

# Office Based Treatment of Opioid Use Disorder

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# Disclosures

- **No financial ties**
- **No conflicts of interest**



# Objectives

- **To validate (and decrease) provider uneasiness in caring for patients with opiate use disorder**
- **To gain knowledge of strategies for helping patients with opiate use disorder**
- **To be convinced that opiate use disorder is treatable and can result in satisfaction for patients and providers**



# Health burden of SUD and opioid use disorders

- ▶ In 2014, an estimated 21.6 million persons aged 12 or older (8.9 percent) were classified with substance dependence or abuse in the past year
  - Despite the high prevalence, the vast majority of individuals who need treatment do not receive it
  - The economic burden of substance use in the US is estimated at \$524 billion/year much of which is attributed to losses in productivity
- ▶ In 2014, 1.9 million Americans aged 12 and older met the criteria for abuse or dependence on opioid analgesics, and over 517,000 met the criteria for abuse or dependence on heroin
- ▶ According to the CDC, drug overdose death rates in the US have more than tripled since 1990 and are at an all-time high, surpassing motor vehicle accident deaths



# What do these people have in common?



- 1. Got in trouble for a frat party
- 2. Voted for Nixon's re-election
- 3. Won a Super Bowl
- 4. Love Uncle John's Band
- 5. Opiate use disorder



# What if he asked you for help?



**According to most firsthand accounts of his days at Johns Hopkins, Halsted was moody, elusive, sarcastic, and prone to dropping out in the middle of an operation ... Most famously, Dr. William Osler recalled in 1890 that he had seen the surgeon having severe chills. Suspecting that Halsted was still addicted to morphine and was going through withdrawal, Osler gained the surgeon's trust and confidence.**



**In a secret diary that Osler kept sometime between 1902 and 1905, which was not unsealed until 1969, Osler wrote, "[Halsted] has never been able to reduce the amount to less than three grains [of morphine] daily, on this he could do his work comfortably and maintain his excellent physical vigor. . . . I do not think that anyone suspected him — not even Welch."**





# Bringing attention to opiate use disorder



“Seventy glassine baggies of heroin packed for individual sale — at least 50 of them unopened — were discovered in the \$10,000-a-month rental where the Oscar-winning actor was found dead Sunday with a needle stuck in his left arm”



# My patient

- 28F seen for first visit. Able to review in prescription monitoring database that she has had multiple ER visits for back pain and scripts for oxycodone. History of HIV (not addressed), abnormal PAP and hypertension (BP 165/84)
- Her agenda- getting script for oxycodone. Admits that she buys heroin when she cannot get oxycodone.
- My agenda- getting her engaged in medical care and treatment for opioid use disorder



# Terminology...

- **Addiction- derived from “reward”**
- **Addiction – compulsive disorder in which person uses/does something despite ultimate negative consequences**
- **Abuse/Dependence/ Use disorder/Unhealthy use/Hazardous use**
- **Disease versus Behavior?**
- **Cultural aspects**
- **Can we understand??**



# A little bit more background...

- Abuse liability- onset/duration of action
- Reinforcing effects – biological aspects
- Negative consequences- health/family/friends/financial/legal
- Who are the people with addiction?  
Stereotype/ non-stereotype



# Opium History

- First cultivation of opium poppies was in Mesopotamia, approximately 3400 B.C., plant called *Hul Gil*, the "joy plant"
- The Greek gods Hypnos (Sleep), Nyx (Night), and Thanatos (Death) were depicted wreathed in poppies
- The Persian physician, al-Razi (845-930 A.D.) made use of opium in anesthesia and recommended its use for the treatment of melancholy.



# Opium History

- **Between 400 and 1200 AD, Arab traders introduced opium to China.**
- **14<sup>th</sup> century Ottoman Empire-opium used to treat headache and back pain.**
- **15<sup>th</sup> century China- first officially recorded use of opium as a recreational drug.**
- **1874- heroin developed**
- **1898-heroin marketed by Bayer as safe pediatric cough suppressant**



# BAYER

## PHARMACEUTICAL PRODUCTS.

We are now sending to Physicians throughout the United States literature and samples of

# ASPIRIN

The substitute for the Salicylates, agreeable of taste; free from unpleasant after-effects.

# HEROIN

The Sedative for Coughs,

## HEROIN HYDROCHLORIDE

Its water-soluble salt.

You will have call for them. Order a supply from your jobber.

Made in Germany.

