The ATTC Network

Ten Regional Centers

Four National Focus Area Centers
- SBIRT
- Hispanic and Latino
- Native American-Alaska Native
- Rural and Frontier

Visit Us Online!

- Upcoming trainings
- The range of training and technical assistance services we offer
- Resources and links on key topics

www.attcnetwork.org/northwest

Personal Views about Addiction

We all have some (maybe a lot) of direct experience with people who are addicted.

We may feel sympathy, anger, and other emotions.

How do my experiences:
- shade how I see addiction?
- influence what I believe <u>as a professional</u> about addiction and what is known to work to improve health and safety?

ADDICTION

"Addiction is a brain disease shaped by behavioral and social context."

Dr. Alan Leshner, Former Director
National Institute on Drug Abuse

"Drug addiction is associated with altered cortical activity and decision making that appears to overvalue reward, undervalue risk, and fail to learn from repeated errors."

Dr. Nora Volkow, Director
National Institute on Drug Abuse

"Any disease that is treated as a mystery and acutely enough feared will be felt to be morally, if not literally, contagious."

Susan Sontag, "Illness as Metaphor" 1978

ELEMENTS OF ADDICTION

1. COMPULSION & CRAVING
   A. BIOLOGICAL (WITHDRAWAL)
   B. CONDITIONED RESPONSE
2. LOSS OF CONTROL OVER USE
3. CONTINUED USE DESPITE ADVERSE CONSEQUENCES
4. SALIENCE OF USE

DURATION of SYMPTOMS

What Does Addiction Feel Like?

Trigger-induced craving

+

Preoccupation - with either staying away from the drug or thinking about getting it

⬇

Drug use because of failures of executive function, impulse control and judgment and misplaced motivation

Terminology
Dependence versus Addiction

- Addiction may occur with or without the presence of physical dependence.
- Physical dependence results from the body's adaptation to a drug or medication and is defined by the presence of
  - Tolerance and/or
  - Withdrawal

Substance Use Disorder – DSM 5

- **Tolerance***
- **Withdrawal***
- **More use than intended**
- **Craving for the substance**
- **Unsuccessful efforts to cut down**
- **Spends excessive time in acquisition**
- **Activities given up because of use**
- **Uses despite negative effects**
- **Failure to fulfill major role obligations**
- **Recurrent use in hazardous situations**
- **Continued use despite consistent social or interpersonal problems**

Severity measured by number of symptoms:
2-3 mild
4-6 moderate
7-11 severe

***not counted if prescribed by a physician**

Opioid Use Disorder: DSM-5

1. Opioids are often taken in **larger amounts** or over a **longer period of time** than intended.
2. There is a persistent desire or unsuccessful **efforts to cut down or control opioid use**.
3. A great deal of **time is spent in activities** necessary to obtain the opioid, use the opioid, or recover from its effects.
4. **Craving**, or a strong desire to use opioids.
5. Recurrent opioid use resulting in **failure to fulfill major role obligations** at work, school or home.

Opioid Use Disorder: DSM-5

6. Continued opioid use despite having **persistent or recurrent social or interpersonal problems** caused or exacerbated by the effects of opioids.
7. Important social, occupational or recreational **activities are given up or reduced** because of opioid use.
8. Recurrent opioid use in **situations in which it is physically hazardous**.
9. Continued use **despite knowledge of having a persistent or recurrent physical or psychological problem** that is likely to have been caused or exacerbated by opioids.

