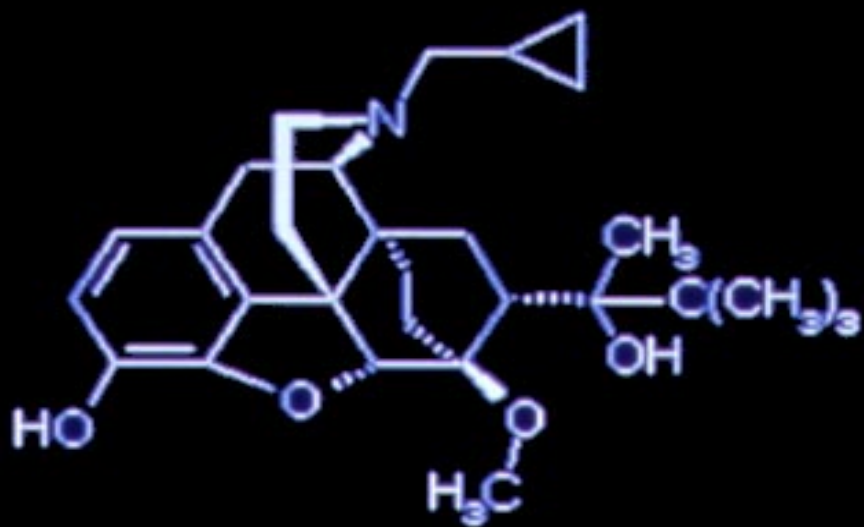


# BUPRENORPHINE

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# **Buprenorphine: View from the Clinician**

**Walter Ling MD**

**Integrated Substance Abuse Programs**

**UCLA**

**Blending Clinical Practice and Research**

**Detroit, Michigan**

**Sept. 27<sup>th</sup> 2004**

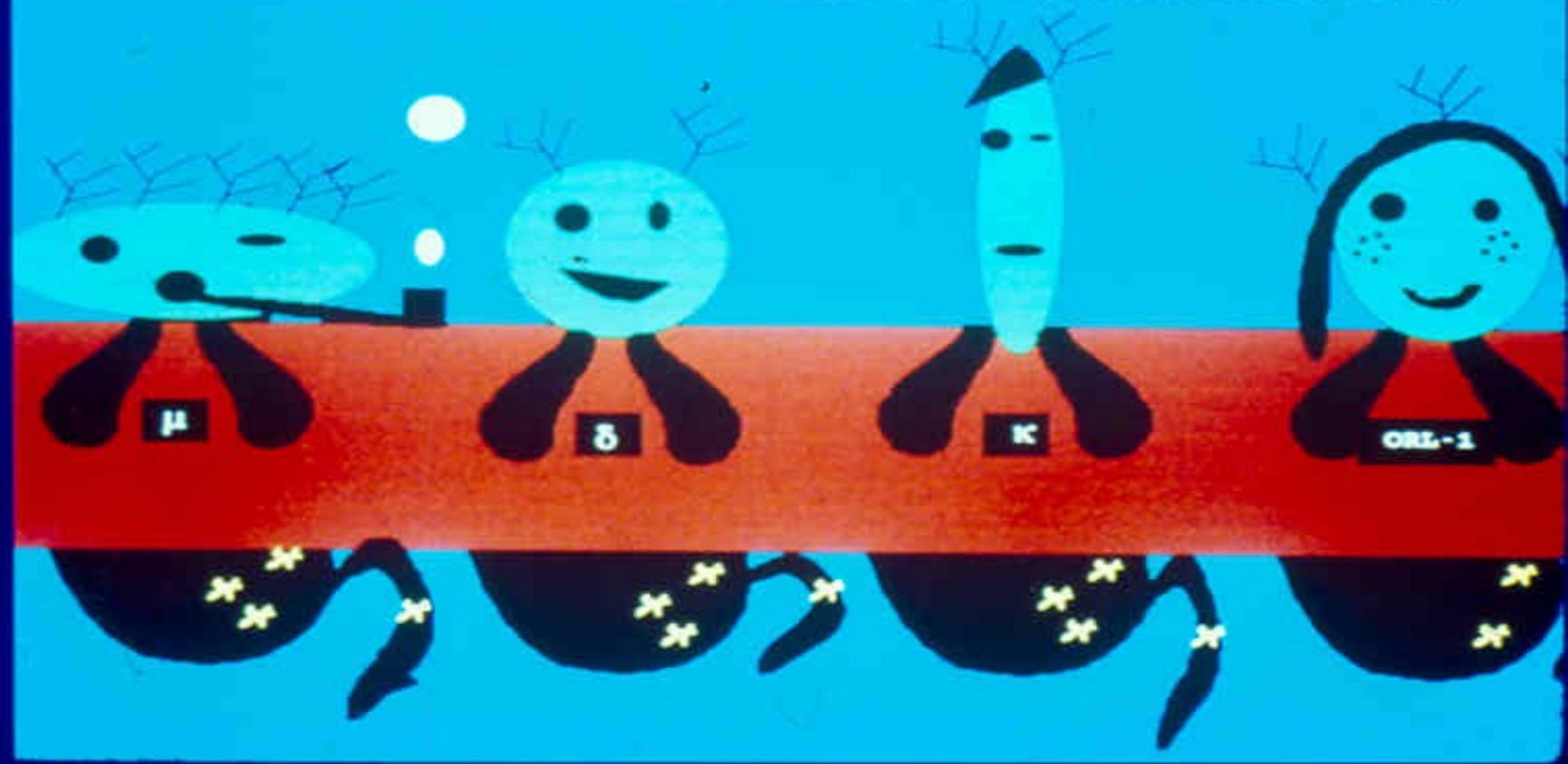
**[lwalter@ucla.edu](mailto:lwalter@ucla.edu)**