### FARBENFABRIKEN OF ELBERFELD CO.

40 Stone Street, New York.

Sole U.S. Agents



# Opiates & Opioids



The sap is extracted  
by slitting the pod

*Highly refined Southwest Asian heroin or  
Southeast Asian heroin*



**Opiates = naturally present in opium**

- e.g. morphine, codeine, thebaine

**Opioids = manufactured**

- Semisynthetics are derived from an opiate
  - heroin from morphine
  - buprenorphine from thebaine
- Synthetics are completely man-made to work like opiates
  - methadone





# Narcotic Regulation in US

- **1914- Harrison Narcotics Tax Act**
- **1925- Linder vs United States**
- **1964- Methadone introduced as experimental treatment for opioid addiction**
- **1968- Bureau of Narcotic and Dangerous Drugs formed (changed to DEA in 1973)**



# Physiological Effects of Opiates

- Euphoria/analgesia
- Nausea/vomiting/stomach turning
- Drowsiness/nodding
- Respiratory depression
- Long term effects- constipation, osteoporosis, hypogonadism



# Which prescription opiates are most likely to be diverted?

## Important Drug Characteristics

- Onset of action
- Intensity of effect
- Ability to convert to injectable form
- Cost and availability of illicit equivalent



# DEFINING the DISEASE: Opiate Use Disorder

1. Tolerance
2. Withdrawal
3. Larger amounts/longer period than intended
4. Inability to/persistent desire to cut down or control
5. Increased amount of time spent in activities necessary to obtain
6. Social, occupational and recreational activities given up or reduced
7. Use is continued despite adverse consequences



# Opioid Efficacy in Chronic Pain



- **Most literature surveys & uncontrolled case series**
- **RCTs are short duration <4 months with small sample sizes <300 pts**
- **Mostly pharmaceutical company sponsored**
- **Pain relief modest**
  - Some statistically significant, others trend towards benefit
  - One meta-analysis decrease of 14 points on 100 point scale



So here is my bias:

SBIRT

VS

SIT (screen, intervene and  
treat)



# Intervention

- Interventions and EDUCATION are effective
- Interventions should emphasize health and relationship benefits
- Use family/friends in a positive way
- “Undo” shame
- Avoid threats- “If you use, you will die”
- Give hope that life can improve
- Acknowledge reasons for use, but...
- Work together to define the benefits of change



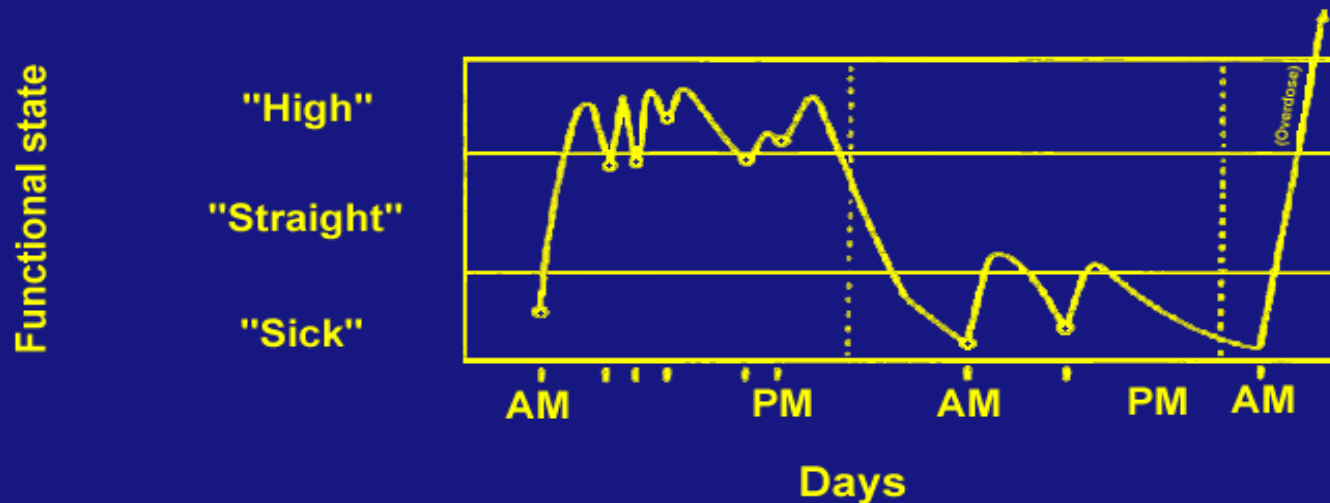
# Rationale for Opioid Replacement Therapy