Opioid Use Disorder: DSM-5

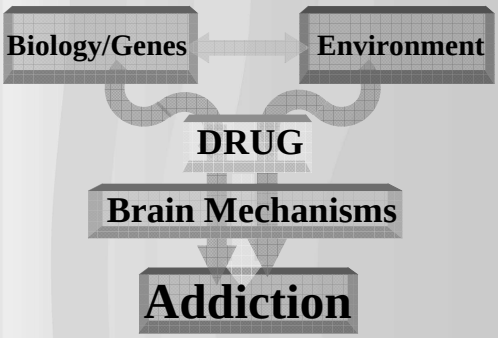
10. Tolerance, as defined by either:
(a) a need for markedly increased amounts of opioids to achieve intoxication or desired effect
(b) markedly diminished effect with continued use of the same amount of an opioid

11. Withdrawal, as manifested by either:
(a) the characteristic opioid withdrawal syndrome
(b) the same (or a closely related) substance are taken to relieve or avoid withdrawal symptoms

Tolerance and Withdrawal

These criterion are **not** considered in OUD diagnosis for patients who are taking opioids solely under appropriate medical supervision for either ad*diction or pain treatment.*

ADDICTION INVOLVES MULTIPLE FACTORS



Drug Dependence: A Chronic Medical Illness

- Genetic Heritability – twin studies
  - Hypertension – 25-50%
  - Diabetes – Type 1: 30-55%; Type 2: 80%
  - Asthma – 36-70%
  - Nicotine – 61% (both sexes)
  - Alcohol – 55% (males)
  - Marijuana – 52% (females)
  - Heroin –34% (males)
- Voluntary Choice – shaped by personality and environment
- Pathophysiology – neurochemical adaptations
- Treatment Response
  - Medications – effectiveness and compliance
  - Behavioral interventions

McLellan, A.T., et.al., Drug Dependence, a Chronic Medical Illness *Journal of the American Medical Association* 284:1689-1695, 2000.

So?

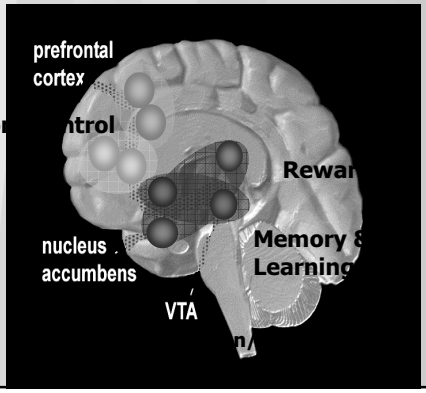
If addiction is a chronic disease:

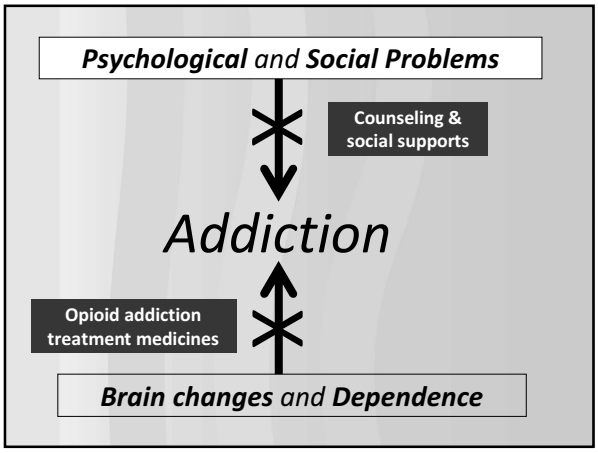
Addiction treatment doesn't cure the disease.

The goal of treatment is to:

- Provide patients the tools to help them manage their addiction – *and medications are among those tools*
- Teach them how to use those tools to achieve and maintain recovery

Circuits Involved in Drug Abuse and Addiction





- Research clearly and consistently shows that medication assisted treatment for opioid use disorder **saves lives and money.**
- "…mortality rates were 75 percent higher among those receiving drug-free treatment compared to those receiving buprenorphine…" (or methadone)

Health Affairs, August 2011 vol. 30 no. 8 1425-1433

Medications for Opioid Addiction

How do Medications for Opioid Addiction Work?

