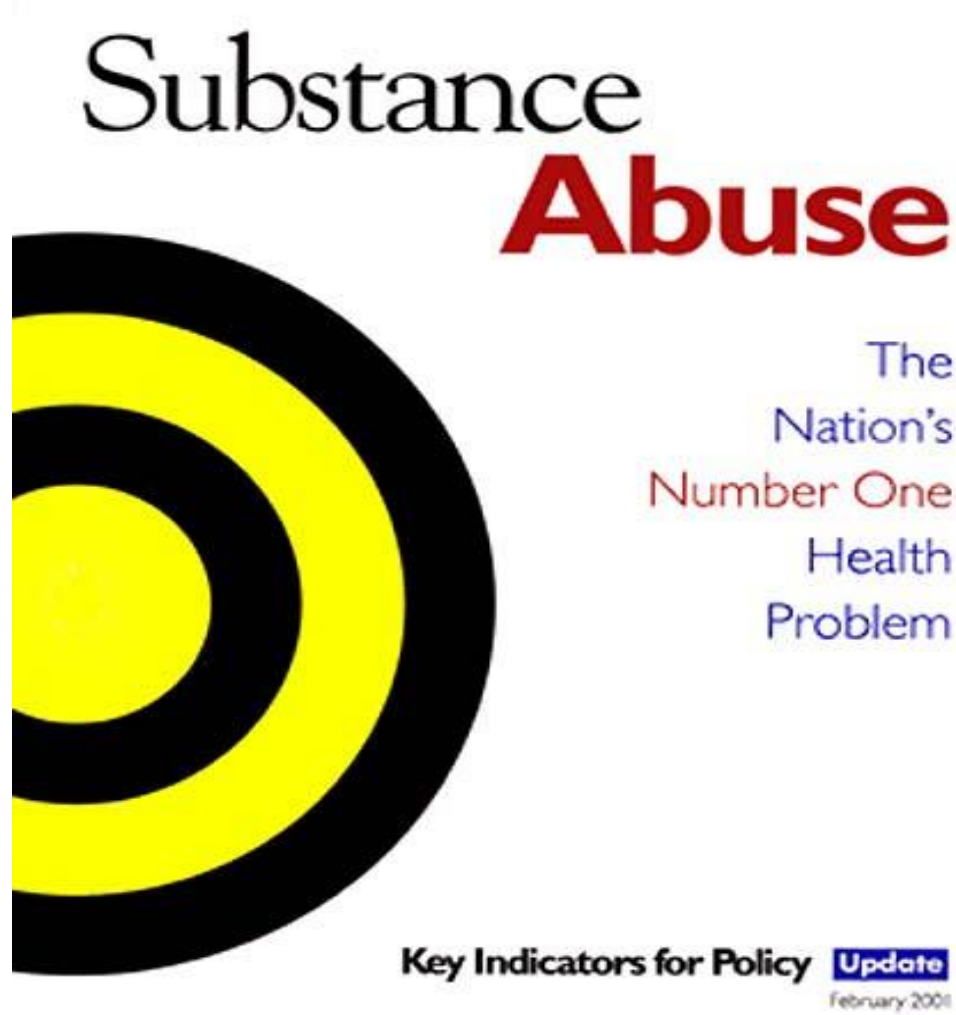
The Robert Wood Johnson Foundation has identified Substance Abuse as the Nation's Number One Health Problem



Opioid Pharmacology

OPIOID: Any chemical compound with pharmacologic actions similar to those of morphine. The term "narcotic analgesic" is often used to refer to opioids.

Sumerians (6000 years ago) called poppy "joy plants." Morphine and codeine are alkaloids of the poppy plant, obtained as opium, referred to as OPIATE.

Opioid Actions

CNS: analgesia, euphoria (dysphoria), sedation, respiratory depression, release of prolactin, nausea, anti-tussive effect

C-V: peripheral vasodilatation

EYE: pupil constriction

LUNGS: respiratory depression

GI: decrease in propulsive contractions in the small intestine and colon. Spasms.