- Medication assisted treatment using opioid agonist therapy
  - Methadone
  - Buprenorphine
- Stabilize neuronal circuitry
  - Mu occupation/blockade
  - Cross-tolerant, long-acting, oral
- Prevent withdrawal and craving
- Prevent spread of HIV and HCV
- Prevent criminal activity





# What the opioid dependent patient feels...

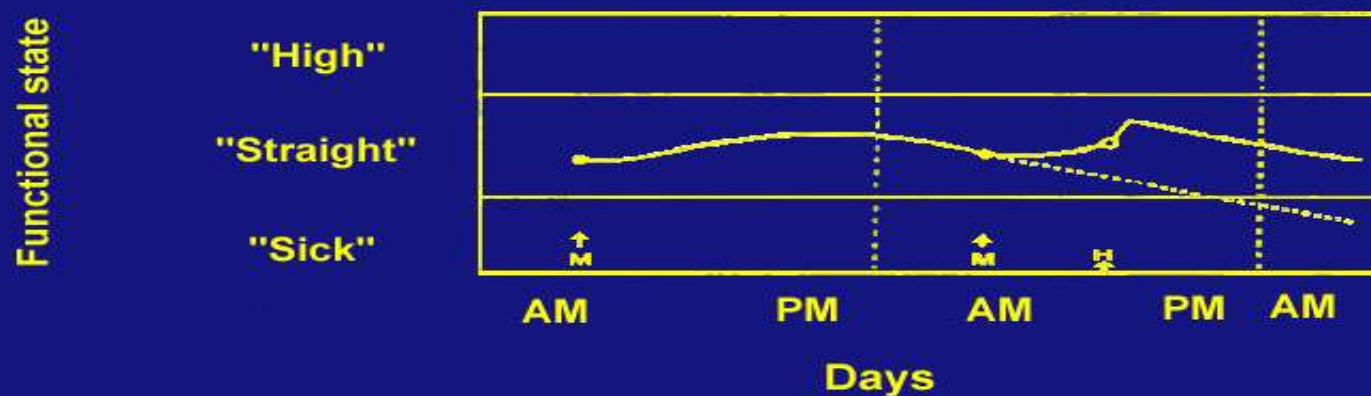


Diagrammatic summary of functional state of typical "mainline" heroin user. Arrows show the repetitive injection of heroin in uncertain dose, usually 10 to 30 mg but sometimes much more. Note that addict is hardly ever in a state of normal function ("straight").

From "Narcotic Blockade," by V. P. Dole, M. E. Nyswander, and M. J. Kreek, 1966, Archives of Internal Medicine, 118, p. 305.



# Stabilization by Blockade Treatment



**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.**

From "Narcotic Blockade," by V. P. Dole, M. E. Nyswander, and M. J. Kreek, 1966, Archives of Internal Medicine, 118, p. 305.



# Traditional 12 Step Drug Treatment

1. Accepting powerlessness
2. Disease identification
3. Surrender to a Higher Power
4. Commitment to AA/NA
5. Commitment to abstinence
6. Sober social support
7. Intention to avoid high-risk situations



# Effective Treatment of Opiate Addiction

NIH Consensus Development Conference

November 17-19, 1997



- **Opiate dependence is a brain-related medical disorder**
- **Treatment is effective-**
  - **“Although a drug-free state represents an optimal treatment goal, research has demonstrated that this goal cannot be achieved or sustained by the majority of opiate-dependent people.”**
- **Reduce unnecessary regulation of long-acting agonist treatment programs**
- **Improve training of health care professionals in treatment of opiate dependence**



# Problems With System Prior to 2000

- **Less than 20% of opioid dependent persons receiving treatment in existing settings**
- **Very limited availability of medication treatment (methadone)**
- **Highly regulated dosing**
- **Limited insurance coverage**



# Drug Addiction Treatment Act of 2000

- **Amendment of Controlled Substances Act**
- **Signed by President Clinton October 2000**
- **Allows prescription of certain narcotics to treat addiction**
  - **States cannot prohibit without specific legislation**



# Drug Abuse Treatment Act

- Allowed “Qualified” physicians to treat opioid dependence outside methadone facilities
  1. Addiction certification from approved organization, or
  2. Physician in clinical trial of qualifying medication, or
  3. Complete 8-hour course from approved organization
- DEA issues (free) to qualifying physicians a new DEA number to use medication for opioid dependence
- As of today, only one medication formulation is approved for this use