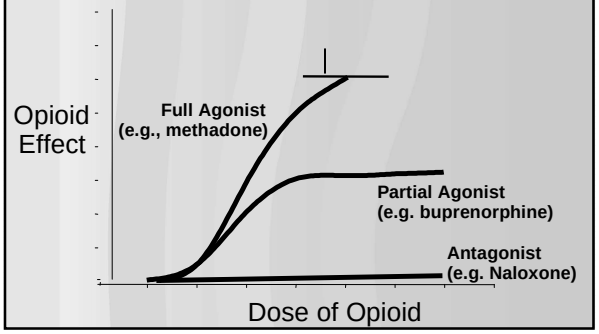
There are three types of medications that can block the "high":

- Agonists
  - produce opioid effects

Partial Agonists
- produce moderate opioid effects

Antagonists
- block opioid effects

How do Medications for Opioid Addiction Work?



NIH Consensus Panel on Effective Medical Treatment of Opiate Addiction

- 12 member multi-disciplinary panel, Nov. 1997
- heard testimony from 25 experts
- reviewed 941 research reports published over the period Jan. 1994 - Sept. 1997

"Of the various treatments available, MMT, combined with attention to medical, psychiatric, and socioeconomic issues, as well as drug counseling, has the highest probability of being effective."

Adapted from JAMA, Dec 9, 1998.280 (22), 1936-1945

How does methadone work?

- Methadone binds to the same receptor sites as other opioids.
- Orally effective
- Slow onset of action
- Long duration of action
- Slow offset of action

Treatment Requirements

- Attendance for observed dosing 6 days a week for the first 90 days
- Take-home doses permitted after 90 days but only to those patients meeting a number of criteria
- At least once per month urinalysis
  - Some clinics observe collection; some don't
  - Some clinics have contingencies (+ & -); some don't
  - Some agencies administer alcohol breath tests; some don't
- Assessment and counseling
- Additional education, i.e., HIV/HCV, family planning

Methadone during Pregnancy

- **Detoxification is contraindicated** unless done in hospital with monitoring.
- Methadone is the **preferred method of treatment for medication-assisted treatment for opioid dependence in pregnant women**. An expert review of published data on methadone use during pregnancy concludes that it is unlikely to pose a substantial risk. There is insufficient data to state that there is no risk.
- It is known that methadone is excreted through breast milk, and a decision should be made whether to discontinue nursing or to discontinue the medication, taking into account the importance of the medication to the mother and continued illicit opioid use.

Methadone & Pregnancy

- Fetal outcomes better on MMT than heroin
- Detoxification from opiates risky for fetus
- Methadone dose adjustments during pregnancy
  - May need "split" dosing to improve serum stability
- Attention to prenatal care during pregnancy
- Some infants have abstinence syndrome within 72 hrs. of birth; may require pharmacotherapy
  - NAS may be associated with mothers' level of smoking during pregnancy (Choo, et.al., 2004)
- Breastfeeding OK with MMT unless otherwise contraindicated, e.g., blood-borne infections

For further information see TIP 43, Chapter 13

Treatment Outcome Data: Methadone

- 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

Methadone Maintenance vs. 180 Day Detoxification

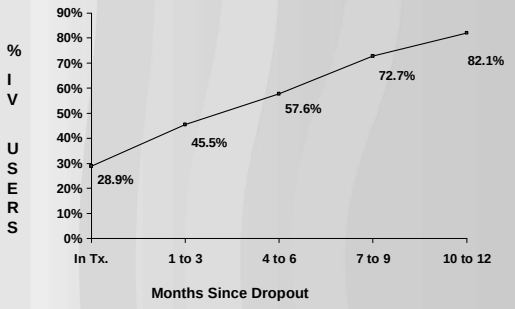
12 month study of 179 opioid dependent patients randomly assigned to:

- **Methadone Maintenance**
  - mean dose=85.3mg
  - for 14 months
- **180 Day Methadone Detoxification**
  - mean dose=86.3 mg prior to taper at 120 days
  - followed by psychosocial Tx for 8 months

➢ **"Methadone maintenance therapy resulted in greater treatment retention and lower heroin use rates than did detoxification."**

