Street Drug Pharmacology 2021

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Emerging Drugs of Abuse discussion group

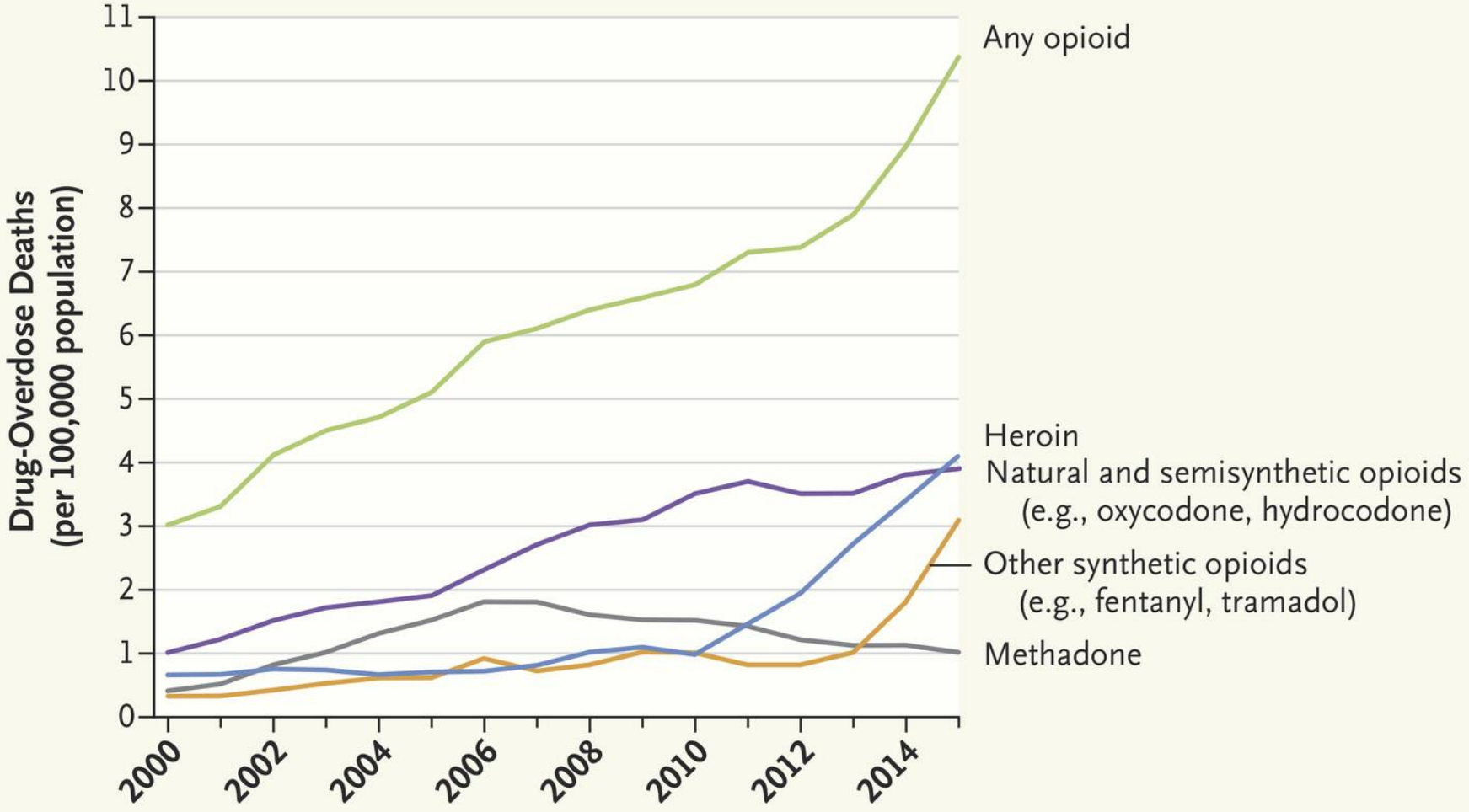
OPIOIDS

Opioids: Basics

- Addiction potential high
- Tolerance develops
- Physical dependence withdrawal symptoms moderate to serious/not life-threatening
- Immediate physical toxicity potential (overdose) moderate to high
- Long-term physical toxicity potential low
- Acute and chronic psychiatric impairment potential low

Opioids

- **Heroin**
- **Hydrocodone/Vicodin/Norco**
- **Oxycodone (OxyContin/Percodan)**
- **Hydromorphone (Dilaudid)**
- **Oxymorphone (Opana)**
- **Fentanyl (Sublimaze)**
- UR-47700
- Other synthetic opioids


Drug-Overdose Deaths
(per 100,000 population)
11
10
9
8
7
6
5
4
3
2
1
0
2000
2002
2004
2006
2008
2010
2012
2014
Any opioid
Heroin
Natural and semisynthetic opioids
(e.g., oxycodone, hydrocodone)
Other synthetic opioids
(e.g., fentanyl, tramadol)
Methadone

Press Release

DEA ISSUES NATIONWIDE ALERT ON FENTANYL AS THREAT TO HEALTH AND PUBLIC SAFETY

WASHINGTON, DC – The United States Drug Enforcement Administration (DEA) today issued a nationwide alert about the dangers of fentanyl and fentanyl analogues/compounds. Fentanyl is commonly laced in heroin, causing significant problems across the country, particularly as heroin abuse has increased.

- **According to DEA, Chicago white heroin is fentanyl laced with heroin**

CBS St. Louis

KMOX NewsRadio 1120

Drug Blamed for Prince's Death Spreading on St. Louis-Area Streets

Brian Kelly (@brpkelly)

June 8, 2016 9:08 AM

Opioids

- March 2016: Fentanyl found in “hydrocodone” and “oxycodone” tablets
- October 2015: Fentanyl found in fake Xanax tablets
- Prince had fake hydrocodone tablets containing fentanyl

Opioids

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- Oxycodone (OxyContin/Percodan)
- Hydromorphone (Dilaudid)
- Oxymorphone (Opana)
- Fentanyl (Sublimaze)
- **UR-47700**
- **Other synthetic opioids (e.g., carfentanil)**

Opioid effects

- Sedation (“nodding”)
- Euphoria
- Pain relief
- Constipation
- Constricted pupils

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- Constipation
- Constricted pupils

Opiate Withdrawal

- Signs of w/d:
  - **Drug hunger (craving)**
  - **Dilated pupils**
  - **Yawning**
  - **Lacrimation (eyes tear)**
  - **Rhinitis (runny nose)**
  - **Fever**
  - **Restlessness**
  - **Stomach, leg and back cramps**

Opiate Withdrawal

- Signs of w/d:
  - **Insomnia**
  - **Nausea**
  - **Diarrhea**
  - **Vomiting**
  - **Chills/cold flashes with goose bumps ("cold turkey“)**
  - **Sweating**
  - **Leg spasms (“kicking the habit”)**

Opiate Withdrawal

- Signs of w/d:
  - **Rapid pulse**
  - **Increased blood pressure**
  - **Anxiety**
  - **Depression**
  - **Muscle and bone pain**

Medication-Assisted Treatment

Medication-Assisted Treatment

Providing opioid agonist or partial agonist medication as an adjunct to psychosocial treatment in order to improve engagement, retention and outcomes.

Treating Opiate Dependency: A Dilemma

- Physical dependence and craving are major barriers to abstaining from opiate use
- Detoxifying addicts with increasingly smaller doses of heroin or morphine is not an effective approach
- “Cold turkey” withdrawal is painful and unpleasant and often results in relapse

Using Medication to suppport opiate dependence treatment

PROFILE FOR POTENTIAL PSYCHOTHERAPEUTIC AGENT

- Effective after oral administration
- Long biological half-life (>24 hours)
- Minimal side effects during chronic administration
- Safe, no true toxic or serious adverse effects
- Efficacious for a substantial % of persons with the disorder

Medications used to treat opiate dependency

- Methadone
- Clonidine
- Buprenorphine
- Naltrexone

Methadone Misconception 1

- MAT clients are still addicted

- Truth: MAT clients will experience withdrawal symptoms if they stop taking methadone. However, withdrawal is not a diagnostic criteriuum when the client is taking opioids solely under medical supervision
- DSM-V requires at least 2 criteria out of a possible 11

DSM-V Criteria: Opiate Abuse

- Mild: 2-3 symptoms
- Moderate: 4-5 symptoms
- Severe: 6 or more symptoms

- Substance taken in larger amount and for longer period than intended
- Persistent desire or unsuccessful efforts to cut down or control use
- Great deal of time spent in activities to obtain, use, recover from effects
- Craving or a strong desire to use

DSM-V Criteria: Opiate Abuse

- Recurrent use resulting in failure to fulfill major role obligation at work, school or home
- Continued use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by effects of the substance
- Important social, occupational, or recreational activities given up or reduced
- Recurrent use in physically hazardous situations
- Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by use

DSM-V Criteria: Opiate Abuse

- Use continues despite knowledge of adverse consequences (e.g., failure to fulfill role obligation, use when physically hazardous)
- Tolerance
- Withdrawal

Methadone Misconception 3

- Opiate dependence is a choice

- Truth: The decision to begin using opiates is a choice. Addiction is a disease.