**[www.uclaisap.org](http://www.uclaisap.org)**

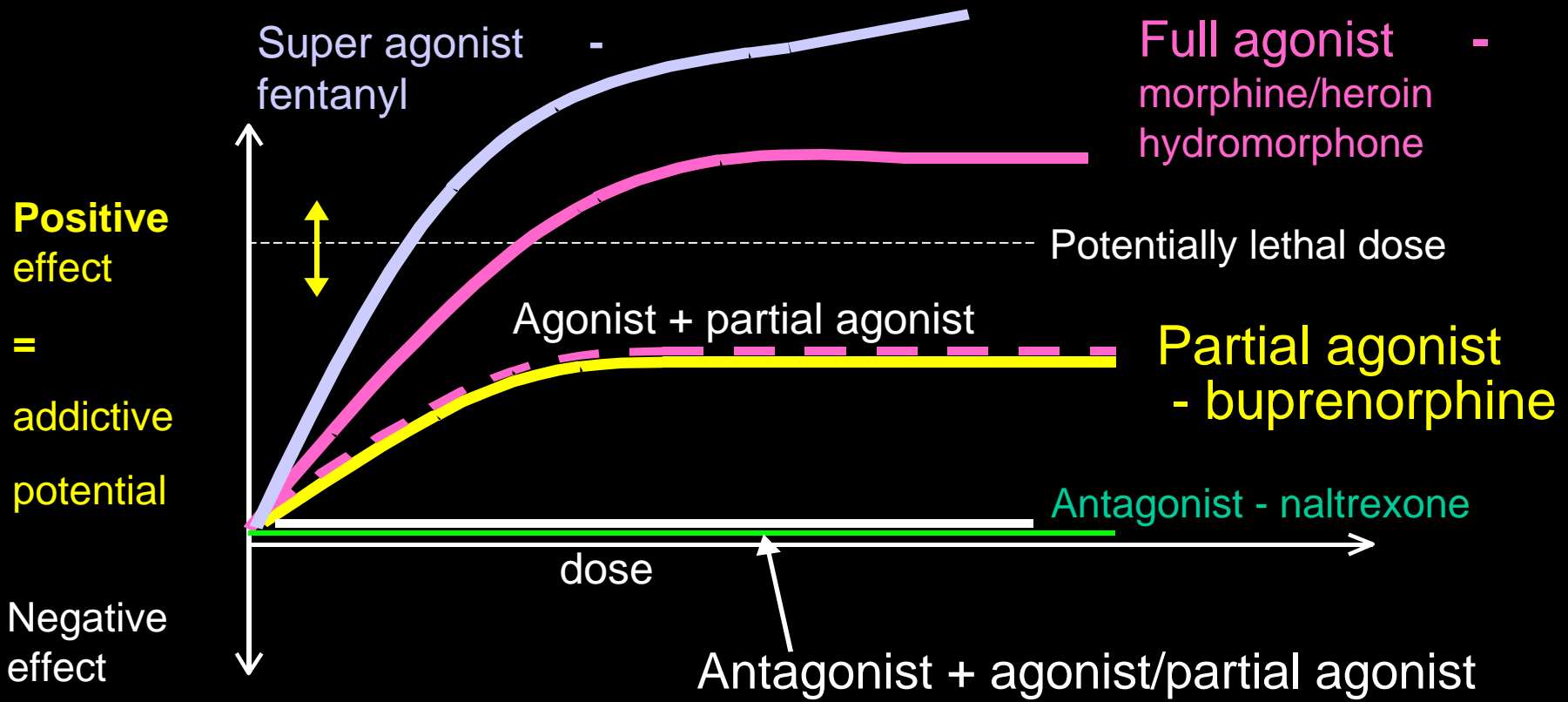
# **Buprenorphine in the Treatment of Opioid Addiction**

- **Buprenorphine as a medication**
  - **Safety and efficacy**
- **Buprenorphine as a Treatment Strategy**
  - **Delivery and patient acceptance**
- **Buprenorphine as a Treatment Philosophy**
  - **The great social experiment and**
  - **The role of the clinicians**

