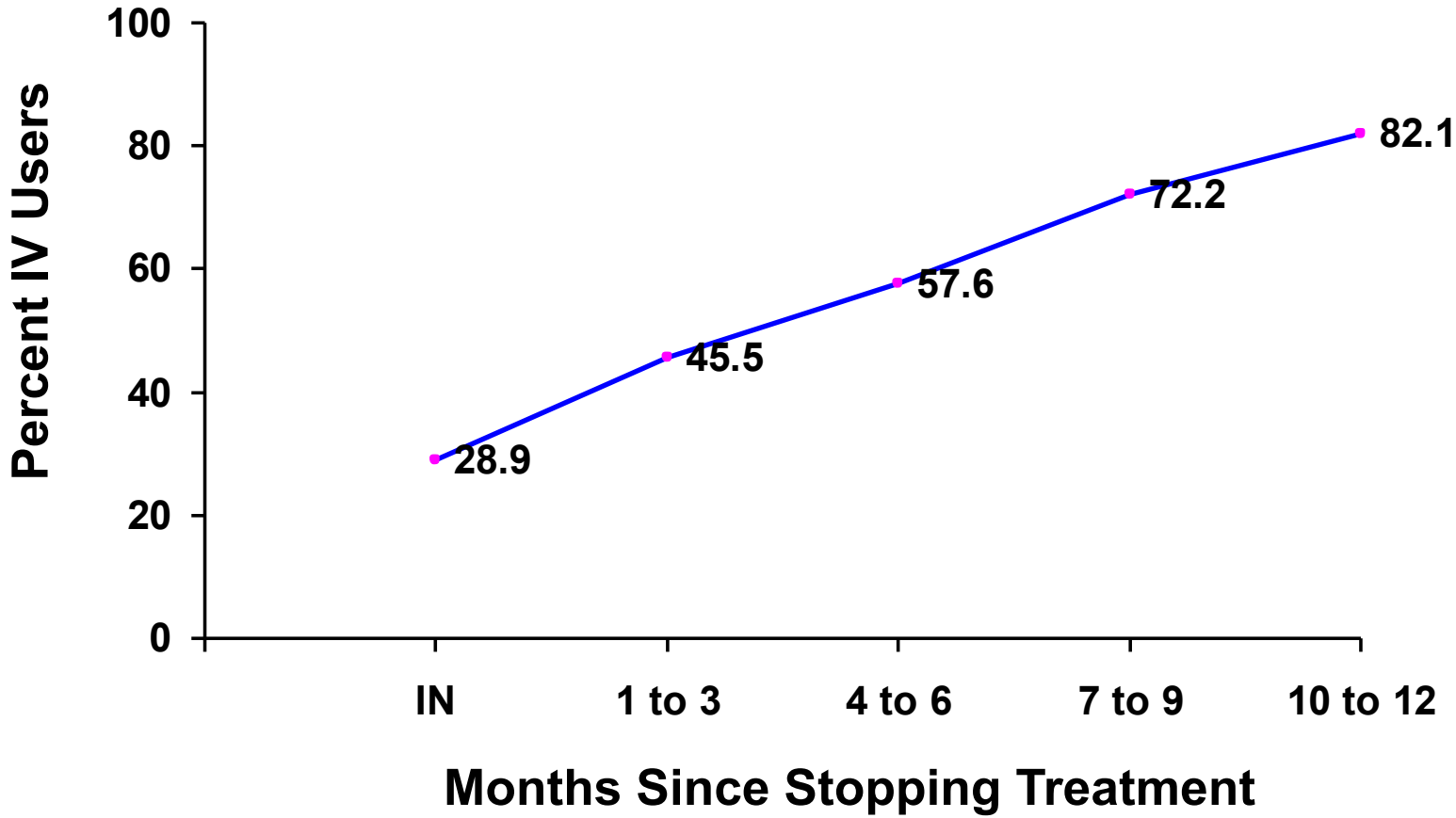
J. C. Ball, November 18, 1988

Crime among 491 patients before and during MMT at 6 programs



Adapted from Ball & Ross - The Effectiveness of Methadone Maintenance Treatment, 1991