What is a Disease?

- Organ
- Defect
- Sx

Diabetes

- Pancreas
  - Islands of Langerhans
  - Glucose
  - Insulin
- Diabetes: Insufficient insulin
- External insulin/lifestyle

Diabetes

- Glucose: the source of the energy we need to keep our bodies functioning
- Homeostasis
  - Hyperglycemia
  - Hypoglycemia

Diabetes

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  - Insulin
- Diabetes: Insufficient insulin
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Opiate Dependence

- Brain
- Neurochemical dysfunction
- Compulsive use, loss of control, continued use despite negative consequences
- Treatment (including MAT)

Methadone Misconception 2

- Methadone is treatment

- Truth: Methadone is an adjunct to treatment ("**Medication-assisted** treatment").

Treatment of Opiate Abuse

- Treatment of only one part of recovery
- Overall approach is Recovery Management
  - Addiction is a chronic (not acute) disorder
  - Multiple pathways in and out of addiction
  - Individualized and culturally appropriate services and features
  - Emphasis on resilience
  - Empowerment of individuals and families to direct their own healing
  - Collaboration with communities of recovery

Evidenced-based psychosocial approaches

- Cognitive Behavioral Therapy
- Motivational Incentives
- Assertive Continuing Care

Untreated opiate withdrawal

- Drug hunger (craving)
- Dilated pupils
- Yawning
- Lacrimation (eyes tear)
- Rhinitis (runny nose)
- Restlessness
- Restlessness
- Anxiety
- Depression
- Muscle and bone pain
- Stomach, leg and back cramps
- Nausea
- Insomnia
- Diarrhea
- Vomiting
- Chills/cold flashes with goose bumps ("cold turkey")
- Sweating
- Leg spasms (“kicking the habit”)

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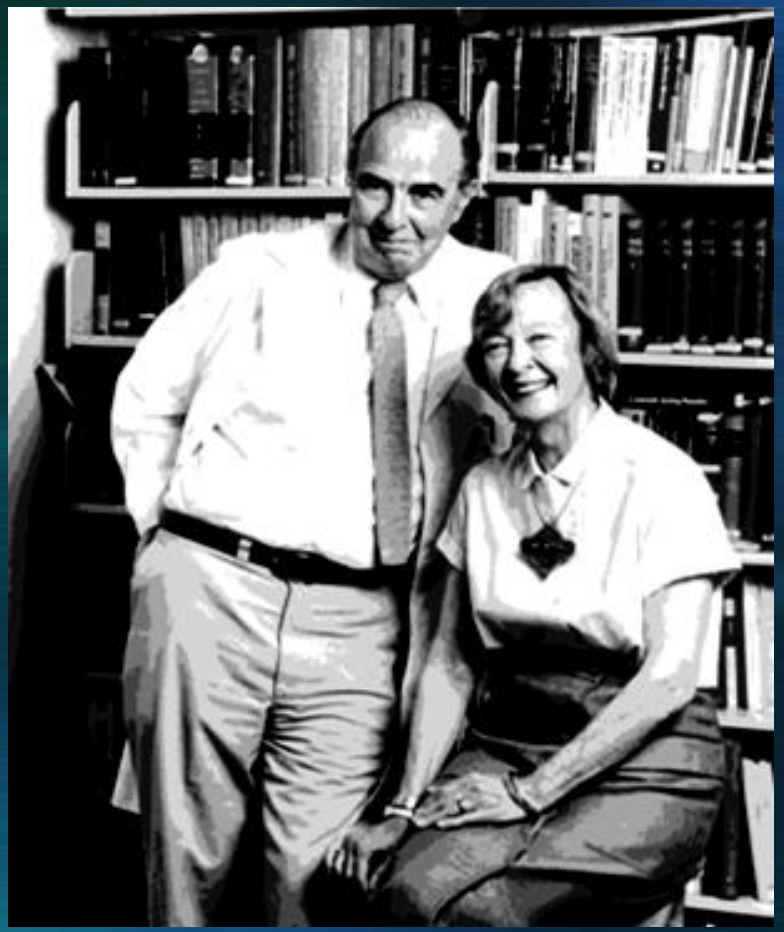


Methadone Pioneers
Drs. Vincent Dole and Marie Nyswander

A brief history of methadone

- 1939: Dolophine is first synthesized in Germany
- 1947: The effects of dolophine (Methadone) are discovered by Dr. Vincent Dole and Dr. Marie Nyswander.
- 1961: Methadone is first used experimentally to treat heroin dependency

A brief history of methadone

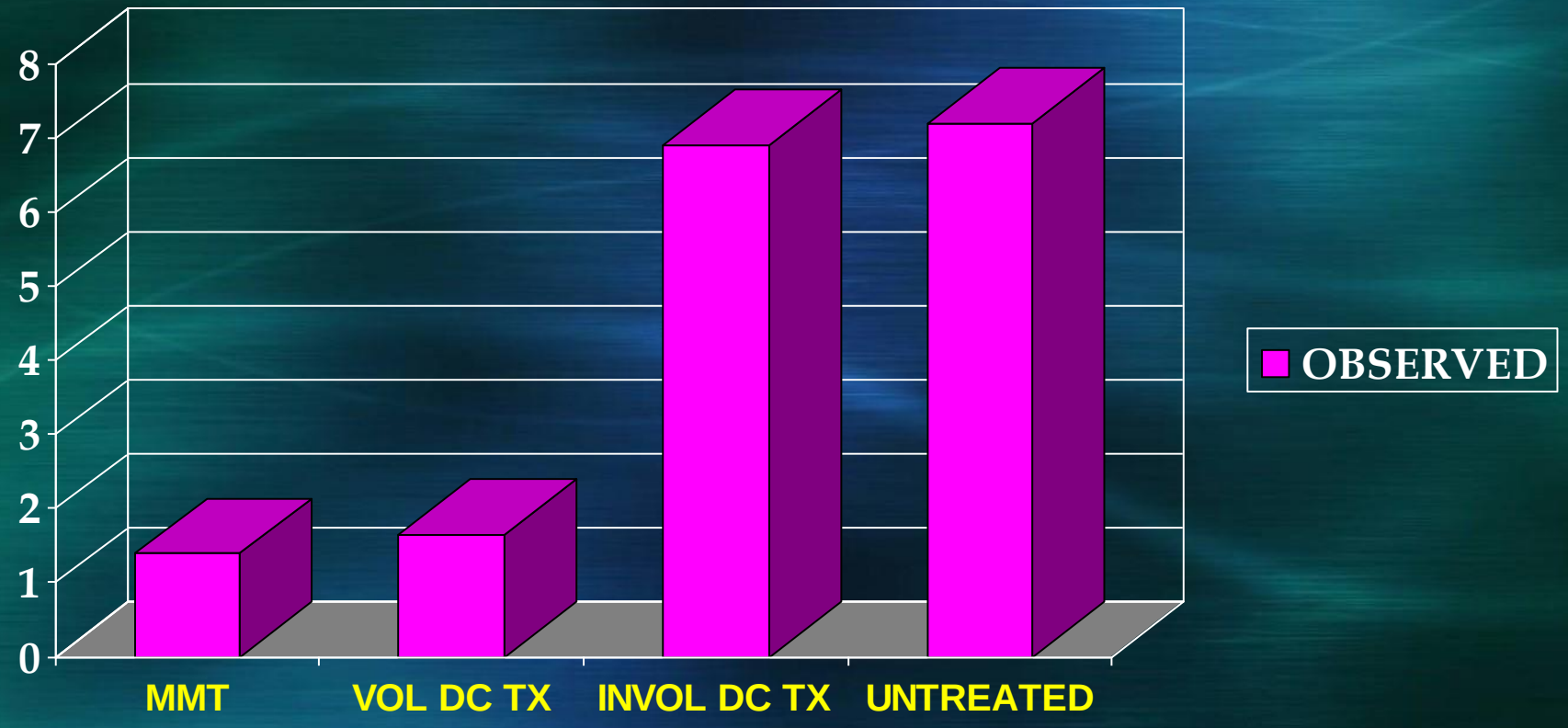
- 1960s and 70s: The Illinois Drug Abuse Program (IDAP) be3comes the nation's leading provider of methadone
- 1970's: A campaign to discredit the use of methadone in heroin treatment publicizes the myth that dolophine was originally called adolphine as a tribute to Adolph Hitler