# THE OPIOID RECEPTOR FAMILY & CLOSE RELATIVE



# Mu efficacy and opiate addiction



# **Buprenorphine as a Medication: Pharmacological Characteristics**

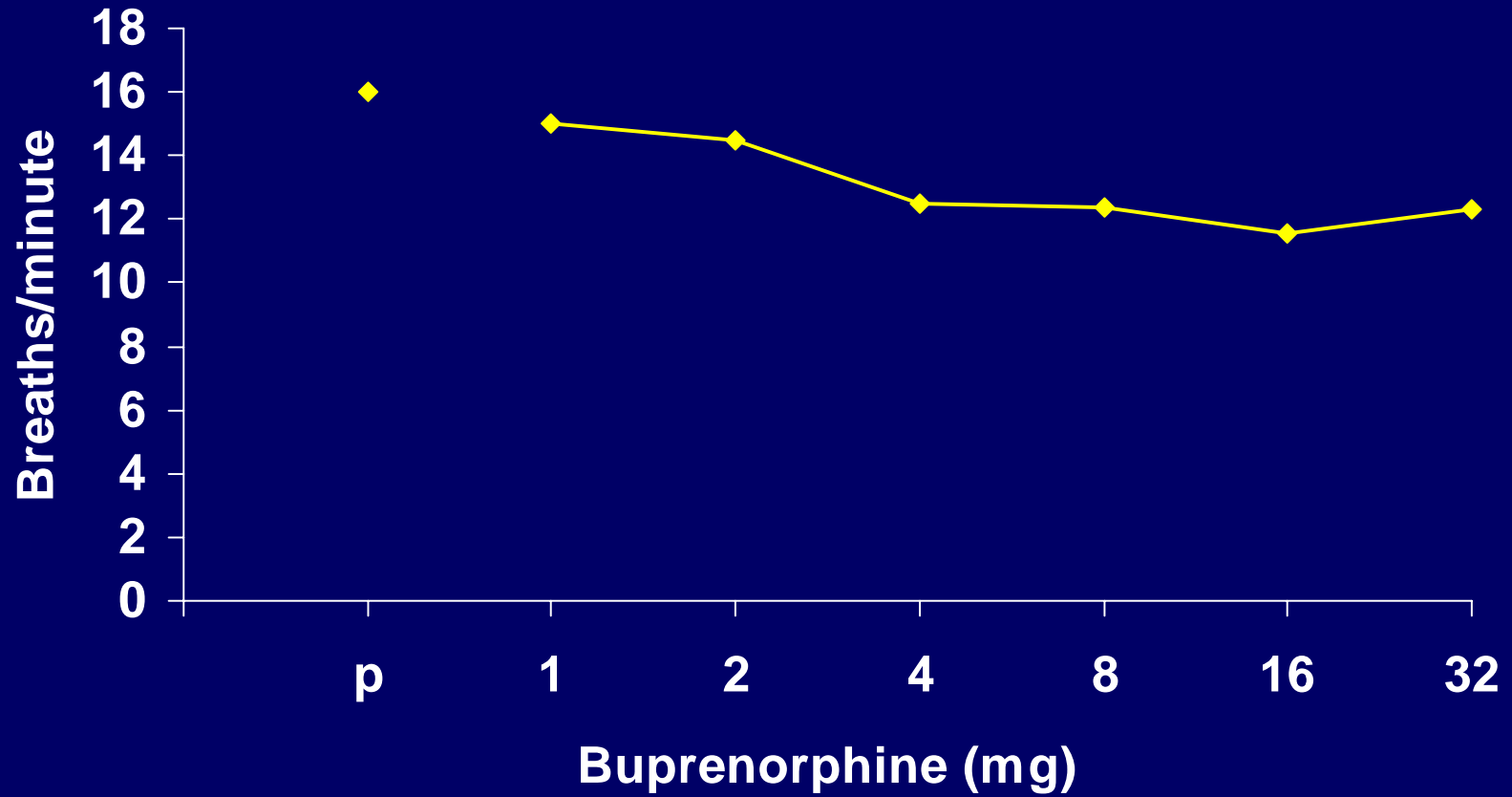
## **Partial Agonist**

- **high safety profile/ceiling effect**
- **low dependence**

## **Tight Receptor Binding**

- **long duration of action**
- **slow onset mild abstinence**

# Respiration



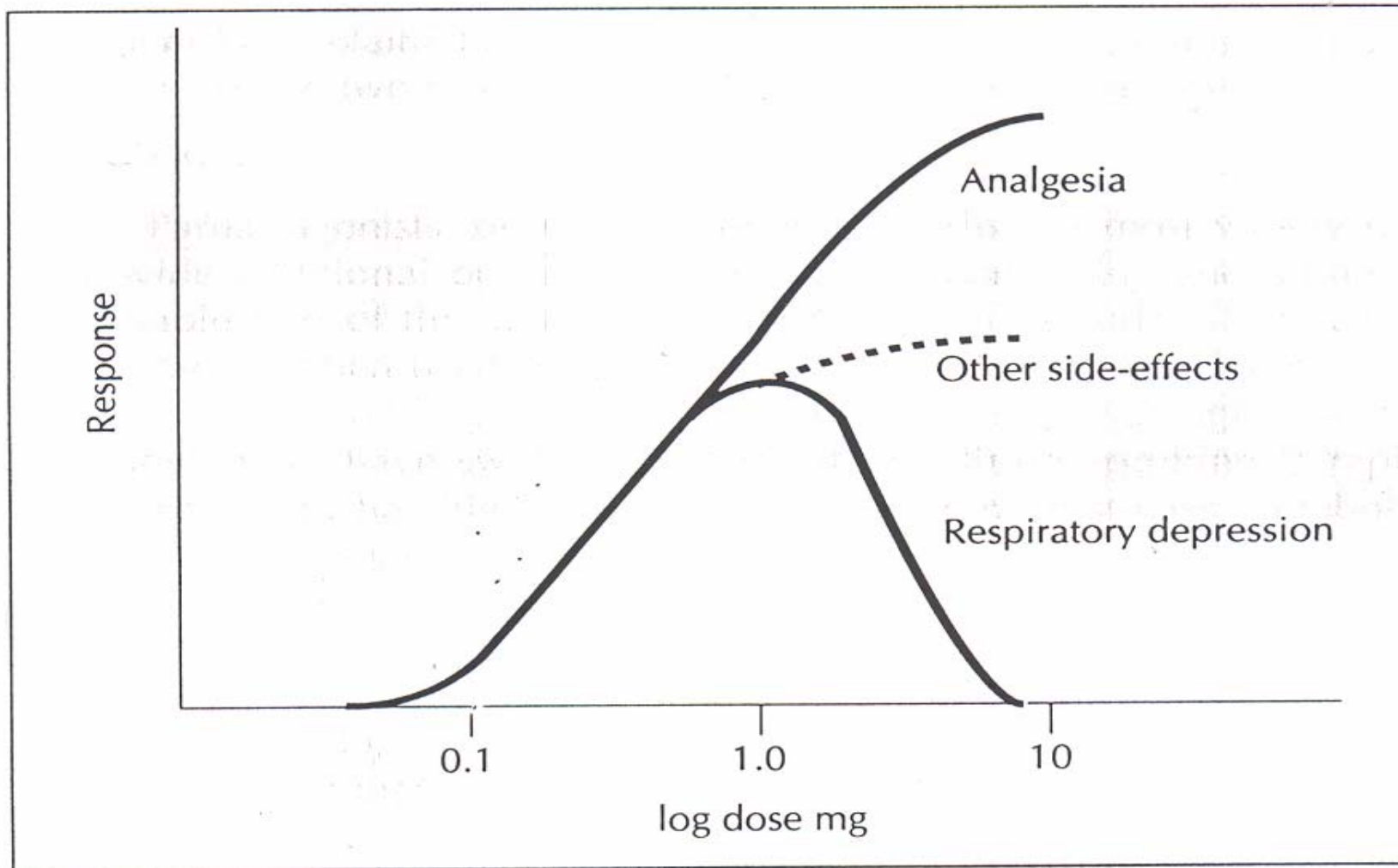
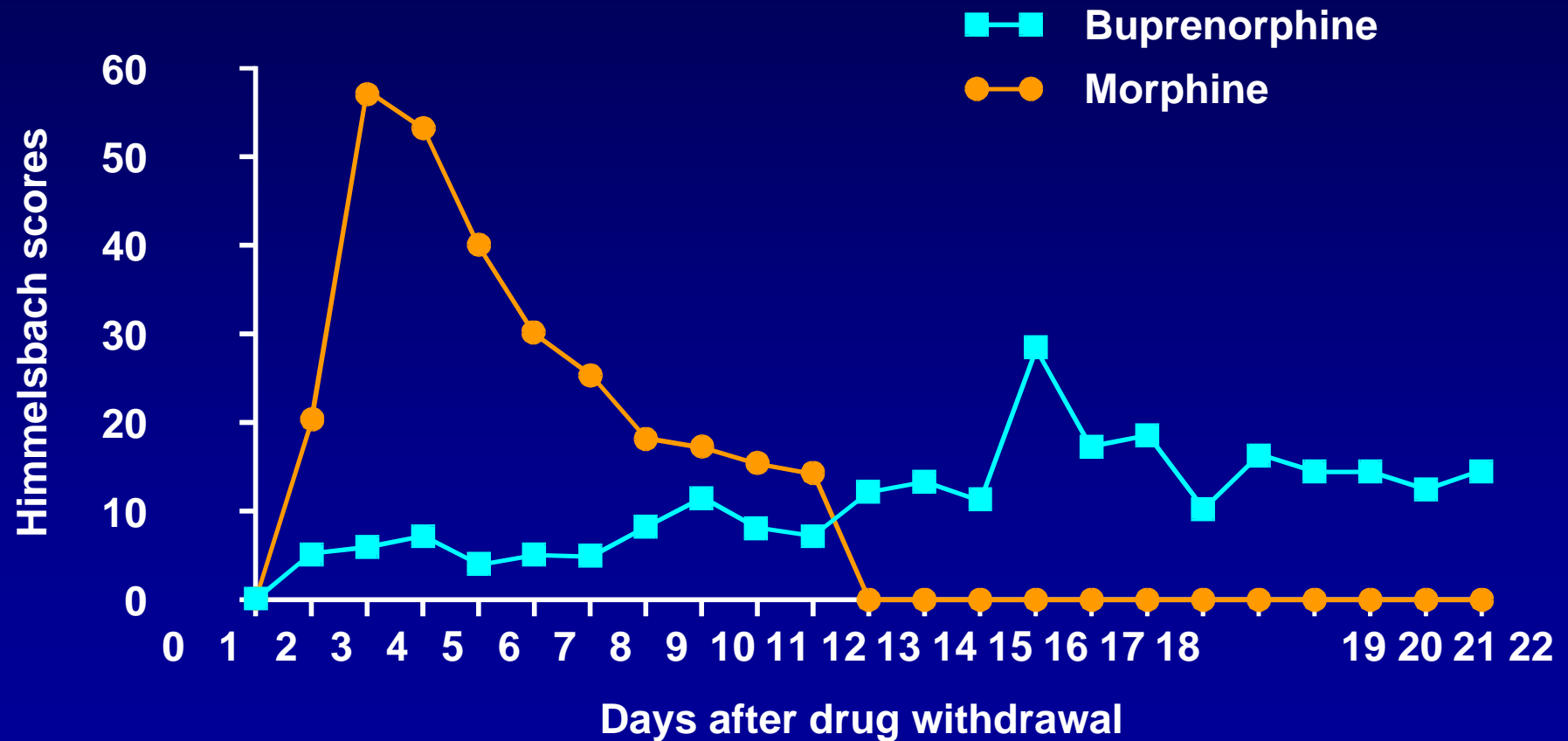


Figure 1. The effect of increasing the dose of buprenorphine on the incidence of side-effects.