# Buprenorphine's Properties

- **Modest  $\mu$  agonist activity with ceiling**
- **Long half life**
- **Precipitated withdrawal if taken after full agonist**
- **Decreased risk of respiratory, CNS depression**
- **Sublingual route of administration**
- **“Combo” film/tablet with naloxone limits abuse by injection**





# Change In Approach

## Methadone Clinic

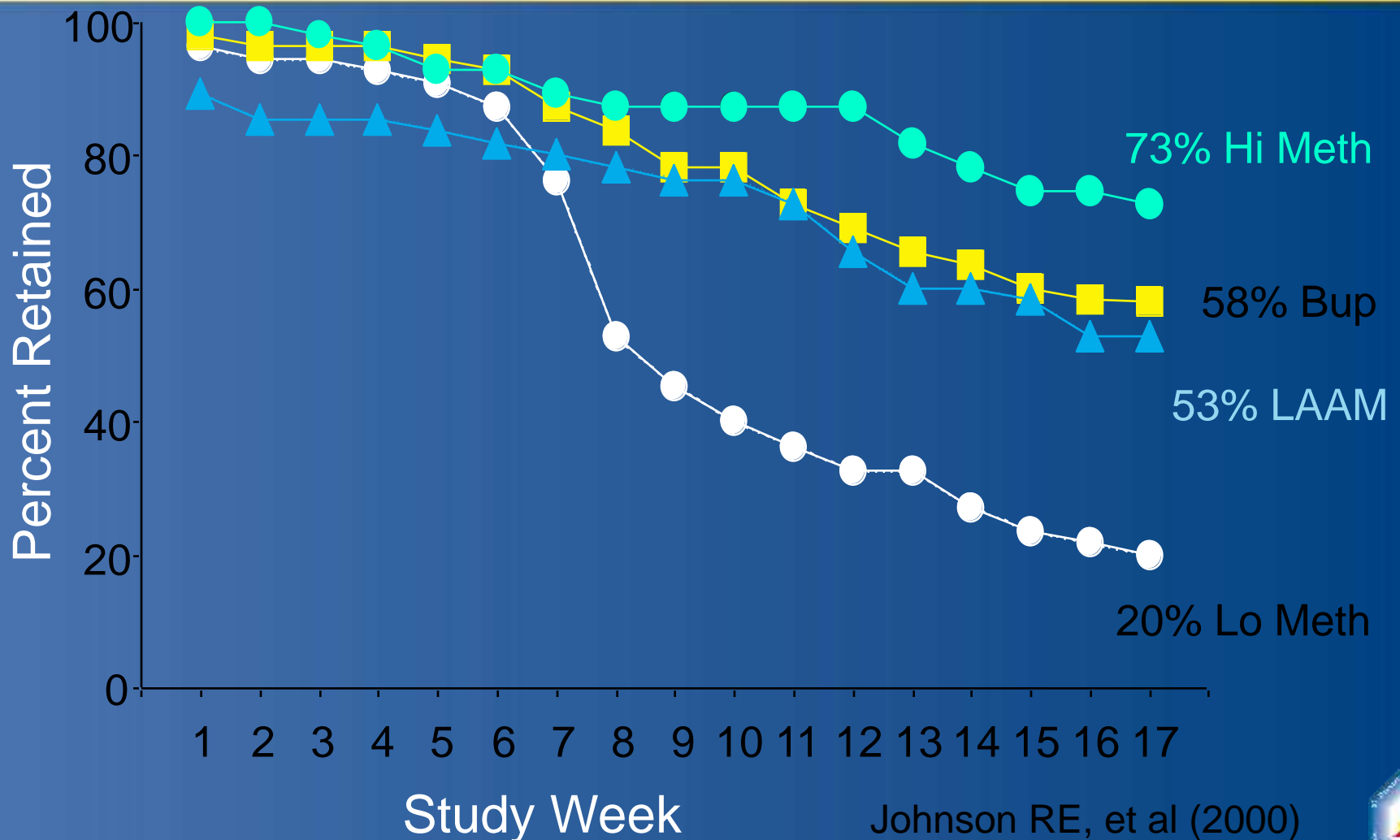
- **Criteria:**
  - 12 months use
- **Dose regulated**
- **Age > 18**
- **Limited take homes**
  - Slow gains
- **Required services**

## Office-Based Bup/Nal

- **Criteria:**
  - No time criteria
- **MD sets dose**
- **Age > 16**
- **Take homes**
  - Up to 30 days
- **Services must be “available”**