Advantages of methadone treatment

- 8-10 fold reduction in death rate
- Reduction of drug use
- Reduction of criminal activity
- Engagement in socially productive roles; improved family and social function
- Increased employment
- Improved physical and mental health
- Reduced spread of HIV
- Excellent retention

Reduction in death rate

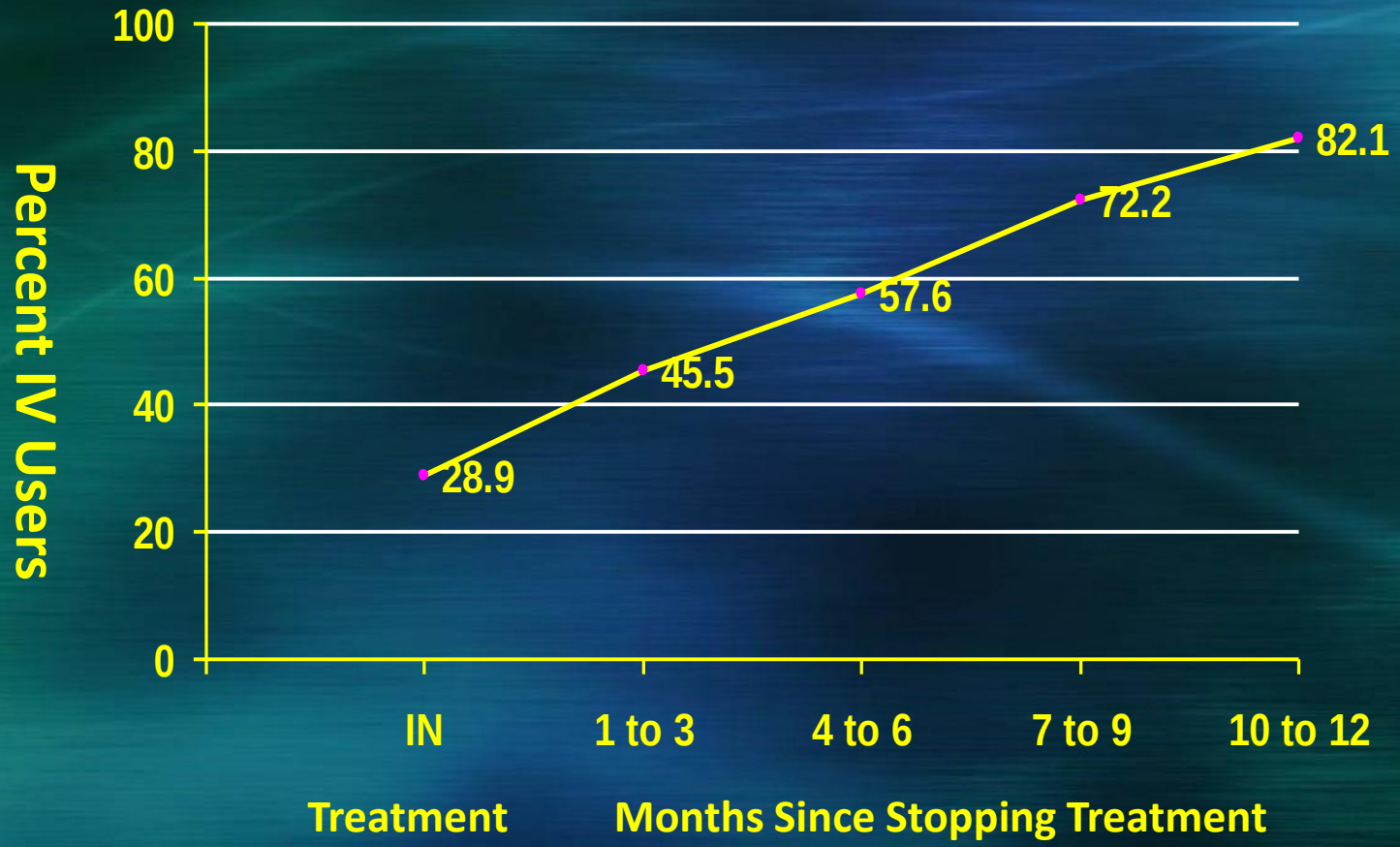
DEATH RATES IN TREATED AND UNTREATED HEROIN ADDICTS



Slide data courtesy of Frank Vocci, MD, National Institute on Drug Abuse

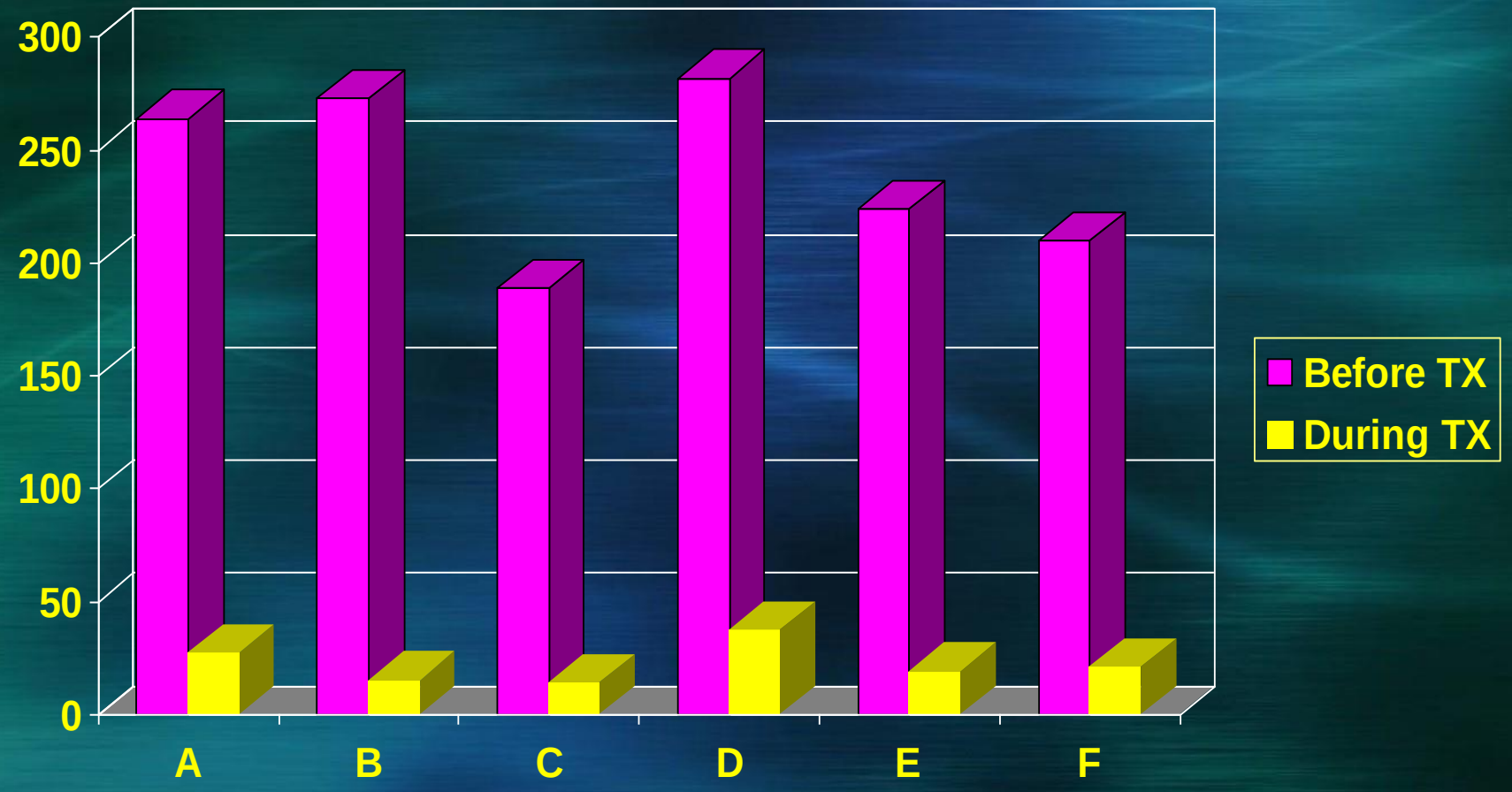
Reduction of drug use

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



Reduction of criminal activity

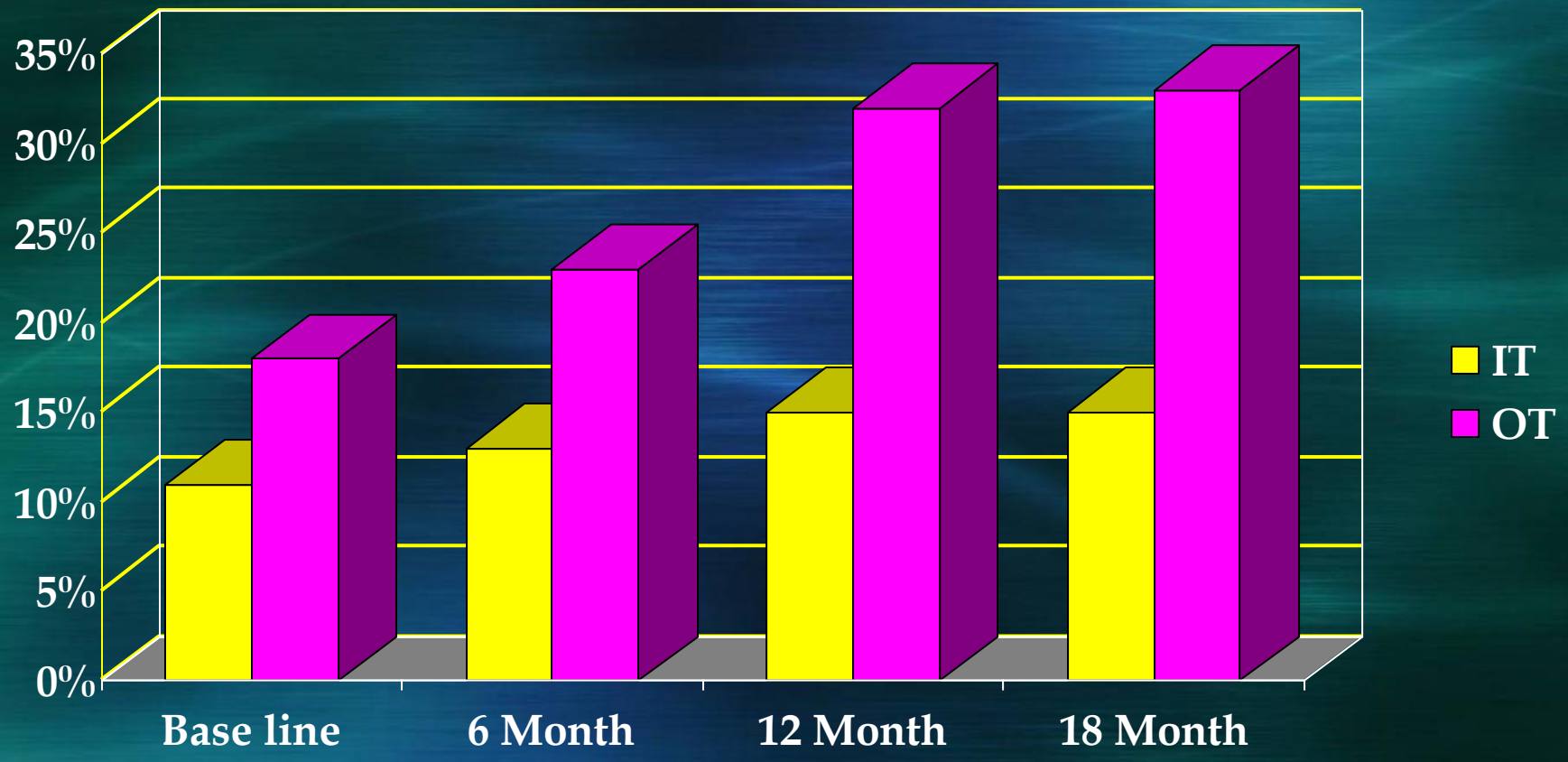
Crime among 491 clients before and during MMT at 6 programs



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

Reduced spread of HIV

HIV CONVERSION IN TREATMENT



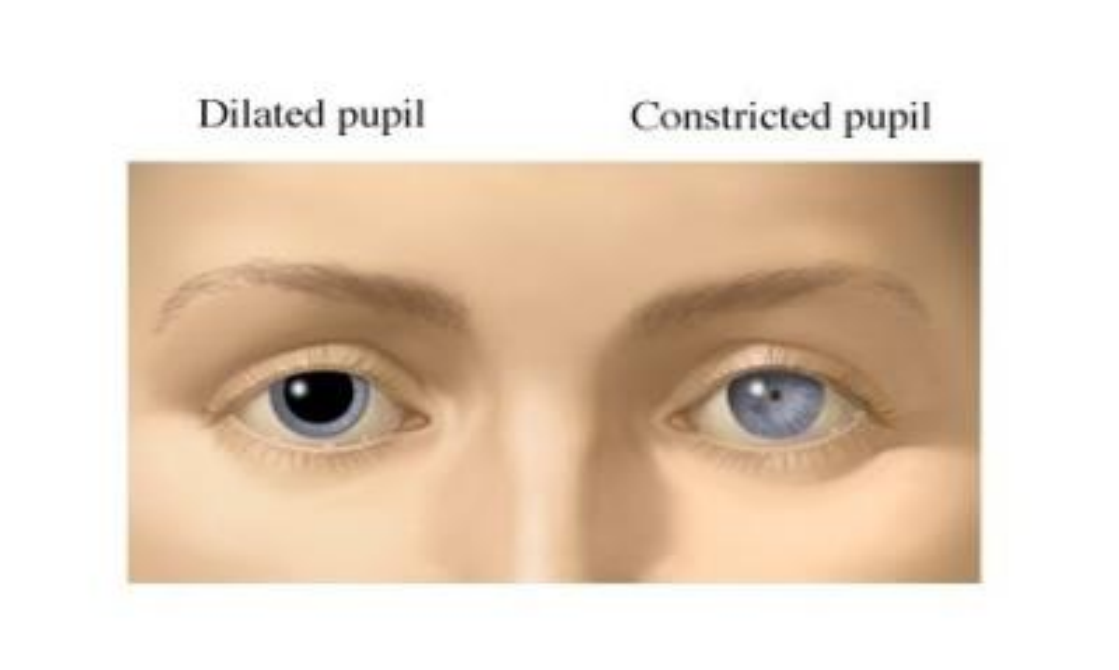
HIV infection rates by baseline treatment status:
In treatment (IT) n=138 not in treatment (OT) n=88

Source: Metzger, D. et. al. J of AIDS 6:1993. p.1052

The methadone maintenance process

- Client is accessed for physical dependency (a requirement for methadone treatment)
- A starting dose is administered
- Client is observed for effects of starting dose

Pupillary constriction/dilation



The methadone maintenance process

- Client is accessed for physical dependency (a requirement for methadone treatment)
- A starting dose is administered
- Client is observed for effects of starting dose
- Dose is increased if necessary
- Client participation in program is ruled out if low dose of methadone causes sedation

Methadone vs Heroin

Heroin	Methadone
Usually administered by injection of smoking	Administered by mouth
Rapid onset of action	Slow onset of action
Tolerance continuously increases	No continuing increase in tolerance levels after optimal dose is reached; relatively constant dose over time
Use is specifically for the sedating & euphoric effect	Client on stable dose rarely experiences euphoric or sedating effects

Methadone vs Heroin

Heroin

- Client
  - feels less physical pain
  - Has blunted emotions
  - Can not drive or perform daily tasks normally and safely

Methadone

- Client able to
  - Perceive pain
  - Experience have emotional reactions
  - Perform daily tasks normally and safely