Pain -- Opioids -- Analgesia

Primary medical use

entire group - morphine, etc.

acute and chronic severe pain

cancer pain --- addiction

Non-medical use = euphoria

Opiate Dependence

- Nationally =
- Heroin but also pharmaceutical opioids fentanyl, oxycodone (esp.. Oxycotin®)
- Male vs. female
- Urban

- **2.3 million Americans reported using heroin ≥ once (1998)**
- **149,000 new users (1999)**
- **980,000 persons using at least weekly (1998)**
- **810,000–1 million chronic users of heroin**
- **Only 170,000–200,000 receiving treatment**

(National Household Survey on Drug Abuse, 1999; Office of National Drug Control Policy, 1997; SAMHSA, Office of Applied Studies, National Household Survey on Drug Abuse, 2000 and 2001)

- **Abuse of Prescription analgesics has risen**
- **OxyContin®, Vicodin®, Demerol®**
- **Dramatic press coverage**
- **Emergency Department visits 1994–2001: 41,687 to 90,232 (117% increase)**

- **Significant diversion and abuse of methadone**

DAWN, 2002

What is the cost to society?

- **$20 billion per year total cost of heroin abuse**
- **The economic cost of drug use and dependence estimated to be $98 billion (Harwood *et al*, 1998)**
- **Figures do not take into account social impact of drug addiction**
  - **Crime / legal costs**
  - **Absenteeism from work / unemployment**
  - **Welfare / medical costs**

Basic Terms 1

- **Abuse — culturally disapproved use**
- **Addiction — meaning varies**
- **Dependence — physiological changes, maladaptive behavior, neuroadaptation, repeat doses or withdrawal**

  (see lecture notes for DSM-IV diagnosis)

Basic Terms 2

- **Tolerance —**
- **Withdrawal Symptoms — abrupt stop --- craving, dysphoria, nervous system over-activity**
- **Cross-Tolerance — another drug substitutes**
- **Rebound — abrupt stop --- exaggerated original symptoms**

Basic Terms 3

- **Detoxification — slow taper to prevent withdrawal**
- **Withdrawal Symptoms — craving, dysphoria, nervous system over-activity**
- **Relapse — return to abuse following full detoxification and stabilization**
- **“slip” —**

Basic Terms 4

- **Agonist — stimulates receptor same as abused drug**
- **Partial Agonist — stimulates but “ceiling” effect**
- **Antagonist — blocks receptor and prevents abused drug effect**

Substance Abuse signs -- General Physician

Medical: infection, nasal/pulm, scars, drug requests

Behavior: poor school/work, marital, family discord

Laboratory: urine*, blood, (hair **, etc.)

* No info regarding tolerance/dependence

** huge issues re: privacy issues, validity

Opioid

- **Detoxification** — agonist, taper and/or clonidine

(transcrainal electro-stimulation -- inc. endorphin)

- **Substitution** — methadone, buprenorphine
- **Antagonist** — naltrexone
- **Relapse Prevention** — naltrexone
- **New** — long-acting buprenorphine, naltrexone

Withdrawal symptoms

- Sweating
- Yawning
- Anxiety
- Increased BP and respiratory rate
- Cravings
- Lacrimation
- Piloerection
- Rhinitis
- Gastrointestinal symptoms

  Abdominal cramps, Diarrhea

Methadone

- Available since 1960's BUT confined to special programs, under federal and state controls.