K.L. Sees et al., JAMA 2000

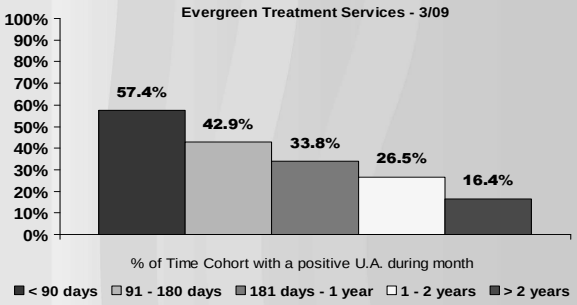
Return to I.V. Drug Use Following Premature Termination of Treatment



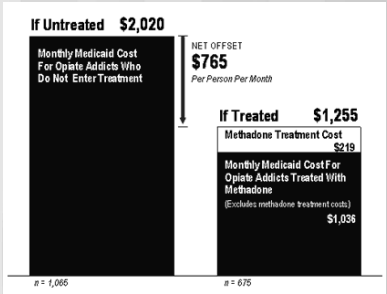
Retention-enhancing

- Opioid dependent patients stay in methadone treatment significantly longer than outpatient psychosocial
  - In King County study, retention for primary opioid dependent patients at 90 days in psychosocial was 45%; in MMT it was 78%
- Longer retention in treatment is associated with improved treatment outcomes.

Drug Use & Length of Time in Methadone Treatment



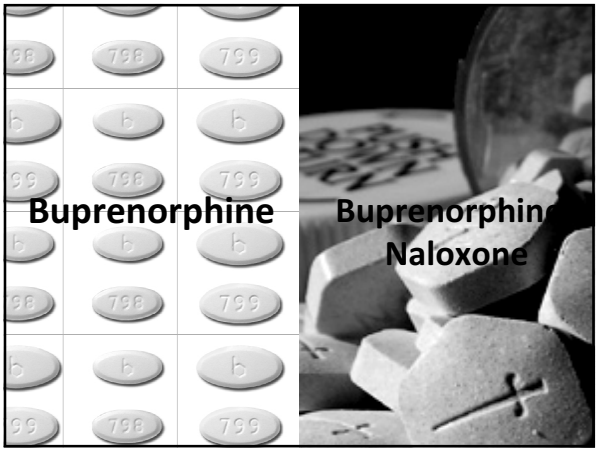
Methadone Treatment For Opiate Addiction Lowers Health Care Costs



Source: State of Washington, DSHS, Research & Data Analysis Division, Report 4.49fs, June, 2004

But aren't they still addicted?

- What is the definition of addiction?
  - Is it simply physical dependence?
- How does the change of lifestyle and psychosocial stability associated with long-term methadone treatment fit with that definition?

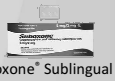


Formulations of Buprenorphine

Buprenorphine is currently marketed for opioid treatment under the trade names:

Subutex®
(buprenorphine)

Suboxone®
(buprenorphine/naloxone)



Suboxone® Sublingual Film
(buprenorphine/naloxone)

Zubsolv® (buprenorphine/naloxone)

5.7 mg. bup./1.4 mg. nalox.

1.4 mg. bup./0.36 mg. nalox.

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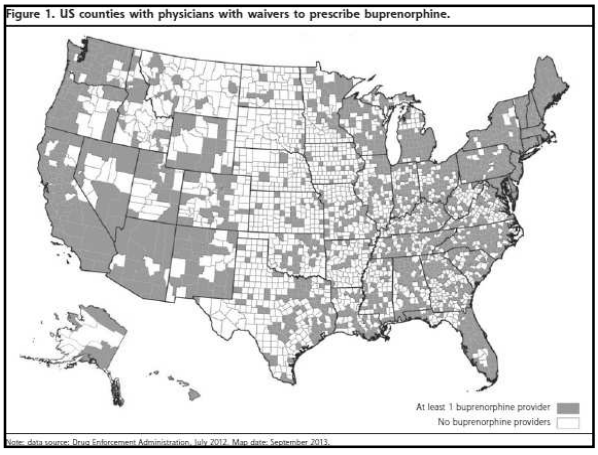
Drug Addiction Treatment Act of 2000 (DATA 2000)