Methadone vs Heroin

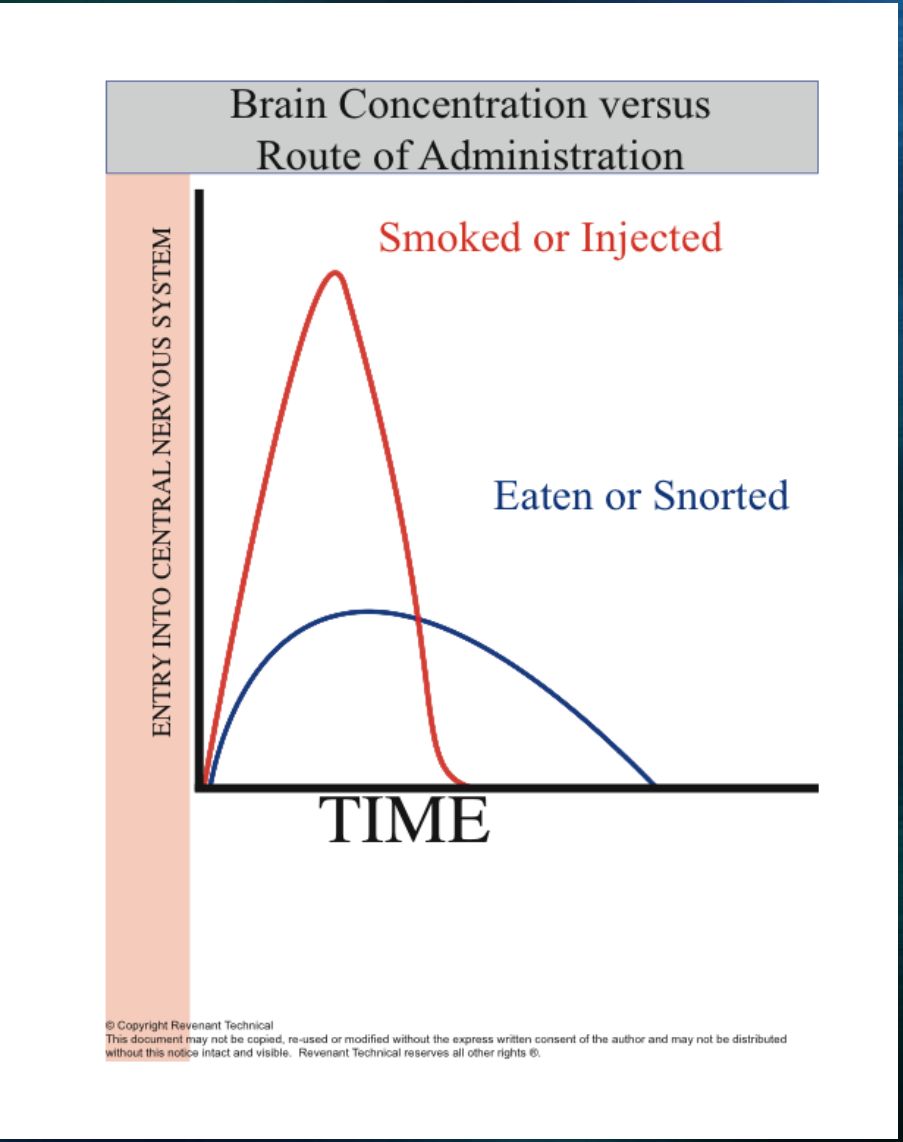
Heroin

- Short-acting: effect lasts 4-6 hours
- May produce medical consequences based on adulteration and method of administration

Methadone

- Long acting: prevents withdrawal for 24 hours, permitting once-a day-dosing
- At sufficient dosage, blocks euphoric effect of normal street doses of heroin
- Medically safe when used on long-term basis (10 years or more)

Rapid onset=More pleasurable reaction



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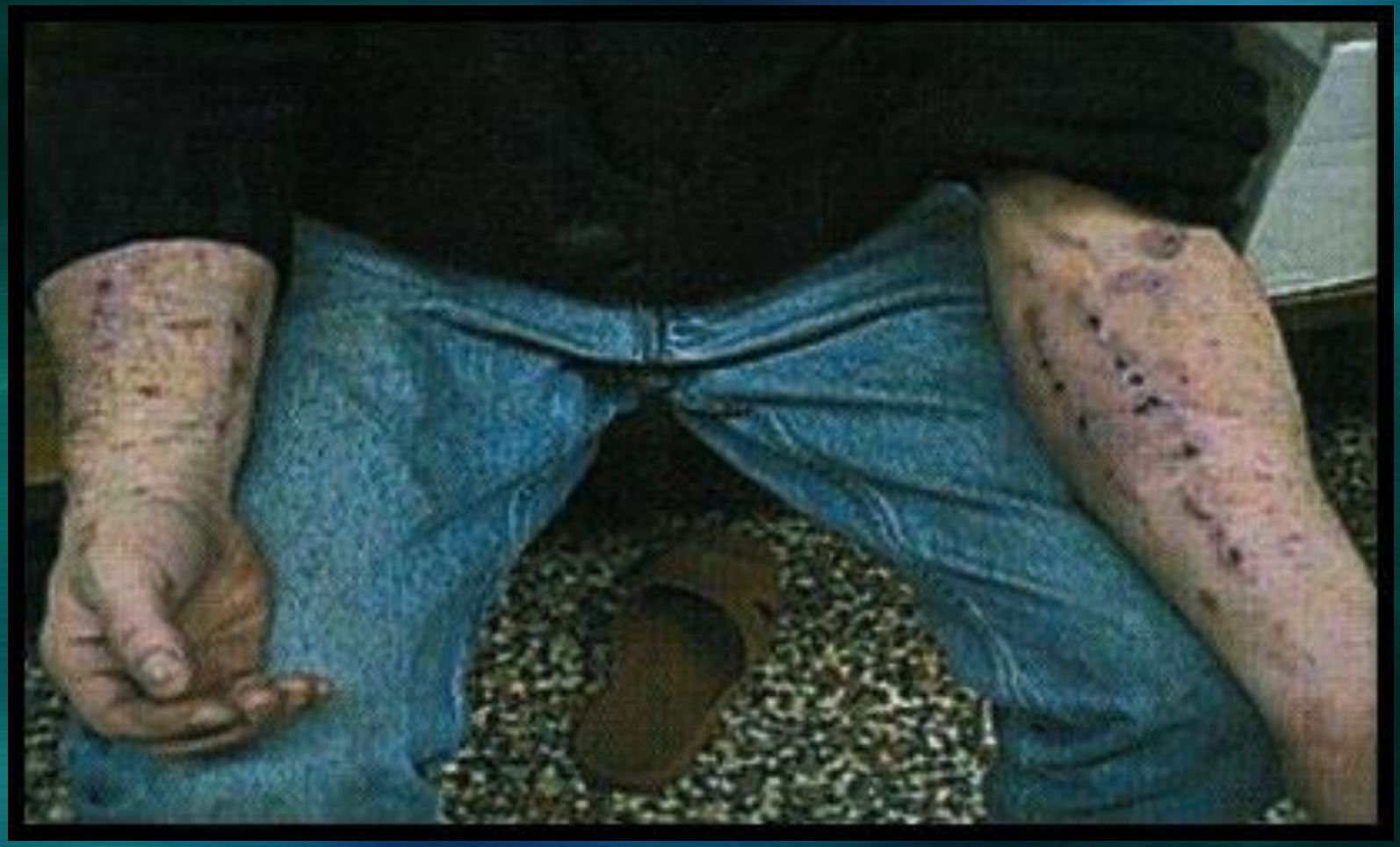
Tracks and abscesses from i.v drug use



