

Arkansas Prescription Drug Abuse Summit

Medication Assisted Treatment for Opioid Use Disorder

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This Presentation Reviews

- **Part I: The problem**
- **Part II: Potential solutions**

Part I: The Problem

- Definitions
- Epidemiology

Part II: Potential Solutions

- Reasons for prescription drug misuse
- Factors in prescription drug misuse
- Intervention strategies
- Treatment

Part I: The Problem

- Definitions
- Epidemiology

Definitions

- Misuse
- Non-medical use
- Use disorder
 - previously abuse/ dependence

Prescriptions

Misuse

- Incorrect use
 - By patient
- Mismanaged
 - By physicians
 - Dated
 - Duped
 - Disabled
 - Dishonest

Non-medical

- Illegal use
 - Not prescribed
 - Took for euphoria
- Most commonly used
- In US, age 12 +:
 - Past month 2%
 - Lifetime: 14%

Use Disorder

2 or more in 12 months

- Failure to fulfill role
- Hazardous use
- Craving
- Use despite relationship problems
- Larger/Longer than intended
- Tolerance
- Withdrawal
- Can't Quit
- Much time spent
- ↓ Activities
- Use despite medical/psychological

Part I: The Problem

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Non-medical use

- 2013 National Survey on Drug Use and Health (NSDUH)
 - 7 % youth 12-17 lifetime non-medical use
- 2013 NSDUH
 - 20 % young adults 18-25 lifetime non-medical use

Emergency Department Visits

2009 Drug Abuse Warning Network

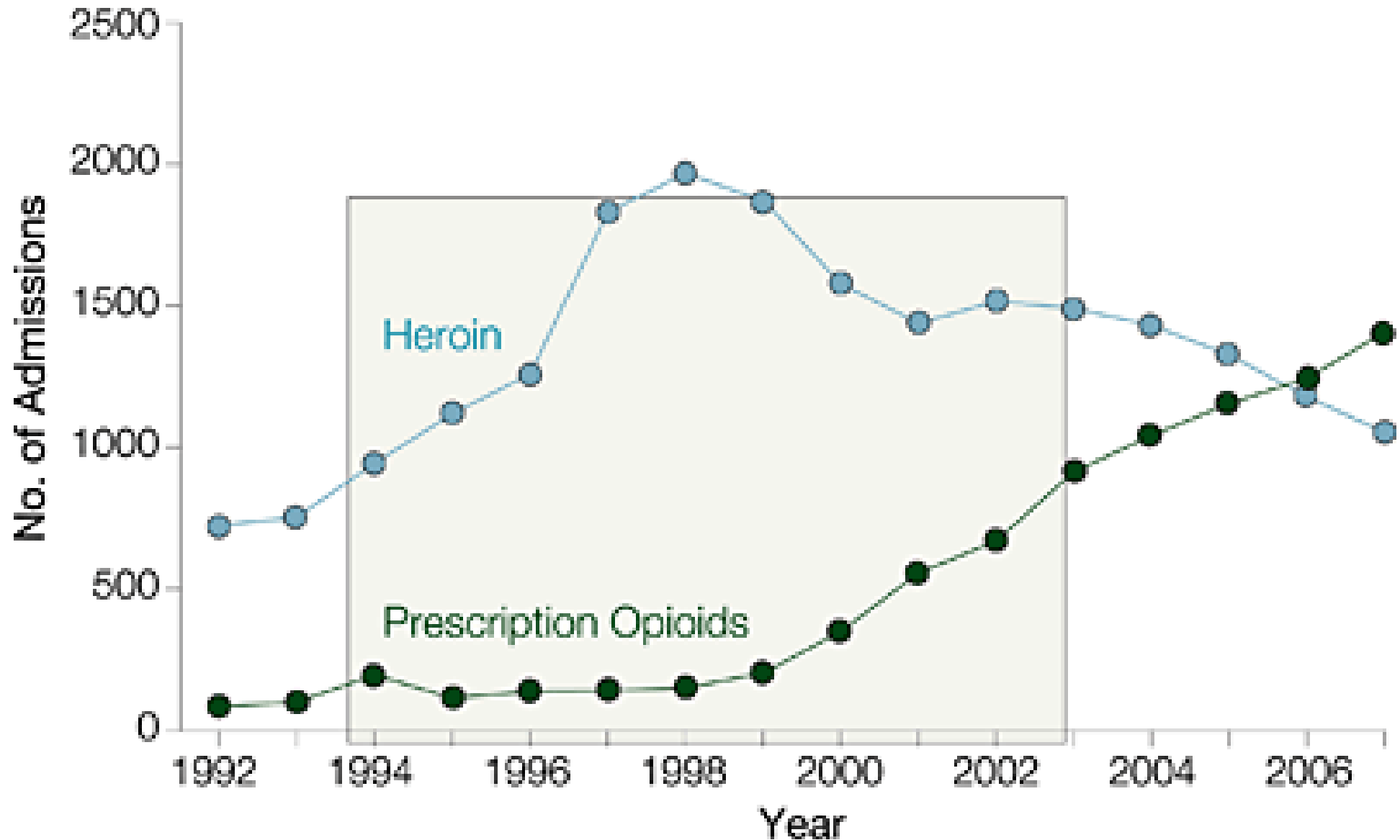
(DAWN)

- 4.6 million drug-related ED visits
- 45 % were drug misuse
 - 27 % non-medical use of pharmaceuticals
 - 50 % of these were opioid analgesics

Prescription Opioids



Opioid Admissions in Adolescents Aged 12 to 17 Years



Source: Subramaniam G. Treatments for adolescents/young adults with opioid use disorder. Presented at: 8th National Institute on Drug Abuse Blending Conference; April 22, 2010; Albuquerque, NM.

Epidemiology

- Heroin Use
 - National Household Survey on Drug Use and Health (NSDUH 2016)
 - 948,000 Americans used heroin at least once
 - 13,000 were adolescents age 12-17
- Prescription Opioids (NSDUH 2016)
 - 11.5 million used prescription analgesics non-medically
 - 891,000 were adolescents aged 12-17
 - 641,000 misused prescription analgesics and heroin
- Opioid use disorder present in 2.4 million > age 12

Arkansas NSDUH Data

- 2006-2007 Data for ages 12 and older
- Past year non-medical use: 169,000 or 7.29% of the Arkansas population
- 66,000 (2.85%) of Arkansans reported needing but NOT receiving treatment for illicit drug use in the past year (2006-2007)
- Admissions to treatment for opiates in Arkansas (TEDS)

	2006	2008	2016
Heroin	40	52	211
Other opiates	778	1441	1572

Opioid dependence: Treatment Gaps

- **Patients with opioid use disorder (NSDUH-2013)**

 - **Pain relievers: 1.9 million**

 - **Heroin: 517,000**

- **Less than half received any treatment**

- **Detoxification: limited effectiveness**

- **Access to treatment restricted**

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Non-medical Use Rx Opioids

- Relieve pain – 63-79 %
- Feel good or get high – 32 %
- Experimentation – 27 %
- M 2X > F to report “get high”
- Get high ↑ other drug use
- Existing addiction/safety < 10 %

Generational Angst?