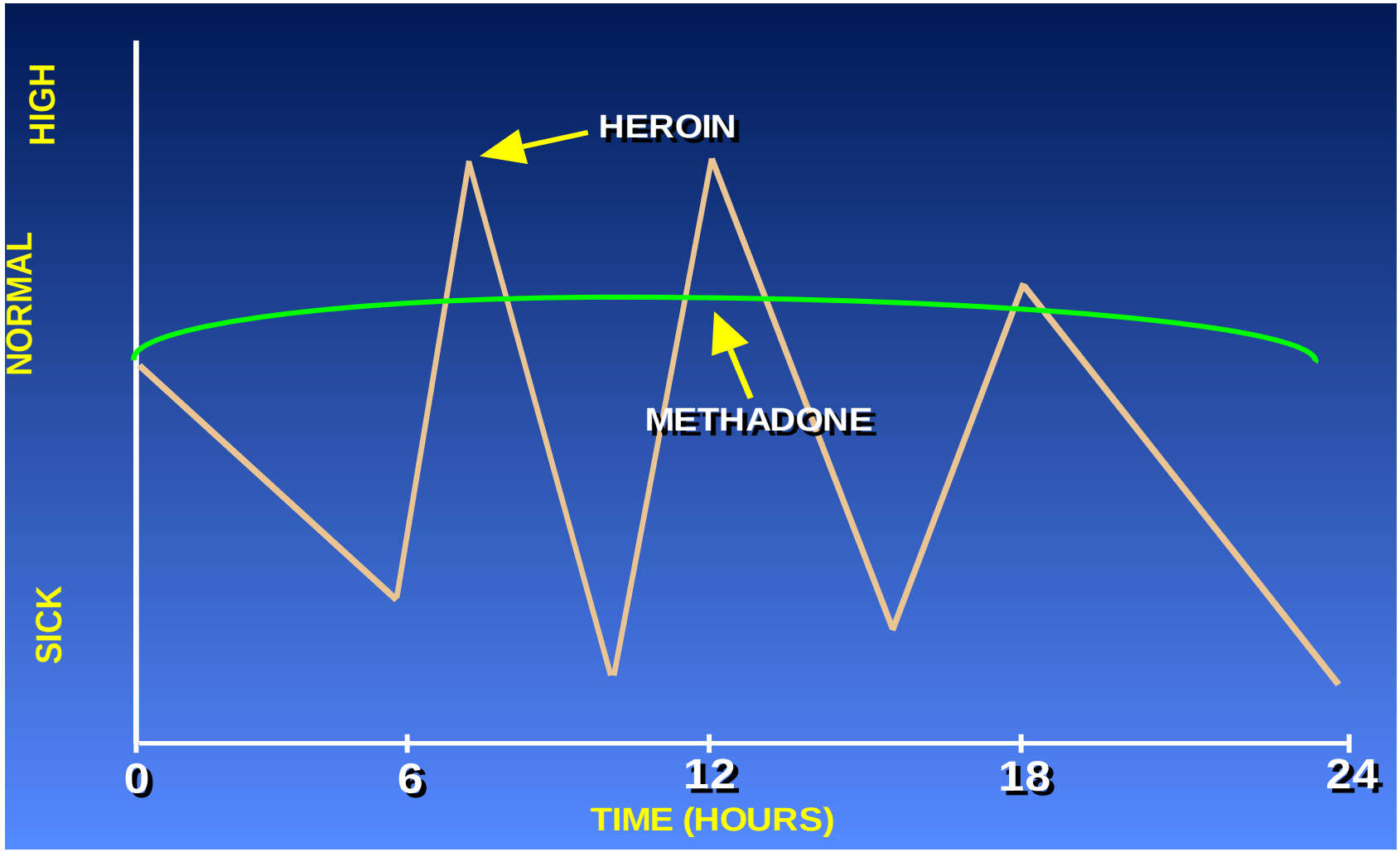
- Primary care and other private physicians unable to treat patients with methadone