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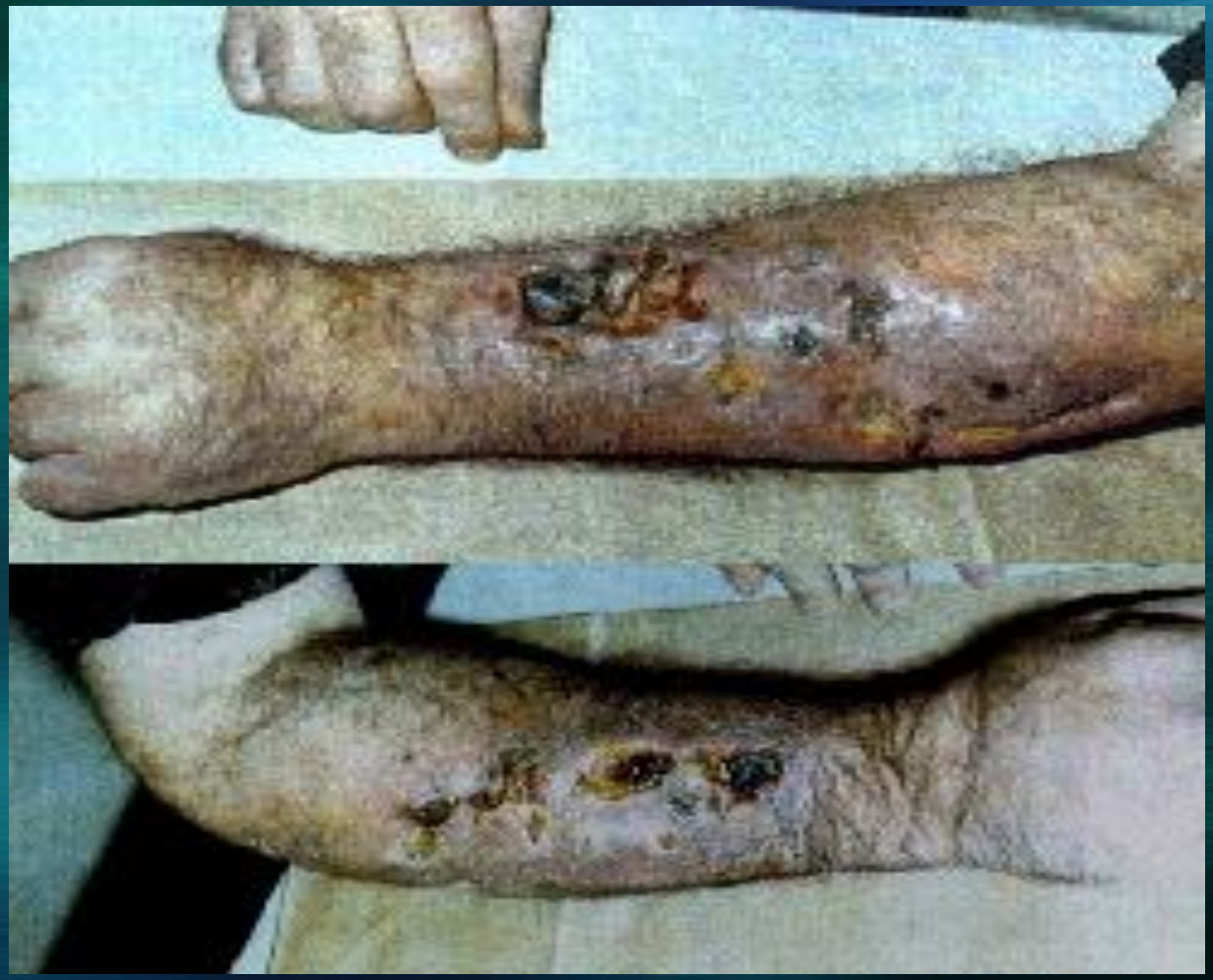
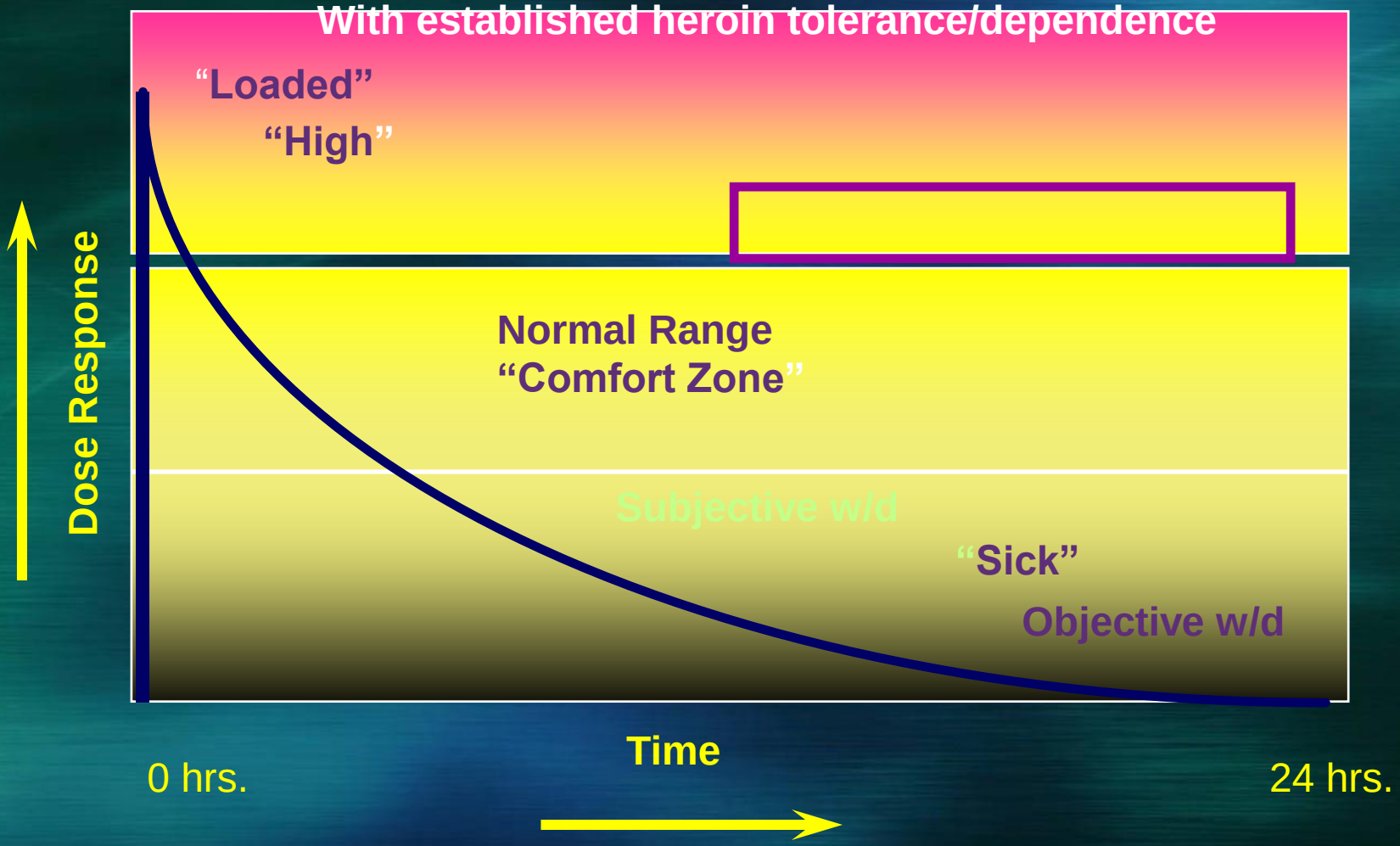
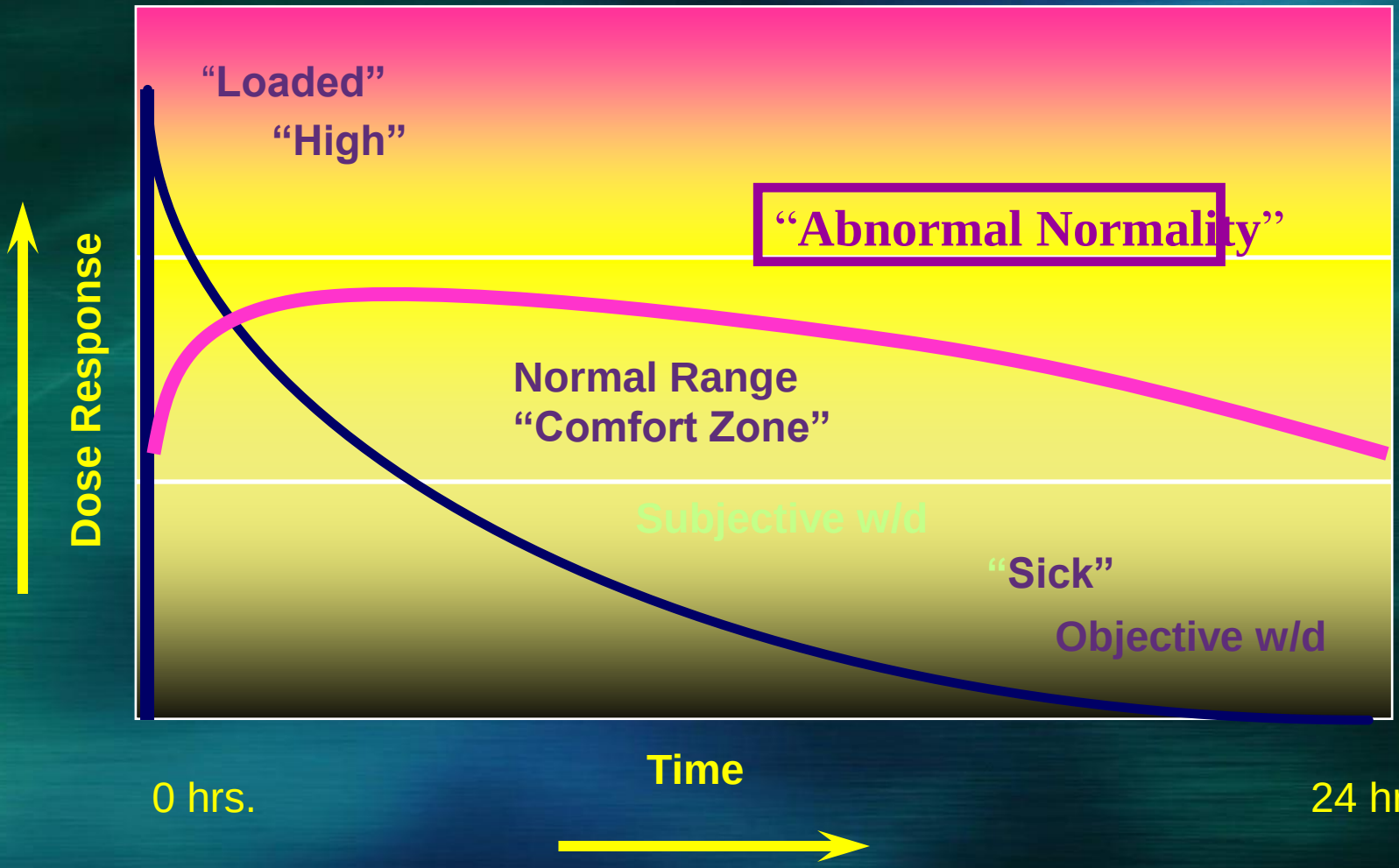