- “We’re living in a time that seems decidedly more apocalyptic, especially since 9/11 and all the recent natural disasters. Maybe we need something to slow down”

- Friedman, 2006

Part II: Potential Solutions

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Contributing Factors

- Parents don't talk about Rx drugs
- Pain management: late 1980's
- New pain meds: early 1990's
 - Hydrocodone RX ↑ 376 %
 - Oxycodone Rx ↑ 380 %
- Media changes
 - DTCA
 - Internet

Protective Factors

- Parental discussion about risks
- Gatekeeper access to Rx drugs
- School based programs
 - Science curriculum
 - Media awareness training
- Pharmaceutical approaches

Awareness of Teens “Lingo”

- Pharming
- Pilz
- Pharm parties
- Trail mix or M & M's
- Chill pills
- Big boy

Part II: Potential Solutions

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Prevention

- ↓ Exposure
- Target high-risk
 - Adolescents
 - Genetically vulnerable
 - Cognitive probs (schizophrenia, brain injury)
 - ↑ Stress reactive (depressed/anxious)

Intervention

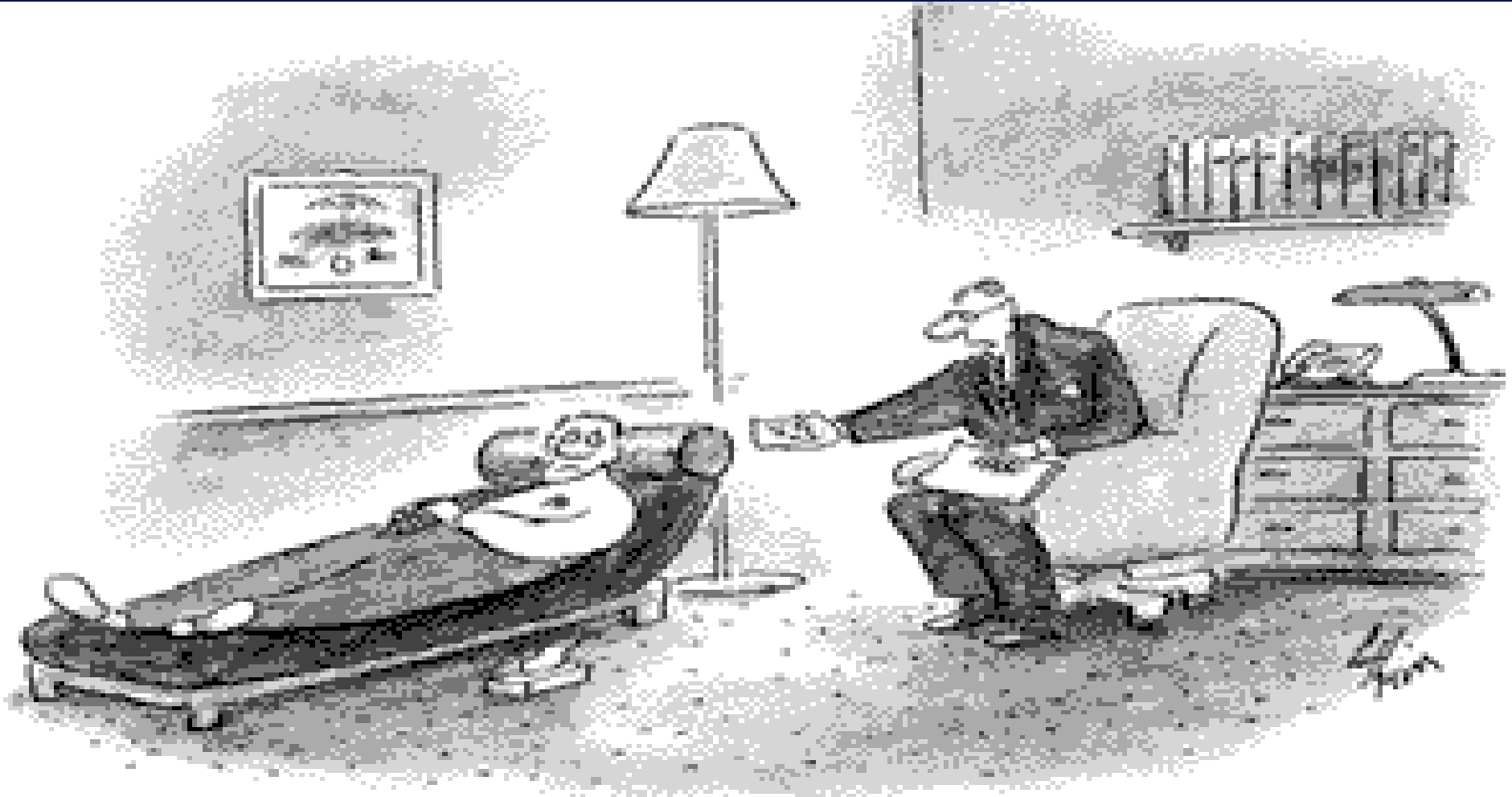
- School Nurses
- Computerized, involve parents
- Cognitive Behavioral Therapy
- Motivational Interviewing
- Medication Assisted Treatment

Questions?

Part II: Potential Solutions

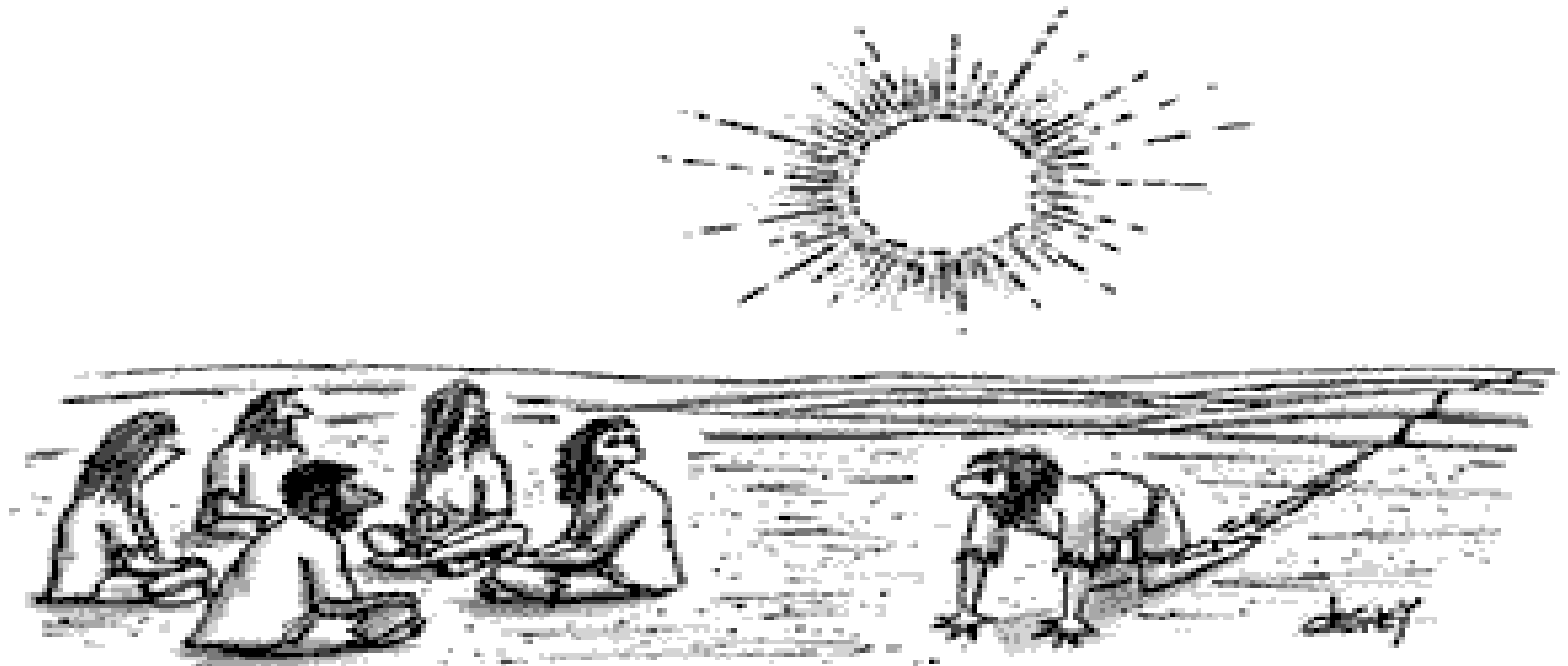
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MEDICATION/PSYCHOSOCIAL