Methadone

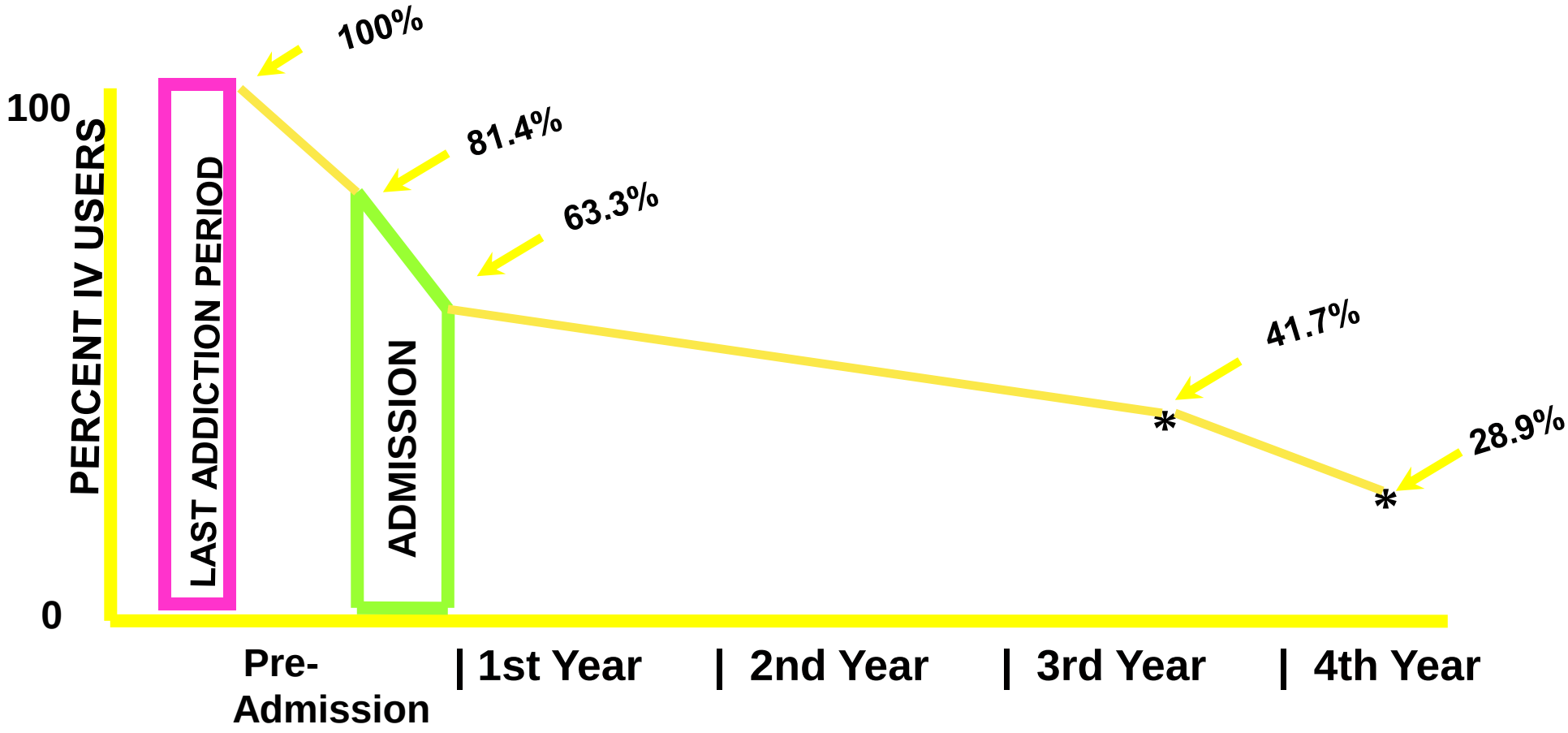
Several, valuable benefits:

- oral, long-acting and cheap
- “blocking dose”
- Eliminate injection risks
- Normalization of body; health
- Life not centered around heroin
- Reduced crime
- Employment