Heroin Simulated 24 Hr. Dose/Response



opiate Agonist Treatment of Addiction - Payte - 1998

Methadone Simulated 24 Hr. Dose/Response
At steady-state in tolerant patient



opiate Agonist Treatment of Addiction - Payte - 1998

How is methadone better than heroin?

- Legal
- Avoids needles
- Known amount ingested
- Slow onset: no “rush”
- Long acting: can maintain “comfort” or normal brain function
- Stabilized physiology, hormones, tolerance

Summary

- Methadone:
  - is a safe medication when used properly
  - Does not cause intoxication if used appropriately
  - Is an adjunct to treatment
  - Blocks withdrawal symptoms/effects of other opiates
  - Reduces crime, death, HIV conversion & costs to society
  - Benefits the client, the community and the human services, child welfare and criminal justice system

Methadone Misconception 4

- Pregnant opiate addicts should discontinue use and detoxify via methadone taper
- Truth: Perinatologists/neonatologists recommend that pregnant addicts be maintained on methadone. Withdrawal from opiates may pose a risk to the fetus

Medications used to treat opiate dependency

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- **Buprenorphine**
- Naltrexone

Narcotic (Opiate) Antagonist

- A substance that has an anti-morphine effect, and that occupies but does not activate the opiate receptor site.
- Antagonists block the effects of opiates by binding to receptors without stimulating them

Types of Narcotic Antagonists

- **Full**: No agonist effect. Completely blocks opiate receptors
  - naloxone (Narcan)
  - naltrexone (Rivea)
- **Partial**: Agonist effect at low doses and an antagonist effect at higher doses.
  - Talwin (pentazocine)
  - Talwin-NX (pentozocine with naloxone)
  - Nubain (nalbuphine)
  - Buprenorphine

Buprenorphine

- Buprenorphine (Buprenex)
- Subutex® (buprenorphine sublingual tablets).
- Suboxone® (buprenorphine and naloxone sublingual tablets).
- Naloxone is not effective as an agonist unless it is injected
  - Guards against cooking and injecting Suboxone

Buprenorphine

- A synthetic opiate partial mu receptor agonist and kappa receptor antagonist.
- At low doses, acts as an agonist, but at higher doses acts as an antagonist.
- Produces many effects associated with morphine/heroin
  - Analgesia,
  - Euphoria,
  - Sedation
  - Respiratory depression.

Buprenorphine

- As a partial mu agonist, it activates receptors to a lesser degree than full mu receptor agonists such as morphine and heroin.
- So what?
- “Bup” produces less of the rewarding and potentially fatal effects

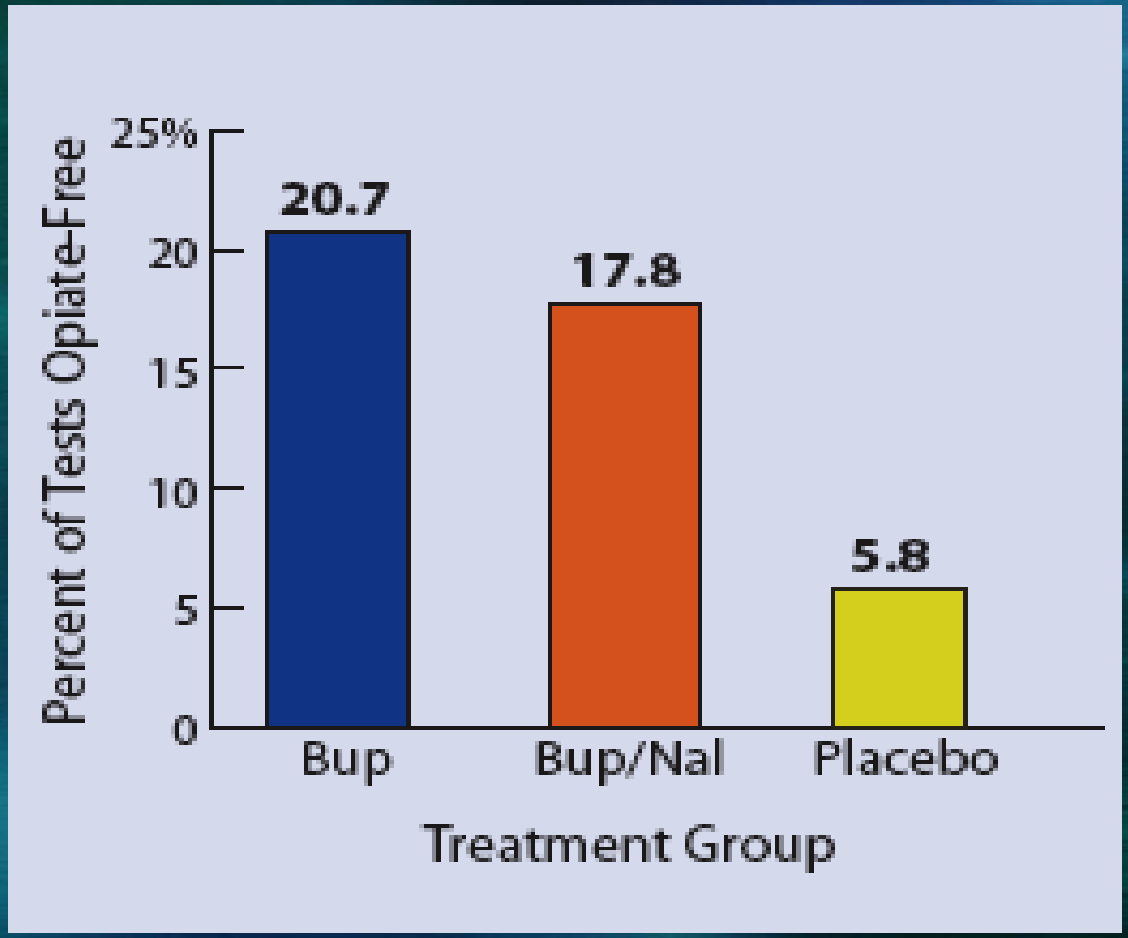
Buprenorphine

- Buprenorphine has duration of 24 hours.
- Buprenorphine produces less euphoria than morphine and heroin.
- Has an “agonist activity ceiling” with no increased benefits on increasing the dose.
- Compared with other opiates, causes a significantly lower degree of sedation and respiratory depression