“I medicate first and ask questions later.”

MEDICATION/PSYCHOSOCIAL



"Sorry, no water. We're just a support group."

Opiate Withdrawal

Early

- Lacrimation
- Yawning
- Rhinorrhea
- Sweating

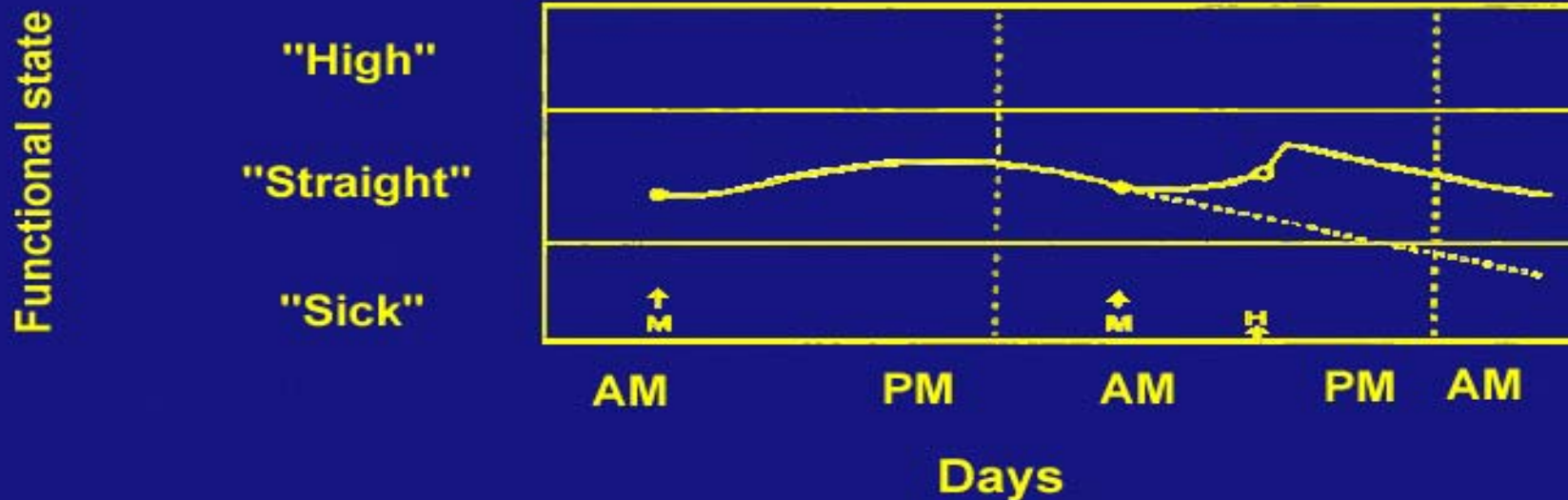
Middle

- Restless Sleep
- Dilated Pupils
- Anorexia
- Piloerection (term cold turkey)
- Irritability

Late Opiate Withdrawal

- ↑all previous S/S
- Abdominal cramps
- Tachycardia
- Labile mood
- Hypertension
- Depression
- Nausea/vomiting
- Muscle spasm
- Diarrhea
- Weakness
- Bone pain

Medication Stabilized Heroin User



Stabilization of patient in state of normal function by blockade treatment. A single daily oral dose of methadone prevents him from feeling symptoms of abstinence ("sick") or euphoria ("high"), even if he takes a shot of heroin. Dotted line indicates course if methadone is omitted.

GOALS FOR PHARMACOTHERAPY

- Prevention or reduction of withdrawal symptoms
- Prevention or reduction of drug craving
- Prevention of relapse to use of addictive drug
- Restoration toward normalcy

Source: MJ Kreek, Rationale for Maintenance Pharmacotherapy of Opiate Dependence, 1992

Medications for Opioid Dependence

- Naltrexone
- Methadone
- Buprenorphine

Medications for Opioid Dependence

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Rationale for Naltrexone Block Pleasurable Drug Effects

- Extinction paradigm: no pleasure→no use
- Craving ↓ if heroin “not available”
- Naltrexone ↓ cue-induced craving
- Naltrexone ↓ priming-induced craving

Naltrexone

- Oral FDA 1984; Injectable FDA 2010
- Derivative of naloxone
- Displaces bound agonists
- Receptor affinity 20 X morphine
- Blocks heroin/opioids
- Peak plasma concentrations in 1hr
- Minimum 7 days abstinence before induction