# Buprenorphine, Methadone, LAAM: Treatment Retention



# Buprenorphine Safety

- **No alteration of cognitive functioning**
  - feel “normal”
- **No organ damage**
  - Early concern of hepatic toxicity unconfirmed
  - No evidence of QT prolongation
- **Ceiling prevents respiratory depression, OD**  
(Overdose reports with combining use with benzodiazepines)
- **No clinically significant interactions with other drugs**



# Most often heard quotes with Buprenorphine

**“Doc, I feel normal”**

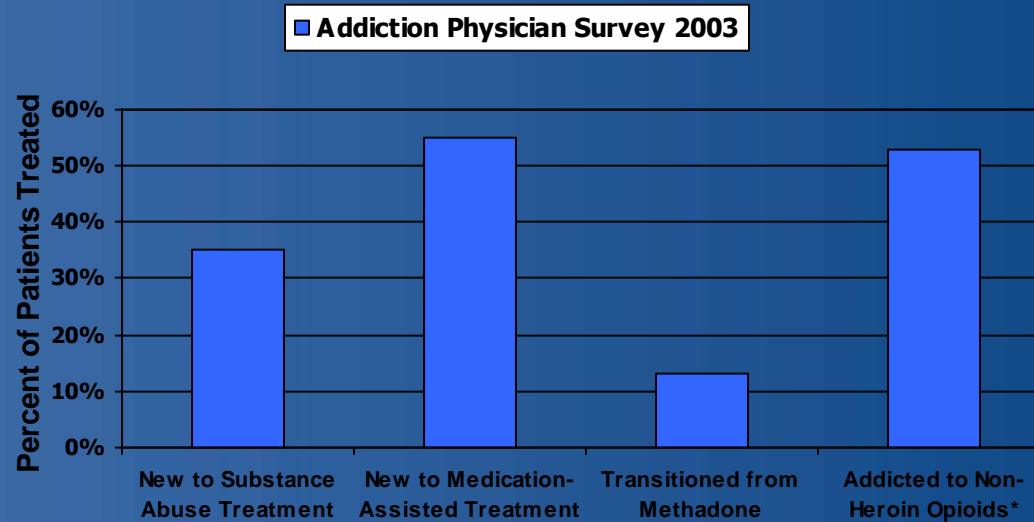
**“I wake up not sick”**

**“I have my life back”**

- Treatment in “normal” medical settings:
  - Encourages continuity of medical/specialty care
  - Encourages relationship building with clinicians
  - Legitimizes opioid dependence as a treatable, chronic illness



# Who were the first patients?



# Starting

- Use a patient treatment agreement
- Check if prior authorization is needed
- Ask specifically about any methadone use
- First dose:
  - 4 / 1 mg of sublingual buprenorphine/naloxone
- Monitor in office or home starting?
- Relief of opiate withdrawal symptoms begins minutes after the first dose of buprenorphine
- Maximum recommended first day dose of 8/2 mg buprenorphine/naloxone



# Intoxication vs Withdrawal

- **Pinpoint pupils**
  - **Somnolence (nod)**
  - **Scratching**
- **Dilated pupils**
  - **Sweating**
  - **Restlessness, anxiety**
  - **Chills**
  - **Myalgias**
  - **Diarrhea**



# Home starting of buprenorphine

- Lee JD, Vocci F, Fiellin DA. Unobserved "home" induction onto buprenorphine. *J Addict Med* 2014; 8:299-308.
- 10 cohort studies
- “There is insufficient evidence supporting unobserved induction as more, less, or as effective as observed induction... Unobserved induction seems to be widely adopted in US and French regional provider surveys. Prescribers, policy makers, and patients should balance the benefits of observed induction such as maximum clinical supervision with the ease-of-use and comparable safety profile of unobserved induction.”





# Buprenorphine Stabilization / Maintenance

- Goal is to stabilize on daily sublingual dose- generally at 16 mg daily by 2<sup>nd</sup> or 3<sup>rd</sup> day
- After 2-3 weeks, patients do not need to “divide” dose over course of day but some patients do feel better taking it twice per day



# Adjunctive counseling?

- **Ling W, Hillhouse M, Ang A, Jenkins J, Fahey J. Comparison of behavioral treatment conditions in buprenorphine maintenance. *Addiction*. 2013 ;108:1788-98.**
- **DESIGN: After a 2-week stabilization, randomization for 16 weeks: cognitive behavioral therapy (CBT = 53); contingency management (CM = 49); both CBT and CM (CBT + CM = 49); and no additional behavioral treatment (NT = 51)**