Buprenorphine

- High doses of buprenorphine (≥100 times the analgesia dose) do not produce dangerous respiratory effects.
- Withdrawal syndrome less rapid and less intense than with a pure agonist such as heroin or methadone.
- Buprenorphine can be given to clients every other day rather daily like methadone

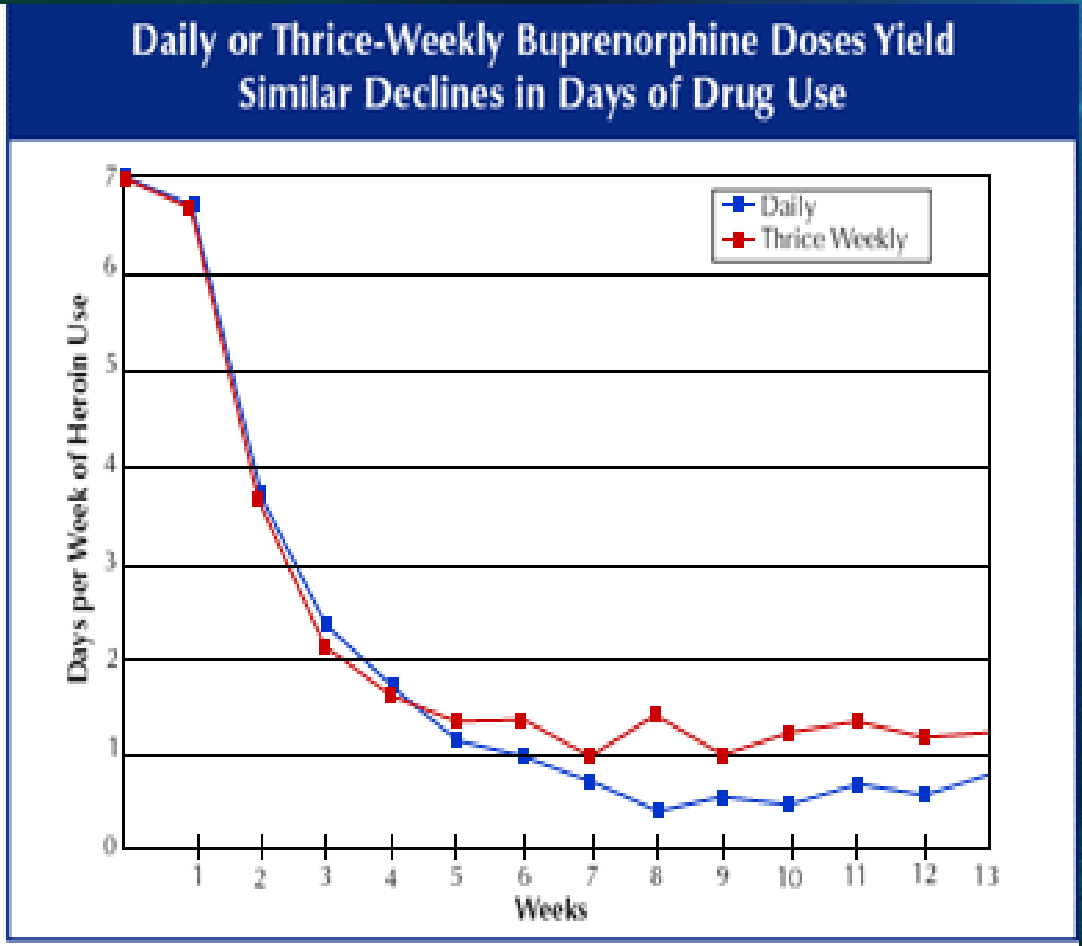
Buprenorphine and Buprenorphine/Naloxone Help Clients Stay Opiate-free



Buprenorphine 3x/week as Effective as Daily Doses

- No significant differences between groups in:
  - Reduction of opioid use
  - Retention in the treatment program
  - Use of cocaine
- Clients couldn't reliably tell whether they were receiving the medication daily or three times each week.

Buprenorphine 3x/week as Effective as Daily Doses

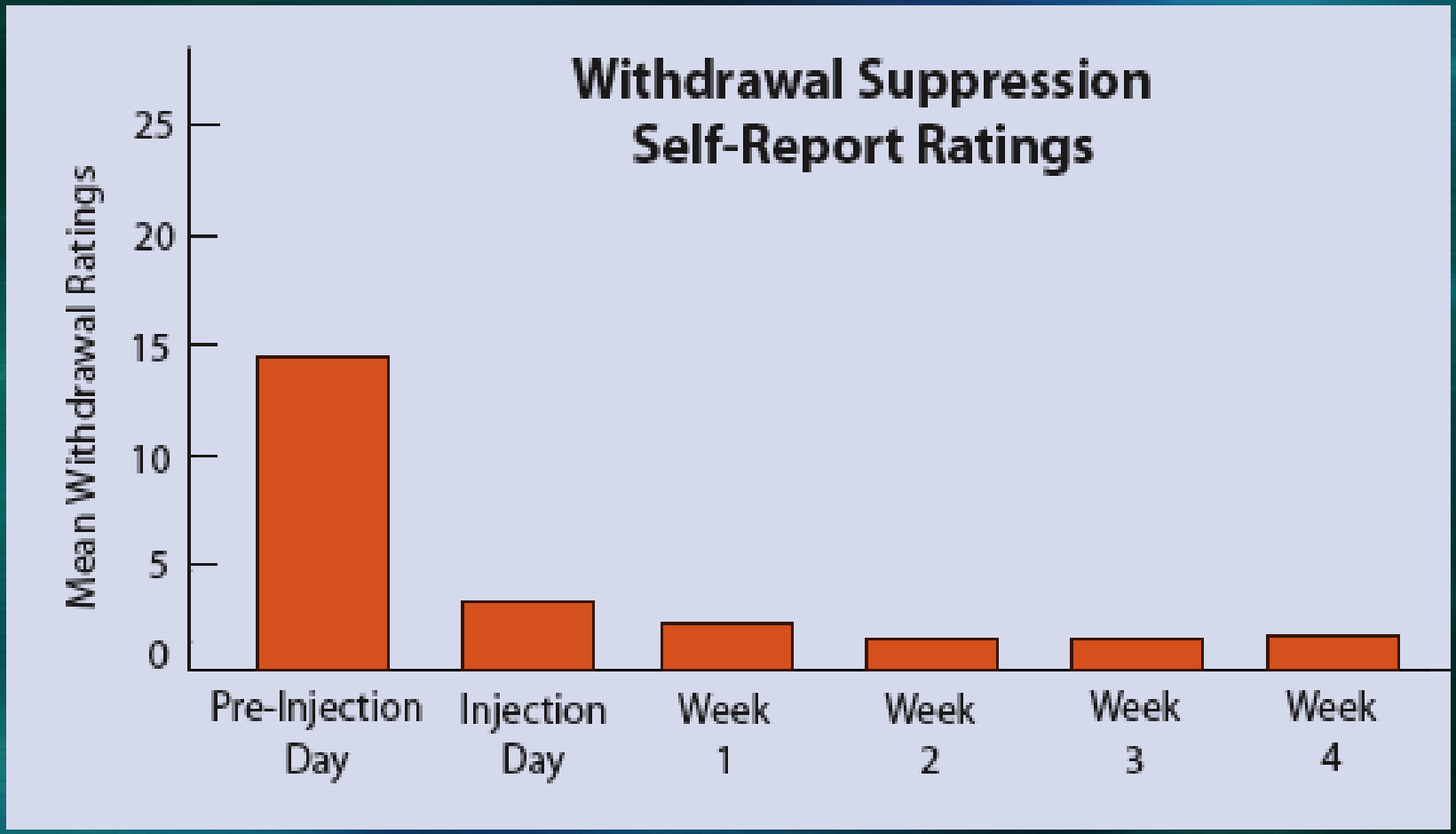


Patients in treatment for opioid addiction received either daily or thrice-weekly doses of buprenorphine. Both groups showed reductions in reported days of heroin use during a 13-week treatment program.

Sustained Release Buprenorphine

- One injection lasts for six weeks
- Treatment consists of a single injection of biodegradable polymer microcapsules containing 58 mg of “bup”
- For 6 weeks clients assessed for signs of heroin withdrawal and clients rated their withdrawal symptoms using a standard questionnaire.
- No client needed additional medication for withdrawal relief.

Long-Lasting Buprenorphine Reduces Withdrawal Symptoms in Heroin-Dependent clients



However:
Buprenorphine is not always the best choice

- Individuals with more severe heroin habits (need methadone ≥ 100 mg)