Naltrexone: Reductions in Opiate Use

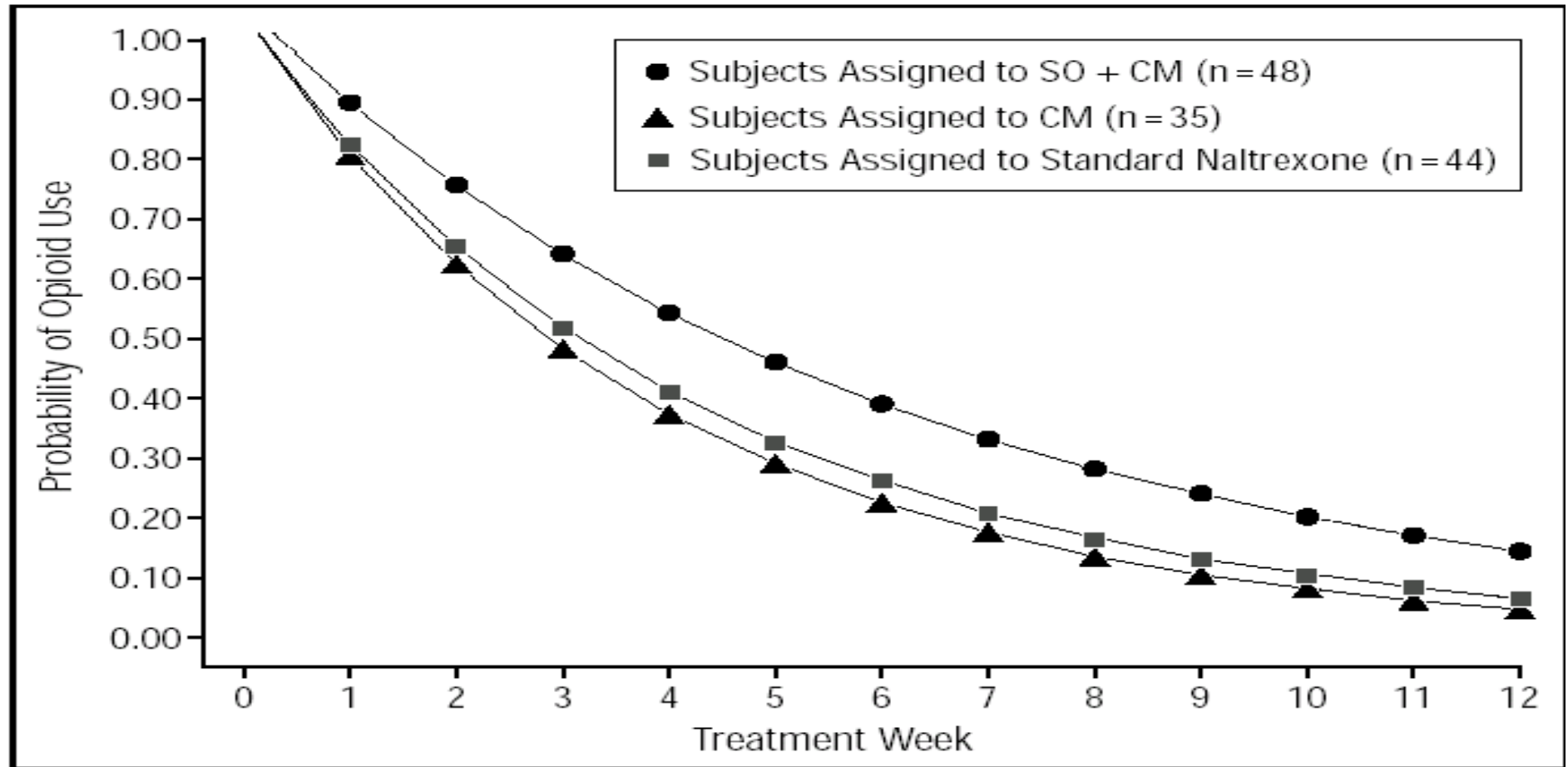


Figure 2. Probability of opioid use by week by treatment group (N=127), result of random regression analyses, using a linear model. All subjects were taking naltrexone 3 times a week as maintenance therapy. CM indicates contingency management; SO+CM, significant other involvement and CM.

Naltrexone: Treatment Retention

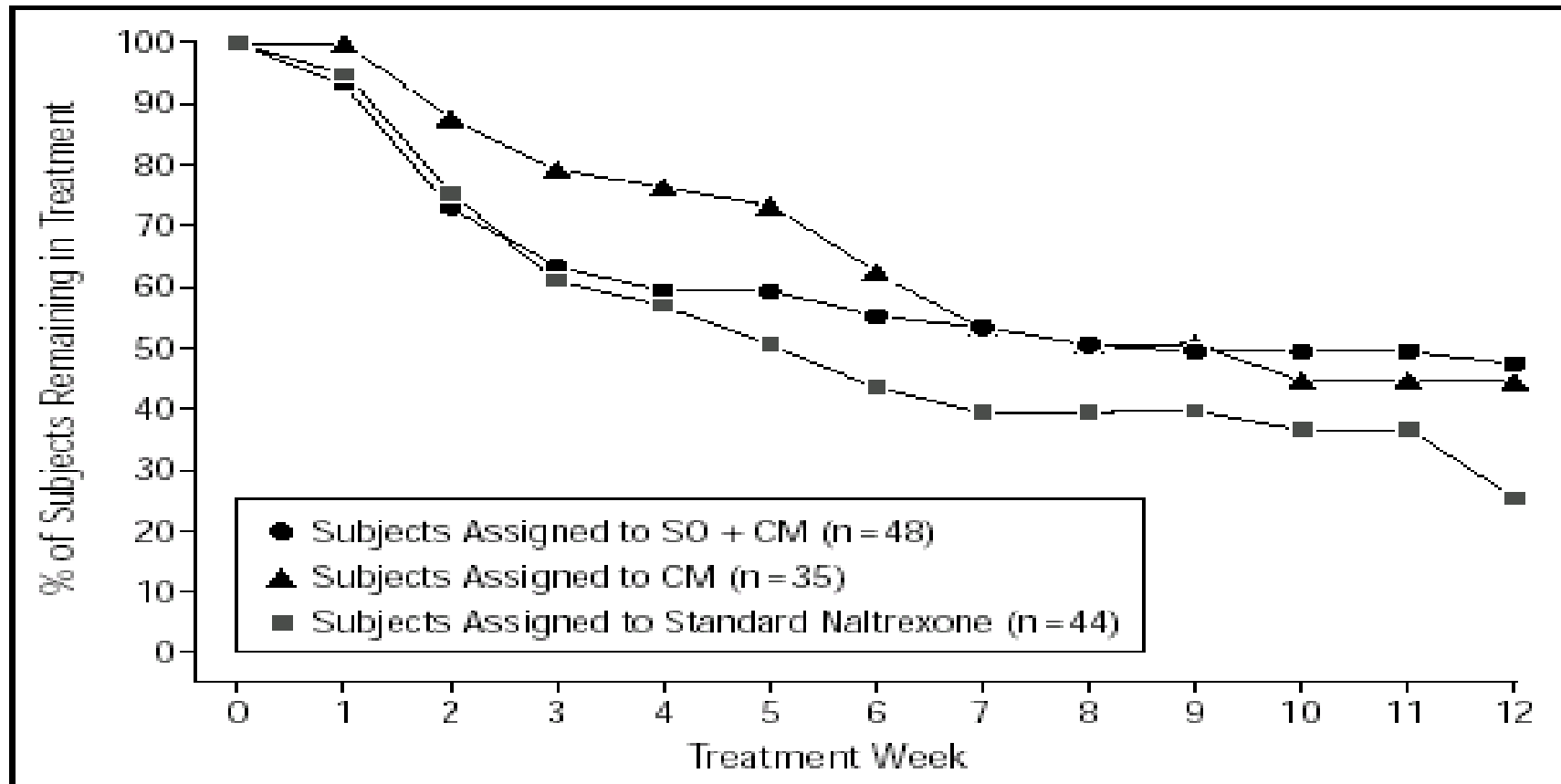


Figure 1. Retention by week by treatment group (N = 127). All subjects were taking naltrexone 3 times a week as maintenance therapy. CM indicates contingency management; SO + CM, significant other involvement and CM.