Methadone Maintenance

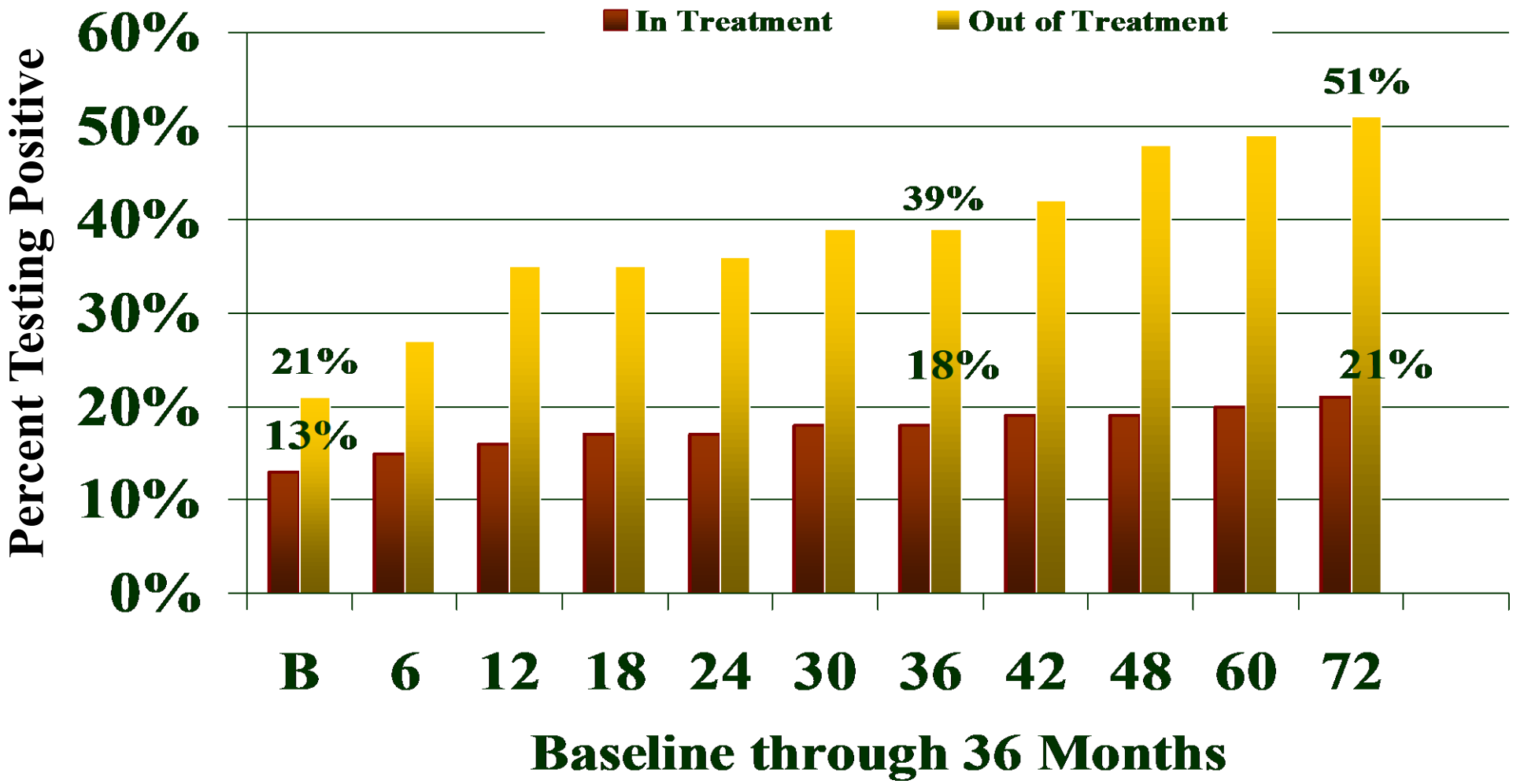


Impact of MMT on IV Drug Use for 388 Male MMT Patients in 6 Programs

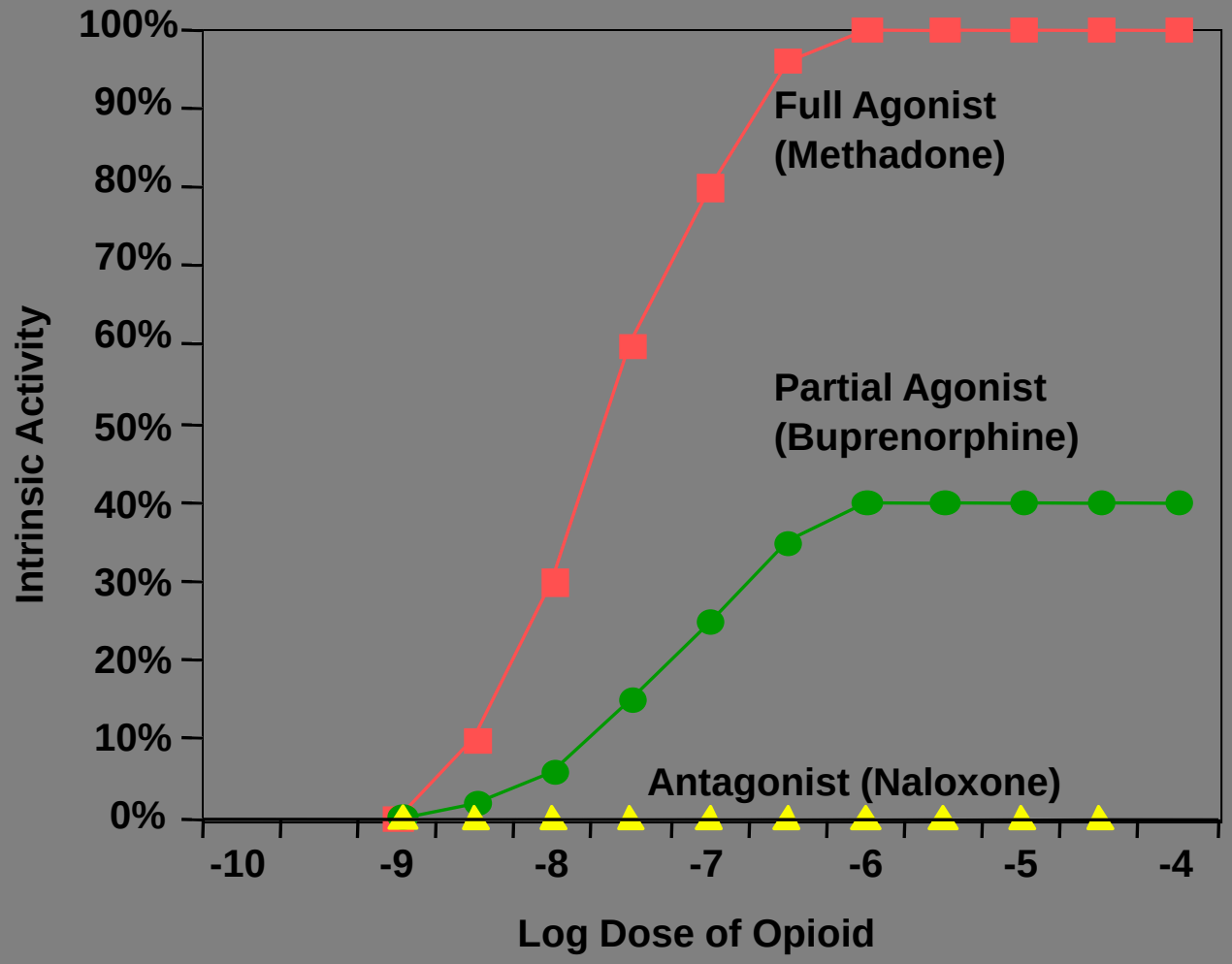


Adapted from Ball & Ross - The Effectiveness of Methadone Maintenance Treatment, 1991

HIV Infection Rates by Treatment Status at Time of Enrollment



Intrinsic Activity: Full Agonist (Methadone), Partial Agonist (Buprenorphine), Antagonist (Naloxone)



Abuse Potential

- Buprenorphine is abusable (epidemiological, human laboratory studies show)
- Diversion and illicit use (by injection) of both of analgesic and substitution forms
- Relatively low abuse potential compared to other opioids

Combination of Buprenorphine plus Naloxone

Combination tablet containing buprenorphine with naloxone – if taken under tongue, predominant buprenorphine effect

If opioid dependent person dissolves and injects buprenorphine/naloxone tablet – predominant naloxone effect (and precipitated withdrawal)

Naltrexone

FDA approved in 1984

- **pharmacologic effects**
- **few studies**

Indications

- **opioid - relapse prevention, detoxification**
- **alcohol (1995) - relapse prevention**
  - **‘anticraving’**

Naltrexone (continued)

Specific antagonism of opiate mu

Competitive antagonism but very tight

Very few AEs (HA, GI, dysphoria)

Oral, relatively long-acting

Non-addicting (no diversion)

Shortened Procedures

- Rapid Opiate Detoxification (ROD)
- Ultra-Rapid (UROD)