# Findings?

- No group differences in opioid use were found between any group.
- **CONCLUSION:** “There remains no clear evidence that cognitive behavioral therapy and contingency management reduce opiate use when added to buprenorphine and medical management in opiate users seeking treatment”



# Common problems

- **Positive drug tests**
- **Problematic urine testing**
- **Appearing intoxicated**
- **Missing or coming late to appointments**
- **Running out of medication too soon**



# Urine Testing

## Develop plan for responding to a positive result

- **Consider stage of treatment**
- **Consider class of drug found in urine**
- **Consider range of consequences (pharmacological, non-pharmacological)**



# Tailor Response:

- Find your place on the continuum (i.e. your limits)
- Increase in treatment intensity is not punitive!
  - Change in visit and dosing schedule
  - Use of “recall” for urine test or pill/film count
  - Increased outpatient counseling or meetings
  - Higher level of care needed
    - Methadone
    - Residential



# Relapse Prevention

- **Coping skills:**
  - What coping skills has the patient already been using (e.g., medication, NA, AA, family support)?
  - Reinforce healthy coping skills and explore alternatives to maladaptive ones.
  - Build self-esteem
- **High risk situations:**
  - Ask about previous and current high-risk situations (triggers) in a neutral, non-threatening manner
  - Develop plans for potential slips



# Relapse Prevention: “Slips”

- **Slip: Limited drug use in an abstinent patient**
- **Common signs of an impending “slip”/relapse**
  - negative affective states
  - interpersonal conflict
  - social pressure
- **Handling “slips”**
  - preventing shame, guilt, and anxiety from becoming a full-blown relapse
  - Reframe “slips” as allowing to learn about triggers
  - develop plans for early warning signs of a slip





# Support Self-Efficacy

- Support patient's belief in ability to succeed in a task
- Change is possible “You can do it.”
  - Coach on the sidelines
- Patient is responsible for choosing and carrying out personal change
  - “I’m here to help but you must decide for yourself -- no one else can do it for you.
- With prior failures, emphasize range of alternative approaches.



# Diversion

- In the US, rare reports of buprenorphine dependence without prior opiate dependence
- Evidence to date points to “therapeutic” use of street buprenorphine
- Street buprenorphine is cheaper than pharmacy bought buprenorphine and cheaper than heroin
- Limit dose to 16 mg generally in patients with polysubstance abuse
- Verify presence of buprenorphine in urine



# Our Buprenorphine Outcomes at One Year

- All patients initiated on buprenorphine August 2003 through September 2007
- Visits 15 minutes; frequency at discretion of provider; non-witnessed urines checked for temperature



# Buprenorphine Outcomes

## Comprehensive Care Practice

- 255 patients-mean age 39.6; 44% female
- Insurance- Medicaid 33%, Medicare 20%, Commercial 42%
- Opiates- heroin 83%; 60% IDU
- Other drugs- cocaine 54%; benzos 9%
- 74% presented as new patients to receive buprenorphine treatment; 26% already established patients
- 42% had received no drug treatment in previous 30 days
- Previous methadone maintenance- 11%



# Outcomes Comprehensive Care Practice

- **Co-morbidities- Hepatitis C-49%; psychiatric disorders 49%; HIV 14%; chronic pain 18%**

## Outcomes-

- **At the end of one year- 145 patients (57%) were still receiving buprenorphine treatment**
- **Overall 65% of month-long treatment blocks were opioid negative**



# Buprenorphine Outcomes

## Comprehensive Care Practice

- Treatment success higher for non-heroin users; all other demographic variables not significantly different
- Non-retained patients (109)- 63 lost to f/u; 10 lost insurance; 21 discontinued; 8 transferred to methadone maintenance; 2 had adverse effect; 5 deaths – 3 overdose (none on buprenorphine at time of death); 1 AIDS; 1 cerebral hemorrhage.



# My patient

- After two months - have seen her 7 times
- On medication for hypertension; adherent with HAART for HIV; had PAP done. No ER visits.
- Doing well on buprenorphine/naloxone. No back pain. Urine drug screens all negative since the first visit. Attends 3 NA meetings/week
- Mood/self-esteem much improved. Better relationship with family.



# Summary

- **Office based treatment of opiate dependence with buprenorphine has revolutionized opioid drug treatment**
- **Reward is great for both patient and provider**
- **Providers must be vigilant in protecting buprenorphine treatment through proper prescribing and treatment practices**