Injectable Naltrexone

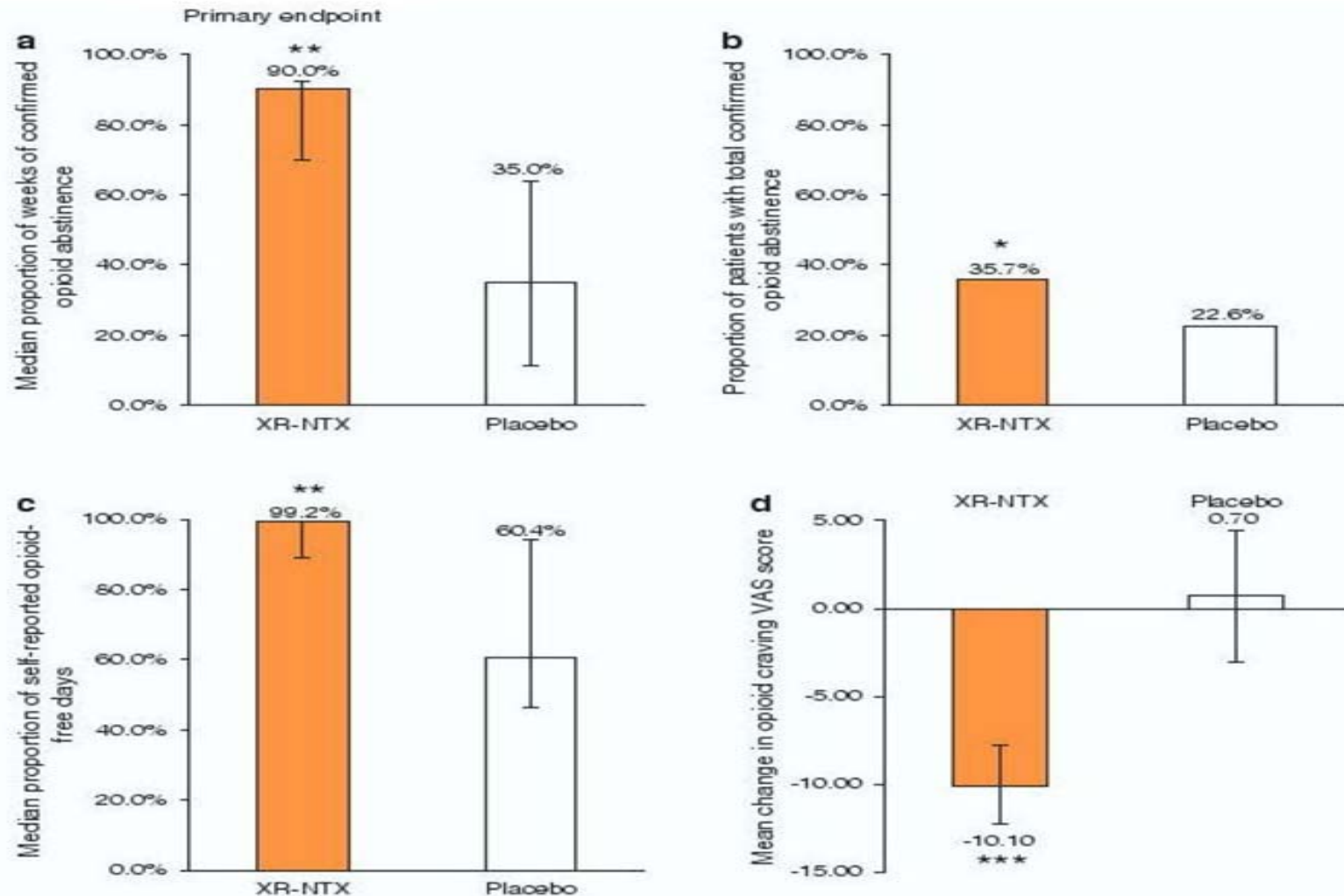


Fig. 1 Efficacy of intramuscular extended-release naltrexone in patients with opioid dependence who had undergone opioid detoxification in a randomized, double-blind, multicentre trial [8]. Patients received extended-release naltrexone 380 mg ($n = 126$) or placebo ($n = 124$) once every 4 weeks for 24 weeks in combination with biweekly psychosocial support. *Error bars* are 95% confidence intervals. **a** Median proportion of weeks of confirmed abstinence during weeks 5–24 (primary endpoint, as defined in Table 1).

b Proportion of patients with total confirmed opioid abstinence during weeks 5–24. **c** Median proportion of self-reported opioid-free days on timeline follow-back survey over 24 weeks. **d** Mean change from baseline in self-reported need for opioids assessed on a visual analogue scale at week 24; see Table 1 for scale description and baseline scores. XR-NTX extended-release naltrexone, VAS visual analogue scale. * $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$ vs. placebo

Naltrexone Side Effects

- Nausea/Diarrhea
- Headache
- Insomnia
- Dizziness
- Possible liver toxicity
- Opioid analgesics NOT effective

Medications for Opioid Dependence

- Naltrexone
- Methadone
- Buprenorphine

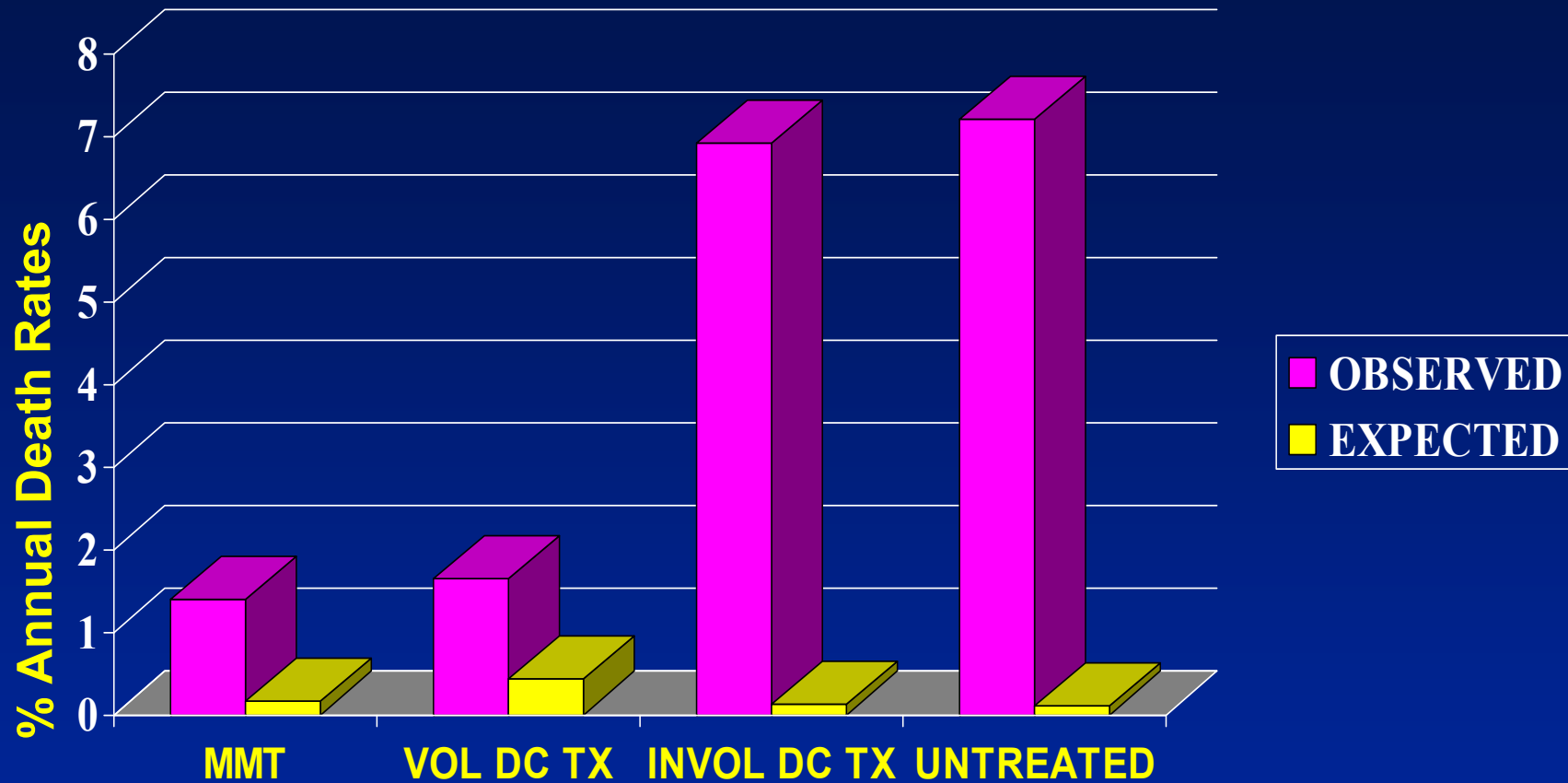
One year outcome randomized controlled trial