- Expands treatment options to include both the general health care system and opioid treatment programs.
  - Expands number of available treatment slots
  - Allows opioid treatment in office settings
  - Sets physician qualifications for prescribing the medication

DATA 2000: Physician Qualifications

Physicians must:

- Be **licensed** to practice by his/her state
- Have the **capacity to refer** patients for psychosocial treatment
- Originally limited to 30 patients later expanded to allow for **100 patients** after the first year of experience
- Be **qualified** to provide buprenorphine and receive a license waiver



The Role of Buprenorphine in Opioid Treatment

- Partial Opioid Agonist
  - Produces a **ceiling effect** at higher doses
  - Has effects of typical opioid agonists—these effects are dose dependent **up to a limit**
  - **Binds strongly to opiate receptor and is long-acting**
- Safe and effective therapy for opioid maintenance and detoxification

Advantages of Buprenorphine in the Treatment of Opioid Addiction

1. **Patient can participate fully in treatment** activities and other activities of daily living easing their transition into the treatment environment
2. **Limited** potential for **overdose**
3. **Minimal subjective effects** (e.g., sedation) following a dose
4. **Available** for use in an **office setting**
5. **Lower** level of physical **dependence**

Disadvantages of Buprenorphine in the Treatment of Opioid Addiction

- **Medication cost**
  - ✓ **$160 – 220/month for 16 mg. dose**
- **Cost of each physician visit for prescription refill**
- **Not detectable in standard urine toxicology screenings**
- **Additional counseling services would mean an additional cost to patient**

Specific Research on Buprenorphine and Pregnancy

MOTHER Study, Jones, et.al., 2010.

- Randomized double blind, double dummy comparison between methadone and buprenorphine (Subutex®) in pregnant women in a large multi-site trial.
- Women dosed daily under observation 7 days per week.
- No difference in NAS frequency in babies born to mothers on either medication.
- Two statistically significant findings: shorter hospital stay for buprenorphine, less NAS medication used.
- No data available to inform determination of patients who should be maintained on methadone rather than buprenorphine
- Comprehensive integrated services and daily observation (methadone clinic) vs. office based medication.

The Prescription Opioid Addiction Treatment Study (POATS)

- **Largest study ever conducted for prescription opioid dependence – 653 participants enrolled**
- Compared treatments for prescription opioid dependence, using buprenorphine-naloxone and counseling
- Conducted as part of NIDA Clinical Trials Network (CTN) at 10 participating sites across U.S.
- Examined detoxification as initial treatment strategy, and for those who were unsuccessful, how well buprenorphine stabilization worked

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Key Features of POATS Design

- Adaptive treatment research design approximates clinical practice
- All subjects receive buprenorphine-naloxone
- Start with a less-intensive treatment to see if it works
- Try a more intensive treatment when needed

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The Prescription Opioid Addiction Treatment Study (POATS): Design

- Subjects who succeed in ***Phase 1*** (1-month taper plus 2-month follow-up) are successfully finished with the study
- Subjects who relapse may go into ***Phase 2***:
  - Re-randomized to SMM or SMM + ODC in Phase 2
  - 3 months of BUP-NX stabilization,
  - 1- month taper off BUP-NX,
  - 2 months of follow-up

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Take Home Messages

- Tapering from buprenorphine-naloxone, whether initially or after a period of substantial improvement, led to nearly universal relapse.
- Medication Management (MM) produced outcomes equal to MM+ individual opioid drug counseling.
- Patients with chronic pain had outcomes equal to those without chronic pain.