Buprenorphine

Scientific point - no proven overall advantage

Penn

- Inpt detox (little methadone)
- naltrexone before discharge

Track Record - very poor acceptance

3% treated

<10% willing to try

many stop drug early

Medication Compliance is a major problem

Subpopulations

Opioid dependent professionals

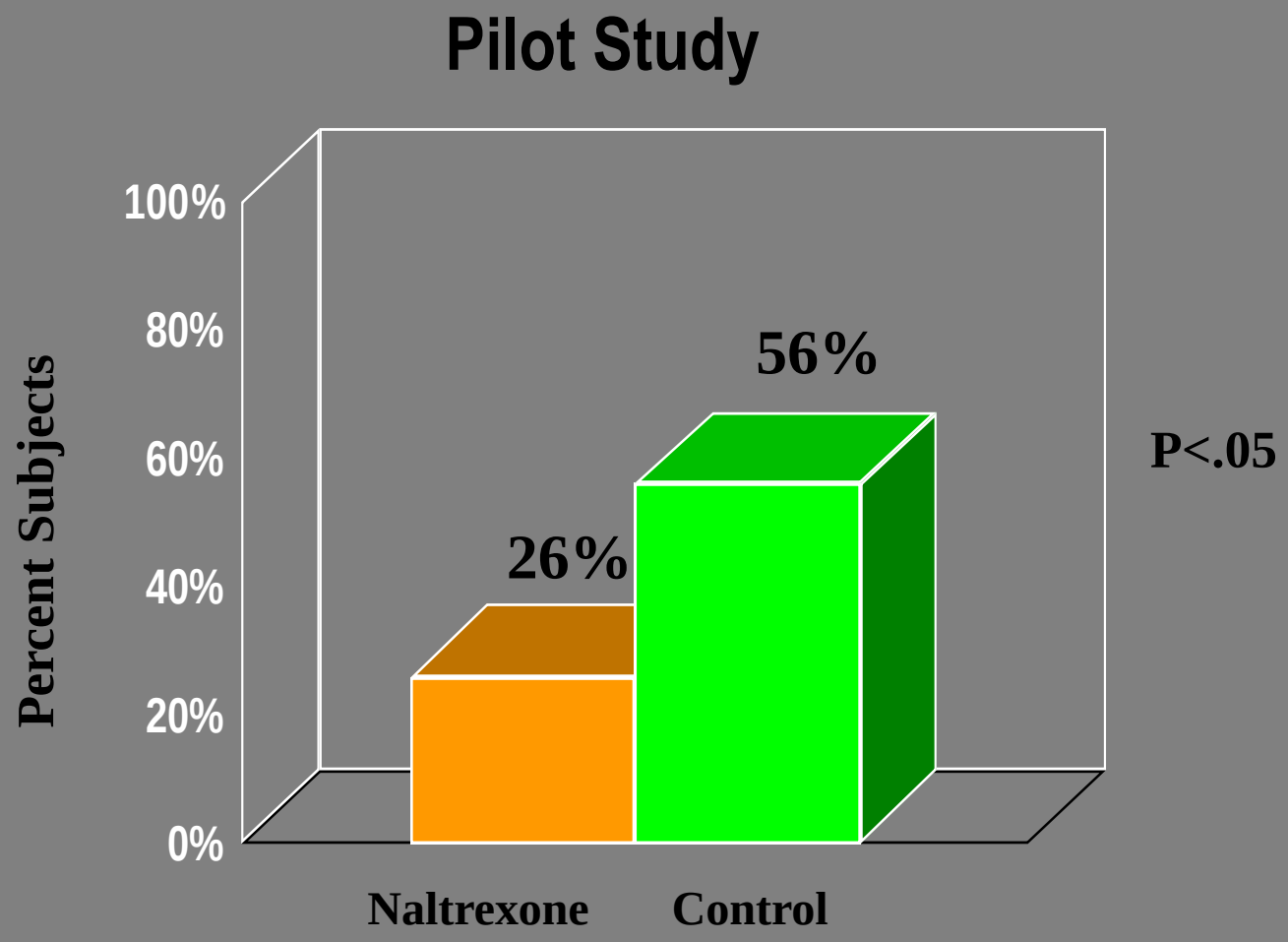
doctors, pharmacists,
lawyers, pilots, etc.