Dole et al., 1969

	<u>Reincarcerated?</u>		<u>Daily Heroin Use?</u>	
	Yes	No	Yes	No
Methadone	6(37%)	10	4(25%)	12
Control	16(100%)	0	16(100%)	0

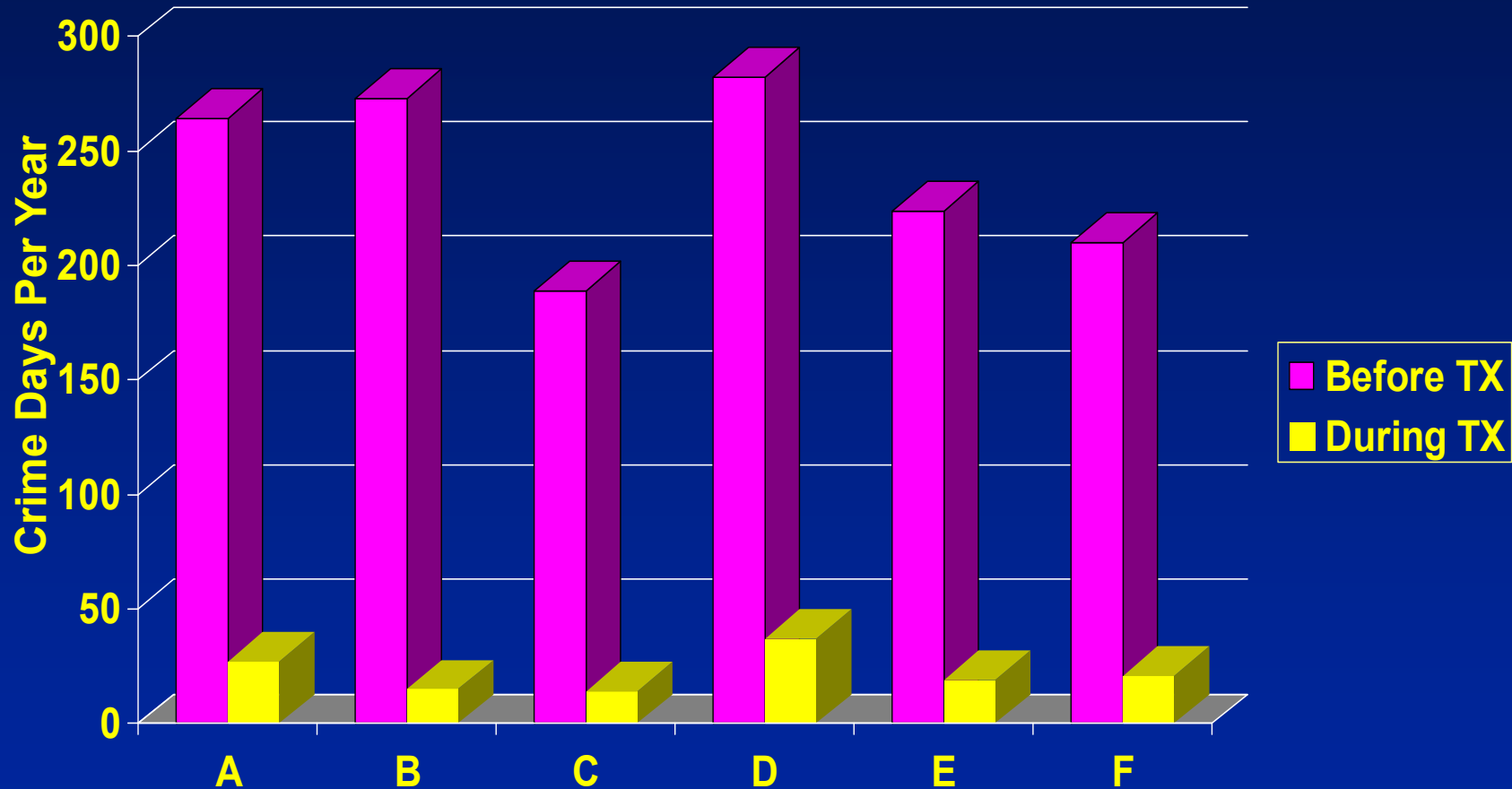
From Key Issues in MMT - Ward, Mattick, and Hall - 1992

DEATH RATES IN TREATED AND UNTREATED HEROIN ADDICTS



Slide data courtesy of Frank Vocci, MD, NIDA - Reference: Grondblah, L. et al. ACTA PSCHIATR SCAND, P. 223-227, 1990