# Intensity of abstinence



# **Buprenorphine Made Safer: Addition of Naloxone Reduces Abuse**

- **Naloxone will block buprenorphine's effects by the IV but not the sublingual route**
- **Sublingual absorption of buprenorphine @ 70%; naloxone @ 10%**
- **If injected, BUP/NX will precipitate withdrawal in a moderately to severely dependent addict**

# **Buprenorphine made Safer: Buprenorphine/Naloxone Combination**

**4 part buprenorphine: 1 part naloxone**

**Sublingual: Opiate agonist effect from buprenorphine**

**Intravenous: Opiate antagonist effect from naloxone**

**Discourage IV use**

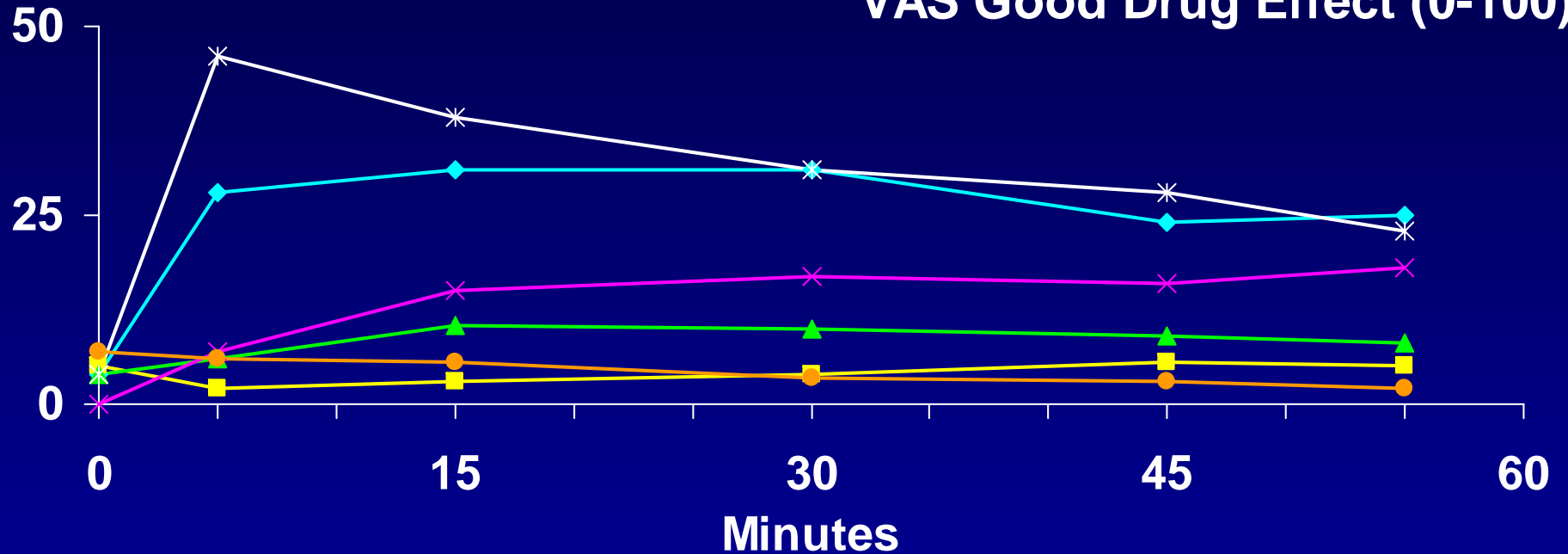
**Diminish street value**

**Diminish diversion**

**Allow for flexible dosing**

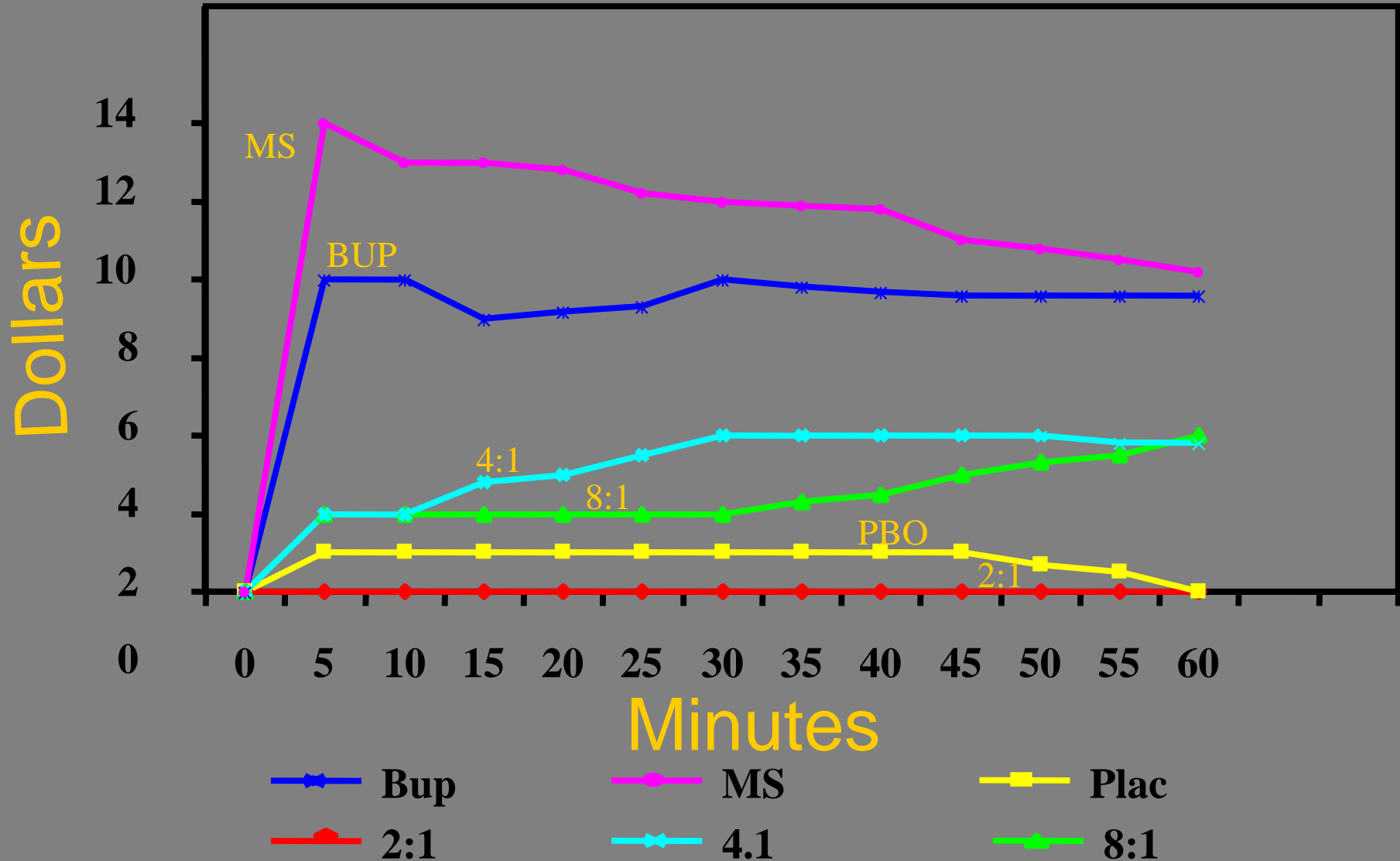
# Opiate Agonist Measures (2)