**** something to loose**

Opioid dependent parole clients

**** leverage of the courts**

Subject Re-Incarceration



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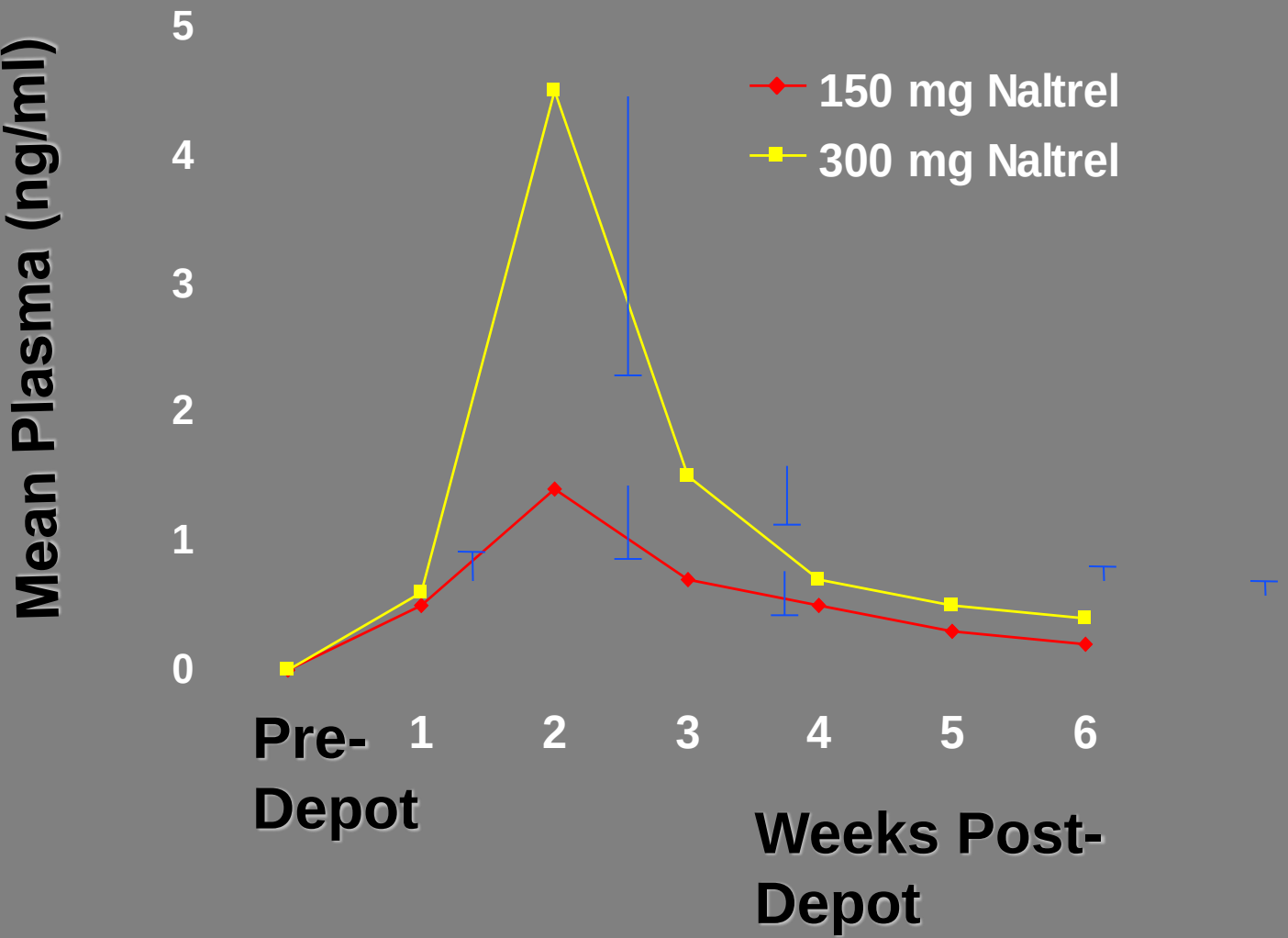
Plasma Levels of Depot Naltrexone



Co-Morbidity Mood Disorders/ SA

- Co-morbidity when presenting for treatment is the “norm”
- Huge literature >3,500 articles, Medline
- Treatment determined by pharmacology + co-morbid condition
- Goal: Practical Guide