Crime among 491 patients before and during MMT at 6 programs



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

Opioid Agonist Treatment of Addiction - Payte - 1998

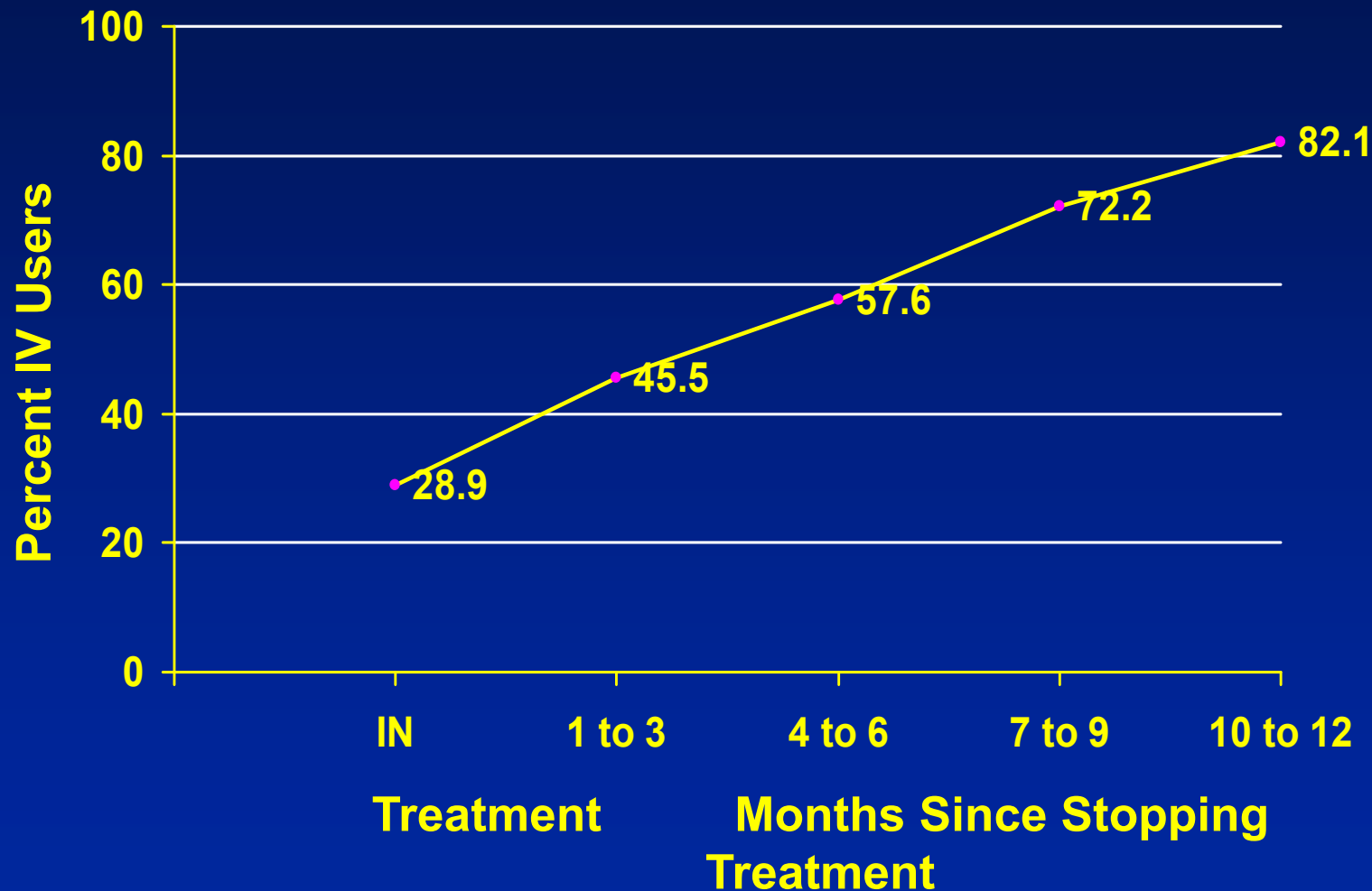
HIV Seropositivity Among Drug Addicts in Bergamo, Italy

Groups	Proportion Positive
Methadone maintenance outpatients	21/74 (28.4%)
Therapeutic Community residents	12/28 (42.9%)
Held in custody	27/66 (40.9%)
Not in treatment	25/51 (52.9%)

Source: Bourne, AIDS and Drug Use: An International Perspective, 1988

Relapse to IV drug use after MMT

105 male patients who left treatment



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

Impact of Medication Assisted Treatment

- Reduction death rates (Grondblah, '90)
- Reduction IVDU (Ball & Ross, '91)
- Reduction crime days (Ball & Ross)
- Reduction rate of HIV seroconversion (Bourne, '88; Novick '90,; Metzger '93)
- Reduction relapse to IVDU (Ball & Ross)
- Improved employment, health, & social function

Methadone Side Effects

- Minimal sedation once tolerance achieved
- Constipation
- Increased appetite/weight gain
- ↓ Libido; May ↓ gonadal hormone levels
- Exhaustively studied: no evidence of harm

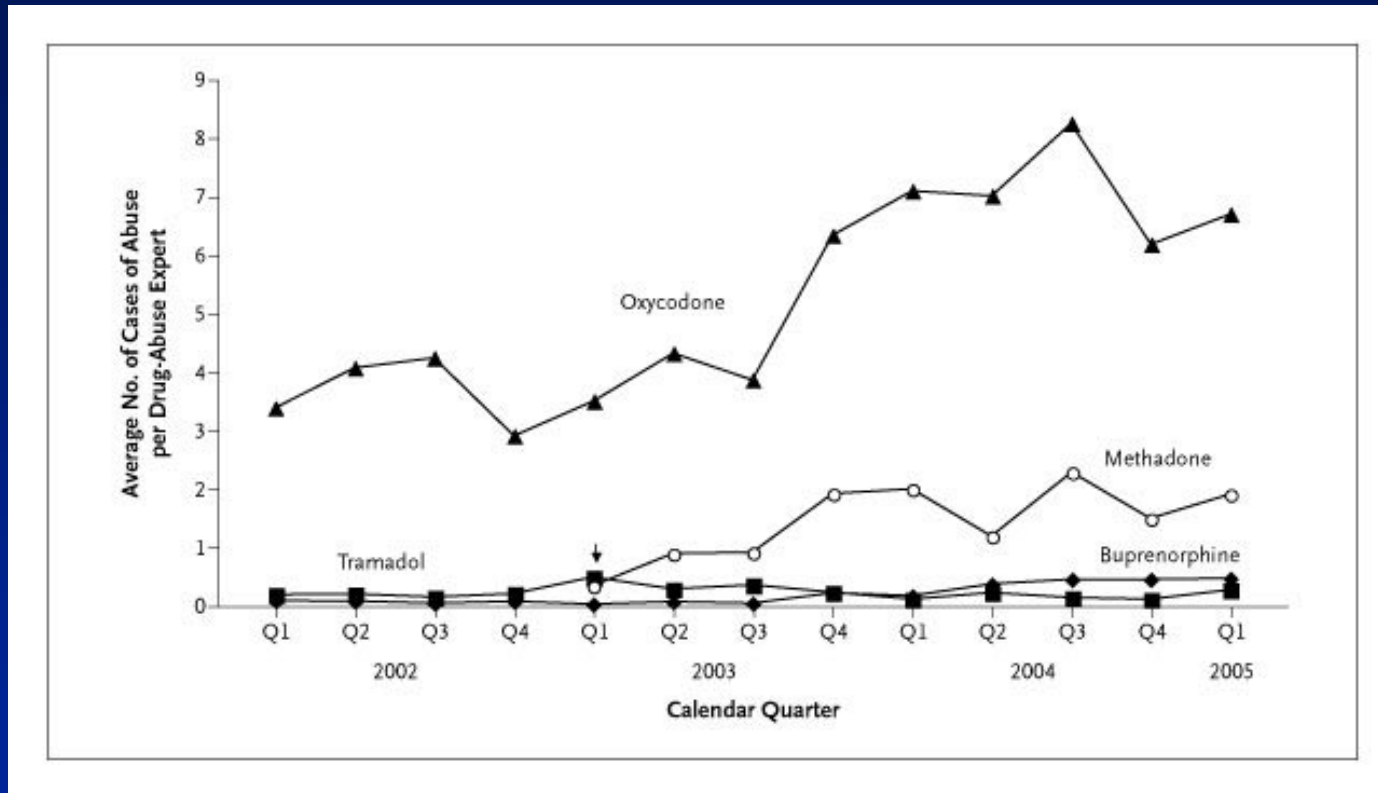
Medications for Opioid Dependence

- Naltrexone
- Methadone
- Buprenorphine (BUP)