VAS Good Drug Effect (0-100)



- ◆— buprenorphine (2mg)
- buprenorphine (2mg) and naloxone (1 mg)
- ▲— buprenorphine (2 mg) and naloxone (0.5 mg)
- ×— buprenorphine (2 mg) and naloxone (0.25 mg)
- \*— morphine (15 mg)
- placebo

# Value of a Dose in Dollars



# **Buprenorphine as Treatment strategy: The First CTN Protocols**

- **Inpatient detoxification:**
  - Buprenorphine/naloxone vs clonidine
  - (CTN 0001)
  
- **Outpatient detoxification:**
  - Buprenorphine/naloxone vs clonidine
  - (CTN 0002)

# Study Design

**Open Randomized Study**  
**Bup/Nx:Clonidine = 2:1**

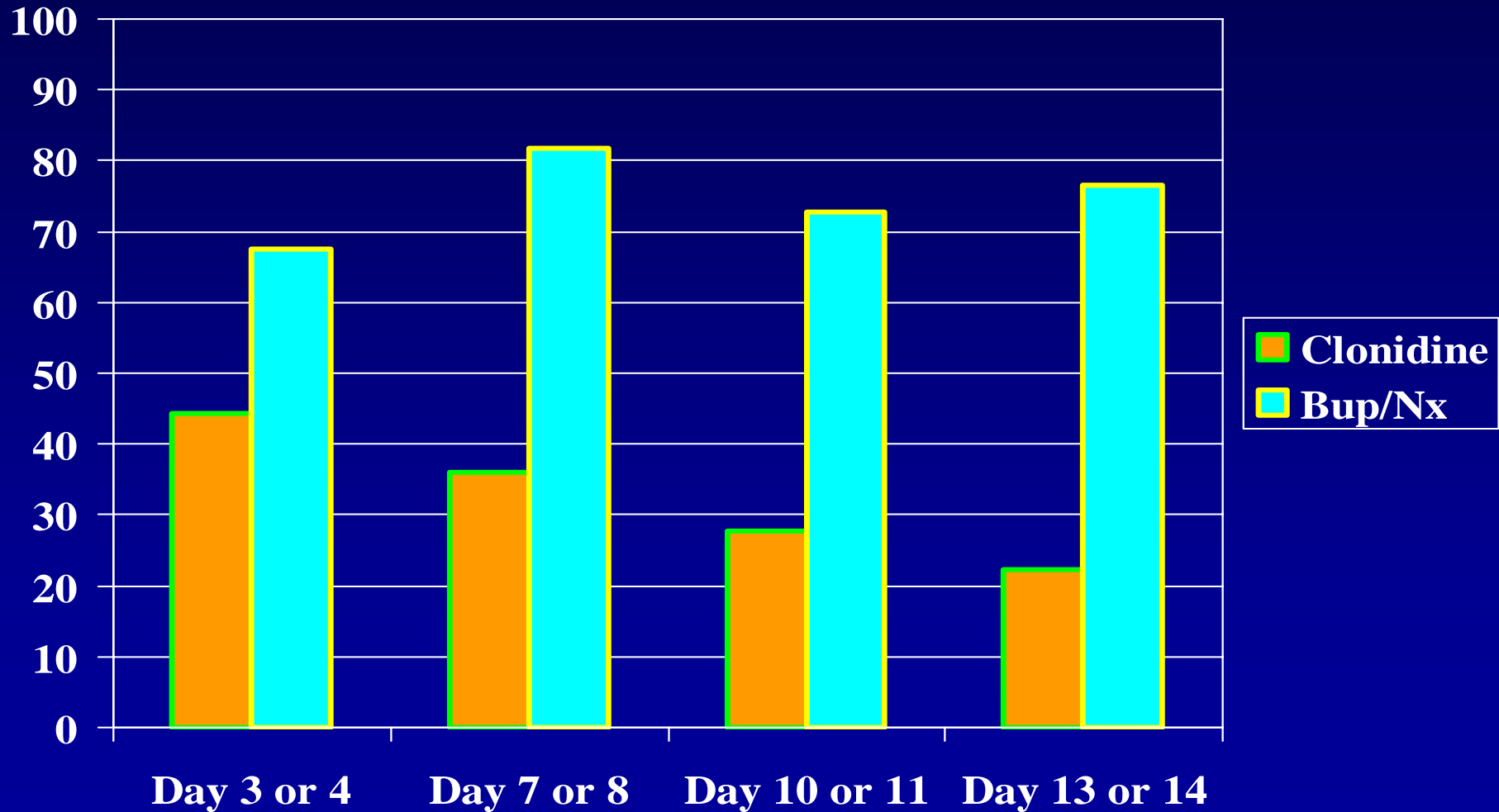
**Buprenorphine/Naloxone**  
**13 days detoxification**