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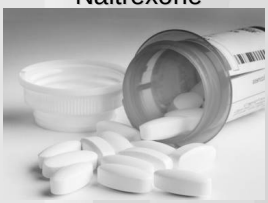
Summary: Opioid Interactions with Psychotropics

Medication	Methadone plasma concentrations	Buprenorphine plasma concentrations
Antipsychotics		
Quetiapine	↑	Not clinically studied
Antidepressants		
Fluoxetine	↑	No reported interaction
Fluvoxamine	Possible ↑ metabolism (associated with onset of opioid withdrawal)	Not clinically studied
Amitriptyline	Could be associated with increases in plasma methadone concentrations	Single report of serotonin toxicity
St. John's Wort	↑ metabolism and elimination	↑ metabolism and elimination
Desipramine	Associated with increased desipramine levels	No reported interaction
Anxiolytics		
Diazepam	Associated with increased sedation and impaired performance on psychological tests	Associated with increased sedation and impaired performance on psychological tests
Alprazolam	Associated with fatalities	Associated with fatalities
Anticonvulsants		
Carbamazepine	Opiate withdrawal	Not clinically studied
Phenytoin	Opiate withdrawal	Not clinically studied
Phenobarbital	Opiate withdrawal	Not clinically studied

Opioid Antagonists

Naltrexone



Revia ® or Depade ®

Naltrexone for Extended-Release Injectable Suspension

Vivitrol®

Naltrexone

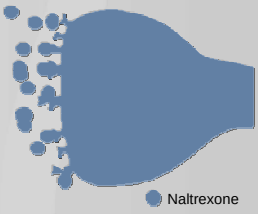
Revia ® or Depade ®

How Does Naltrexone Work?

- Naltrexone is an opioid receptor antagonist and blocks opioid receptors.

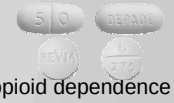
This prevents the effects of self-administered opioids.

It also diminishes release dopamine when alcohol is consumed, reducing the pleasurable effects



Medication Assisted Treatment of Opioid Use Disorders
Ron Jackson, MSW, LICSW

Naltrexone Hydrocholoride



Marketed As: ReVia® and Depade®

Indication

Used in the treatment of alcohol or opioid dependence and for the blockade of the effects of exogenous administered opioids and/or decreasing the pleasurable effects experienced by consuming alcohol.

Has not been found to be addictive or produce withdrawal symptoms when the medication is ceased.

Administering naltrexone will invoke opioid withdrawal symptoms in patients who are physically dependent on opioids.

Additional Information

Cost:
$40 - 60 per month
Third-Party Payer Acceptance:
Covered by most major insurance carriers, Medicare, Medicaid, and the VA.

Dosing:

One 50mg tablet, once a day
Can be crushed, diluted or mixed with food.

Abstinence requirements: must be taken at least 7-10 days after last consumption of opioids; abstinence from alcohol is not required;

What Does the Research Say?

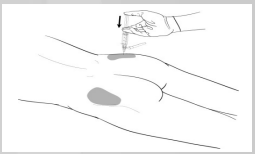
- Naltrexone is effective for opioid and alcohol addiction:
  - Reduces risk of re-imprisonment
  - Lowers risk of opioid use, with or without psychological support
  - Extended-release naltrexone addresses the issue of patient compliance

Naltrexone for Extended-Release Injectable Suspension

Vivitrol®

Extended-Release Naltrexone

Dosing:



One 380mg injection deep muscle in the buttock, :
every 4 weeks

Must be administered by a healthcare professional and should alternate buttocks each month.

Blocks opioid receptors for **one entire month** compared to approximately 28 doses of oral naltrexone.

It is **not possible to remove** it from the body once extended-release naltrexone has been injected.

Pricing: $800 – 1200 per month (one injection)

Special Precautions for Extended-Release Naltrexone

- During clinical trials, there was an increase in adverse events of a suicidal nature in patients taking extended-release naltrexone. Counselors should continue to closely monitor and record all suicidal events for patients, including those taking extended-release naltrexone.
- If opioid analgesia is required, it should be noted that the patient may necessitate greater than usual amounts of opioids to achieve desired effect, and the resulting respiratory depression may be deeper and more prolonged.