Potential for Abuse and Dependence

- **Buprenorphine is abusable**
- **Diversion and illicit use (by injection)**
- **Low abuse potential vs other opioids**

Average Number of Cases of Abuse of Buprenorphine Products, Methadone, Tramadol, and Oxycodone per Drug-Abuse Expert



Cicero, T. J. et al. N Engl J Med 2005;353:1863-1865



The NEW ENGLAND
JOURNAL of MEDICINE

Combination of Buprenorphine plus Naloxone

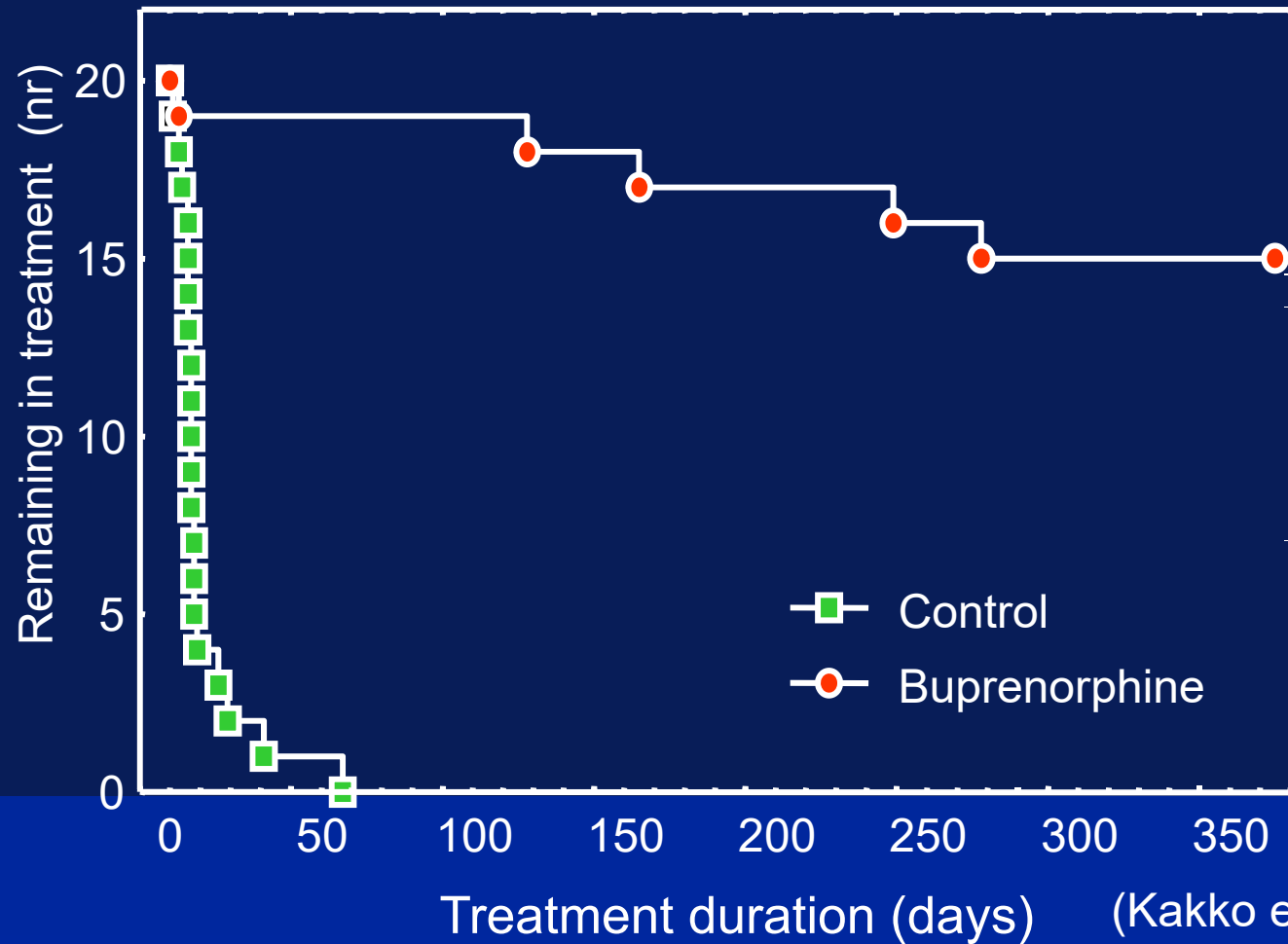
- **Sublingual buprenorphine good bioavailability**
- **Sublingual naloxone relatively poor bioavailability**
- **Combination ratio is 4/1 (buprenorphine/naloxone)**
- **Suboxone (2/0.5, 4/1, 8/2, 12/3 mg films)**
- **Generic BUP and BUP/naloxone available**
- **Sublingual naloxone has a bitter taste**
- **New brands available**
 - **Minty flavored tablet (Zubsolv®)**
 - **Buccal film (Bunavail®)**

Combination of Buprenorphine plus Naloxone

- **Sublingual use → predominantly BUP effect**
- **Dissolves/injects → predominantly naloxone effect**

Efficacy and Safety of Buprenorphine

BUP Maintenance/Withdrawal: Retention



Treatment duration (days) (Kakko et al., 2003)

Buprenorphine Safety

- Highly safe medication
 - Acute dosing
 - Chronic dosing
- Primary side effects:
 - Nausea
 - Constipation
 - Headaches
- No disruption in cognitive or psychomotor performance
- No evidence of organ damage with chronic dosing

Overdose Risk Minimal

- Very low risk
- High dose BUP → no respiratory depression
- No respiratory depression BUP vs methadone
- Overdose BUP + other CNS depressants:
 - Benzos
 - Etoh
 - Barbs

Buprenorphine

- **Partial mu agonist**
- **Effects similar to other mu agonists**
- **↓ risk of respiratory depression**
- **Lower physical dependence**
- **BUP/naloxone combination preferred**
 - **Unsupervised dosing**
 - **↓ diversion**

Opiate Addiction Treatment Outcome*

Methadone Maintenance	50 – 80%
Naltrexone Maintenance	10 – 20%
“Drug Free” (non-pharmacotherapeutic)	5 – 30%
LAAM Maintenance	50 – 80%**
Buprenorphine-Naloxone Maintenance	40-50%
Short-term Detoxification (any mode)	5 – 20% (limited data)

** One year retention in treatment and/or follow-up with significant reduction or elimination of illicit use of opiates*

*** Maximum effective dose (24mgsl) equal to 60 to 70 mg/d methadone. Data base on 6 month follow-up only.*

Kreek, 1996; 2001

This Presentation Covered

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 - **Treatment**

Opioid Agonist Therapy



For Some Patients OAT Can Be An
Effective and Durable Band-Aid.....
But More Is Usually Needed For
Stable Remission—"Recovery"

MEDICATION ASSISTED ADDICTION TREATMENT

“All Treatments Work For Some
People/Patients”

“No One Treatment Works for All
People/Patients”

Alan I. Leshner, Ph.D
Former Director NIDA

Questions?