**Clonidine**  
**13 days detoxification**

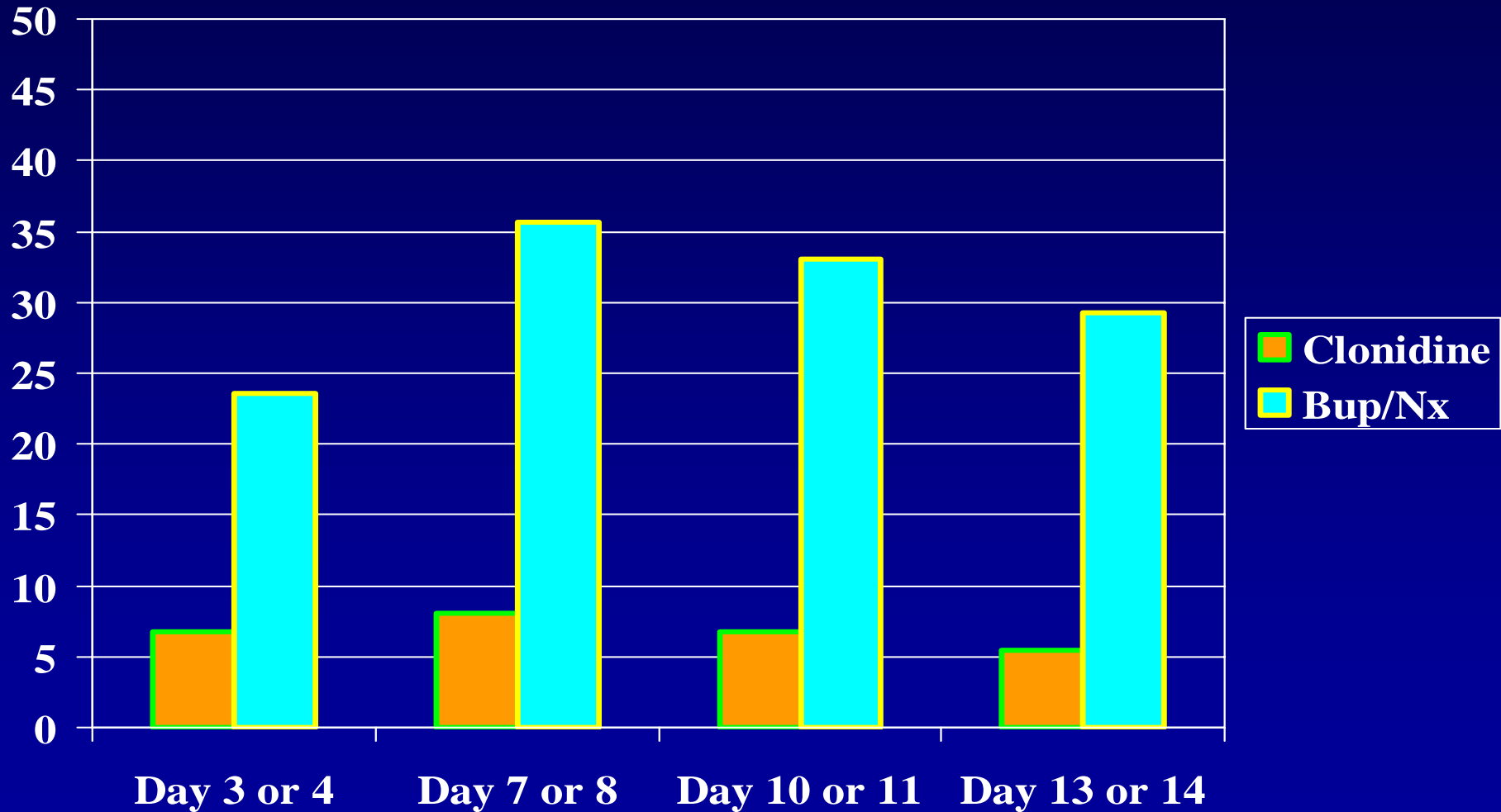
# Joint Probability

$$\frac{\text{N remaining in treatment}}{\text{Total N of subjects}} \times \frac{\text{N giving drug free urines}}{\text{N remaining in treatment}}$$

# Percent Present and Clean 0001 (Inpatient)



# Percent Present and Clean 0002 (Outpatient)



# NNT: Number Needed to Treat

## CTN 0001 (Inpatient)

- NNT for Bup/Nx  $77/59 = 1.31$
- NNT for Clonidine  $36/8 = 4.5$

$$\text{NNT Clonidine : BupNx} = 3.44$$

## CTN 0002 (Outpatient)

- NNT for Bup/Nx:  $157/46 = 3.4$
- NNT for Clonidine:  $74/4 = 18.5$

$$\text{NNT Clonidine : Bup/Nx} = 5.44$$

*NNT= Number of patients needed to treat to achieve 1 treatment success*

# **Buprenorphine: A New Treatment Philosophy**

- **The great social experiment**
  - Drug addiction treatment act of 2000
- **The role of the clinician**
  - Medication and recovery
  - Changing lives

# **Our Treatment Philosophy**

**Addicts are sick; they need help**

**They also sin; don't help them too well**

# **Drug Addiction Treatment Act of 2000**

—

**An Amendment  
to the Controlled Substances Act  
(October, 2000)**

***“The Great Social Experiment”:  
The return of the physician***

# Classification of Addicts and Recommended Treatment

## Types of Addicts

- Correctional cases
- Mental defectives (degenerates)
- Social misfits
- Otherwise normal

## Treatment

- Internment camps
- Sterilization
- Vocational guidance
- Psychoanalysis

# **Pharmacotherapy and Recovery**

- **Medications and recovery: incompatible?**
- **“Medication is not recovery”**
- **The great chemistry paradox**
- **How people change**

# Pharmacotherapy & Recovery

- **Experience (recovery) creates memory**
- **Memory means new protein synthesis**
- **Protein synthesis leads to gene expression**
- **Gene expression determines new behavior**
- **New behavior produces new experience**

*You can change your brain with chemistry or with experience; they are the same thing*

# **Pharmacotherapy and Recovery: Nature via nurture**

- **Our genes and our jeans are closer than we think; our gene were our grandfathers' jeans**
- **How do people change?**