Relapse to IV drug use after MMT
105 male patients who left treatment



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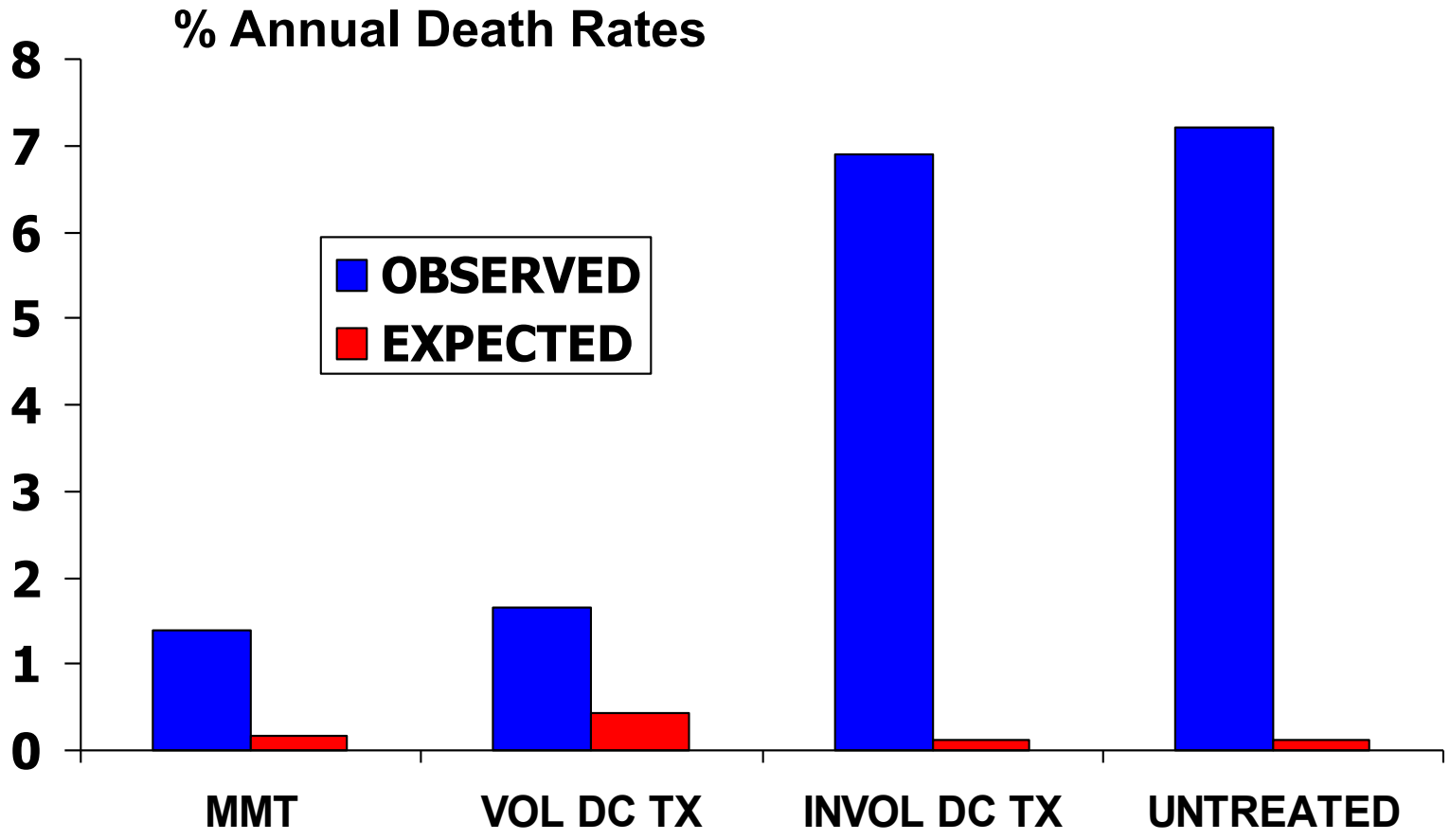
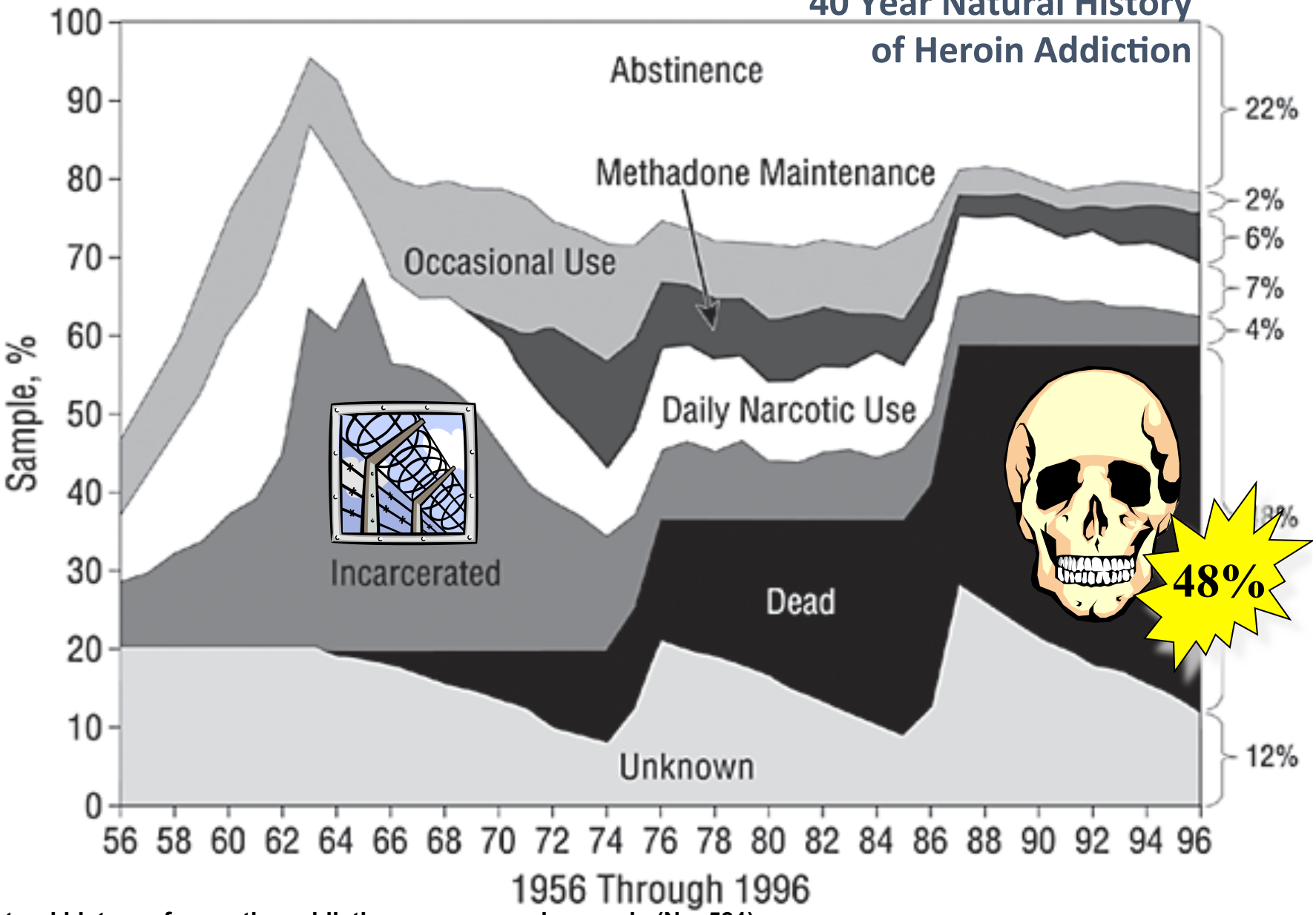
Death Rates in Treated and Untreated Addicts



Slide data courtesy of Frank Vocci, MD, NIDA –
Reference: Grondblah, L. et al. Acta Pschiatr Scand, P. 223-227, 1990

40 Year Natural History of Heroin Addiction



The natural history of narcotics addiction among a male sample (N = 581).
From: Yih-Ing, et. al., 2001. A 33-Year Follow-up of Narcotics Addicts. Archives of General Psychiatry, 58:503-508)

THANK YOU!

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QUESTIONS?

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NARTC Webinar

January 24, 2017

David Kan, M.D., D.F.A.S.A.M.

Diplomate Am. Bd. Psychiatry & Neurology in Psychiatry & Forensic Psychiatry
Asst. Clinical Professor Psychiatry, UCSF School of Medicine
Associate, Forensic Psychiatric Associates Medical Corporation
President-Elect, California Society of Addiction Medicine
655 Redwood Hwy., Suite 271,Mill Valley, CA 94941
415 812 1092 dkan@fpamed.com

Mark I. Levy, M.D., D.L.F.A.P.A

Medical Director, **fpamed**
Asst. Clinical Professor Psychiatry, UCSF School of Medicine
Inquiries: 415 388 8040 mlevy@fpamed.com

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