Selection of Candidates for Naltrexone

- Patients who are not interested or able to be on agonist maintenance
  - ✓ Those with high degree of motivation for abstinence (active in 12-step programs)
  - ✓ In professions where treatment with agonist is controversial (healthcare professionals, pilots)
- Patients successful on agonist but who want to try abstinence
- Patients who failed prior treatment with agonist
  - ✓ Continued use of heroin, did not improve/dropped out
- Patients who are abstinent but at risk for relapse
  - ✓ Moving to old neighborhood, increased stress, worsening psychiatric problems
- Patients for whom relapse would be disastrous (e.g., physicians, pilots, parolees)

Selection of Candidates for Naltrexone

Who is most likely to benefit from naltrexone?

- ✓Highly motivated patients who are committed to abstinence
- ✓Older patients with long history of use and multiple relapses
- ✓Those with longer periods of abstinence between relapses
- ✓Patients who relapsed and returned to treatment do better

Resistance to Medications

- **Many reasons for resistance to medication**
  - Anticipated unpleasant side effects
  - Cost of medication
  - Burden of taking daily medication
  - Denial about condition or disease
  - Influence of others
  - **Negative perception of addiction medications**

Addressing Concerns: "It's Just a Crutch"

"Medication is a crutch; I need to be completely drug free for true recovery."

- Some medication may only be needed for the early stages of recovery.
- AA has issued a clear statement supporting the use of medication in recovery.

"One man's crutch is another man's wing."
Guy Clark

Addressing Concerns: "I'm Not a Pill Popper"

"I don't want to get hooked on a medication."

- Approved medications for alcohol dependence are not physically addictive.
- Addictive medications are usually given only after multiple unsuccessful attempts to quit or a long history of use.
- The harm associated with continued substance use often exceeds the harm of replacement therapies.
- Substitution therapies for opioid dependence reduce harmful consequences, improve quality of life, and increase the chances of eventual abstinence.

Final Note: Behavioral Treatments

The FDA labeling on these medications is clear:

The medications should be used in combination with behavior treatments for addiction

Good treatment is **holistic, integrated and multifaceted**, taking into account the physical, behavioral and spiritual wellbeing of the individual.

Medications can help us **take care of the physical**…we need to do the rest

Treatment, not *Just* Medication

"The problem was one of rehabilitating people with a very complicated mixture of social problems on top of a specific medical problem, and that (practitioners) ought to tailor their programs to the kind of problem they were dealing with. The strength of the early programs as designed by Marie Nyswander was in their sensitivity to individual human problems. The stupidity of thinking that just giving methadone will solve a complicated problem seems to me beyond comprehension."

Vincent P. Dole, M.D., 1989

Source: Courtwright, et. al. Addiction: Who Survived

Resources

Buprenorphine

- SAMHSA - www.buprenorphine.samhsa.gov
- Reckitt Benckiser
  - www.suboxone.com
  - www.heretohelpprogram.com
- Zubsolv - http://www.zubsolv.com/

Extended-Release Injectable Naltrexone

- Clinical Use of Extended-Release Injectable Naltrexone in the Treatment of Opioid Use Disorders: A Brief Guide
  - http://store.samhsa.gov/shin/content//SMA14-4892/SMA14-4892.pdf

More Resources

- TIP 40: Clinical Guidelines for the Use of Buprenorphine for the Treatment of Opioid Dependence (SAMHSA-CSAT)
- TIP 43: Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs (SAMHSA-CSAT)
  - http://store.samhsa.gov/
- Medication-Assisted Treatment for Opioid Addiction: Facts for Families and Friends (SAMHSA-CSAT)
- ONDCP Fact Sheet: http://www.whitehouse.gov/sites/default/files/ondcp/Fact_Sheets/medication_assisted_treatment_9-21-2012.pdf