**Remember....**

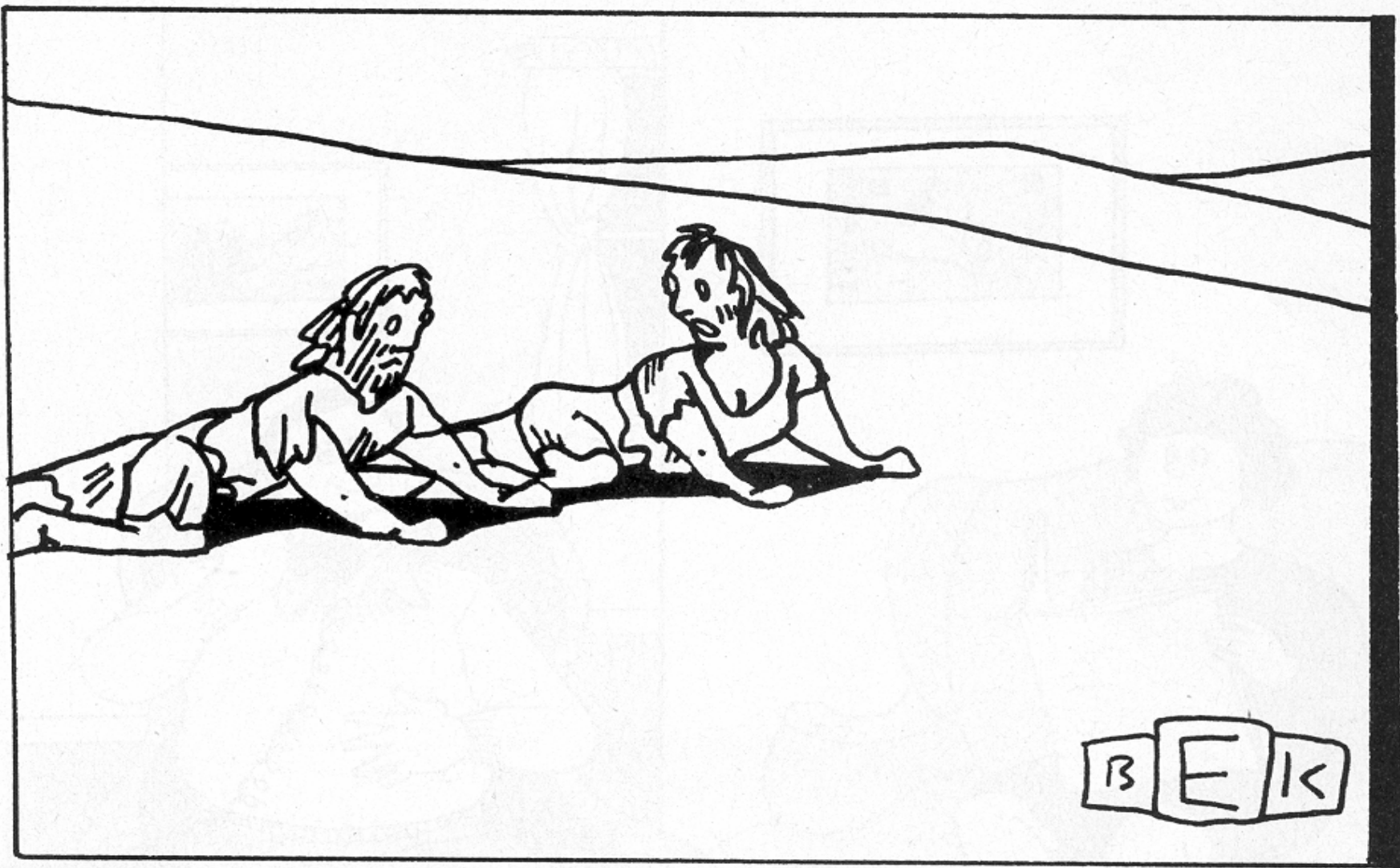
***You Can Change the Brain with Either  
Biological or Behavioral Treatments***

**Alan Leshner**

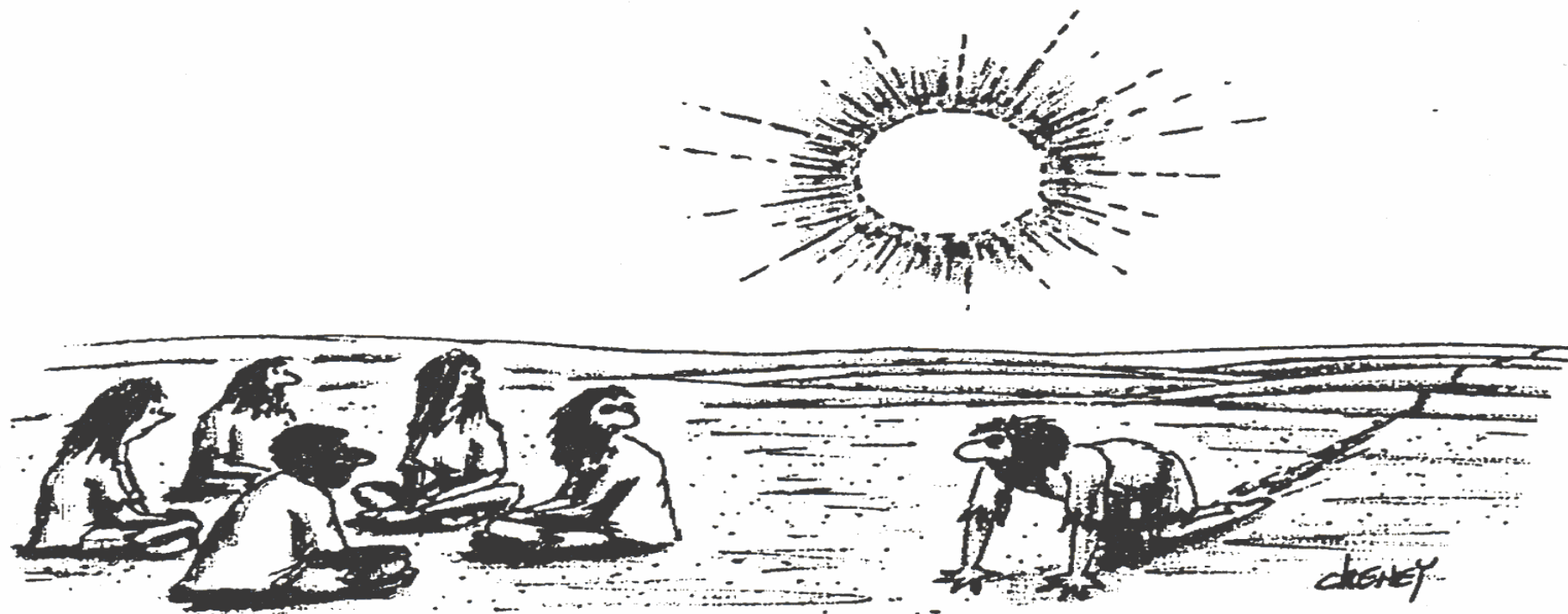
# Changing Lives

- *“You can change some one’s life by altering his genes; but you can also do that by paying off his credit card”*

**James Watson**



*"This isn't really about water. It's about what's going on between us."*



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

# **Thanks to**

**National Institute on Drug Abuse**

**NIDA Clinical Trials Network Staff**

**CTN Publications Committee**

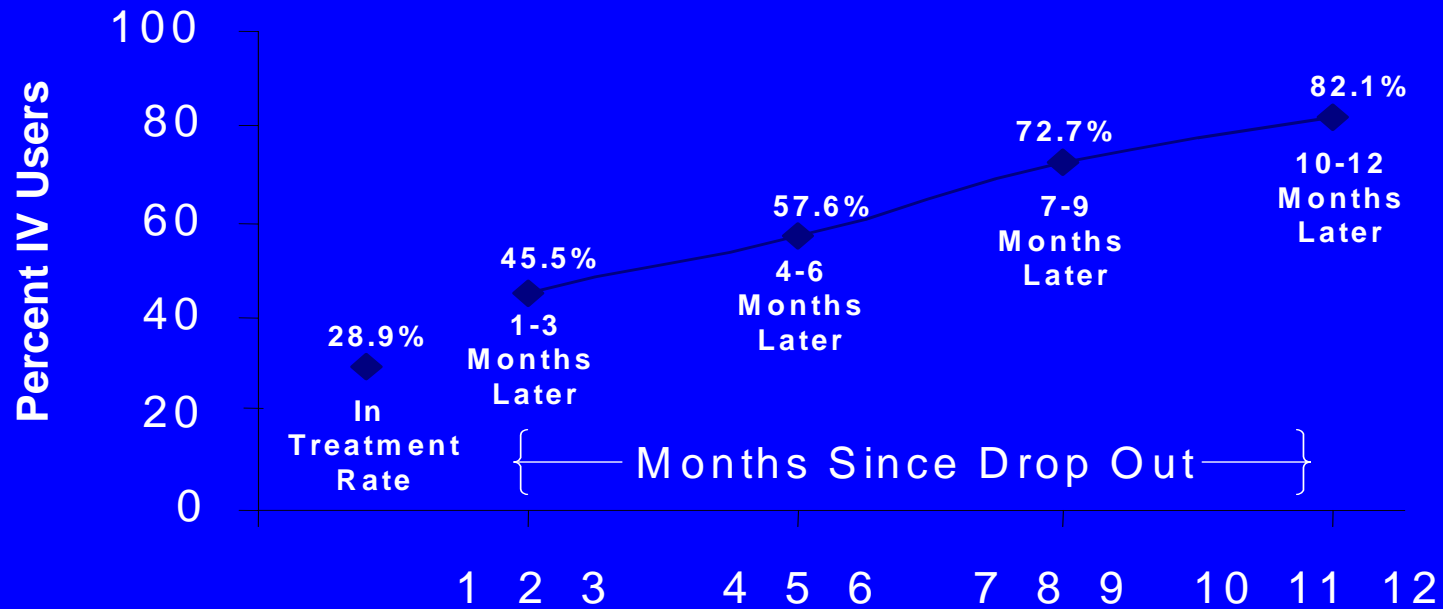
**Participating CTN Nodes and CTPs**

**Reckitt Benckiser**

**Participating Patients**

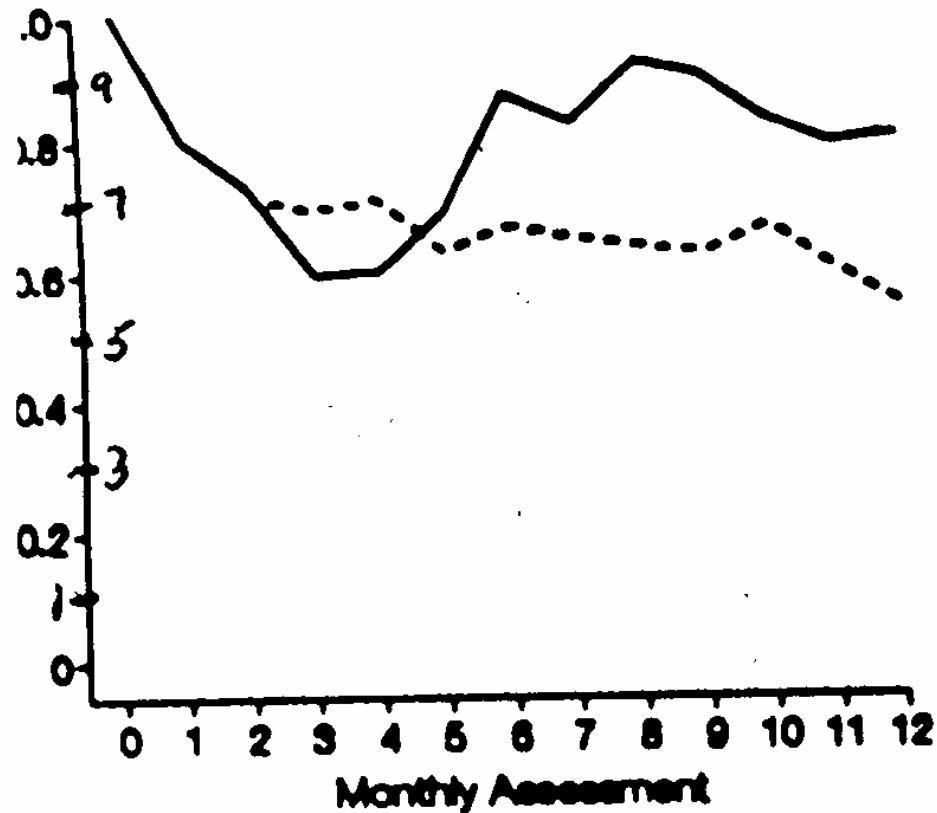
**You the audience**

# Relapse to IV Drug Use After Termination of Methadone Maintenance Treatment



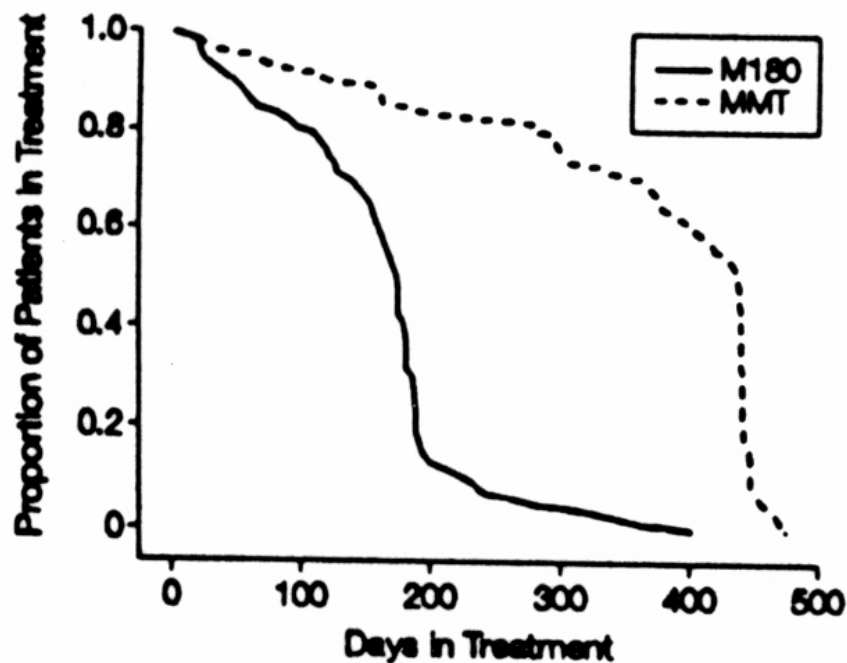
Ball, JC, Ross A. The Effectiveness of Methadone Maintenance Treatment, Springer-Verlag, New York, 1991

### Heroin Use



SD indicates 180-day methadone-assisted detoxification; MMT, methadone maintenance treatment. Test parameter estimates ( $P$  value,  $<.001$  for all estimates): group,  $-0.15$ ; assessment,  $-0.005$ ; and group  $\times$  assessment,  $0.003$ .

**Figure 3. Survival Function by Treatment Group**



Proportion of study participants in treatment by group over time. M180 indicates 180-day methadone-assisted detoxification; MMT, methadone maintenance treatment. For significant differences between conditions, Wilcoxon  $\chi^2_{1, 85.0}$  ( $P < .001$ ).

# Detoxification

**Detoxification is good for a lot of things;  
staying off drugs is not one of them.**

# Pentazocine: T's Blues

- **Pentazocine: mixed angonist/antagonist analgesic**
- **Pentazocine use and abuse**
- **T's and blues**
- **Pentazocine/nx**

