

# Doing the Same Thing Expecting Different Results: Examining All the Treatment Options for Opioid Use Disorder



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# Goals for the Training



- Understand the neurobiology of opioid use disorder (OUD) and treatment.
- Become familiar with the various medications used to treat OUD
- Become familiar with the use of Naloxone and the concept of “Harm Reduction” in the context of OUD.
- Explore the efficacy of the various treatment options for OUD, including abstinence based behavior modification medication assisted treatment.
- Explore specific treatment issues related to women who are pregnant and have OUD such as Neonatal Abstinence Syndrome(NAS) and the use of opioid medications during pregnancy.
- Explore personal biases regarding the use of medication in addiction treatment.

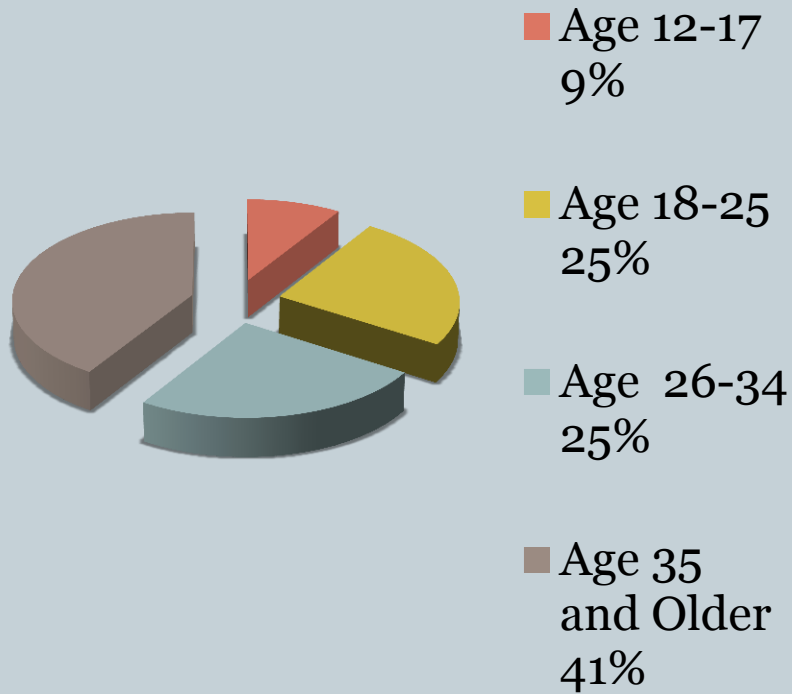
# What Does Opioid Use Look Like



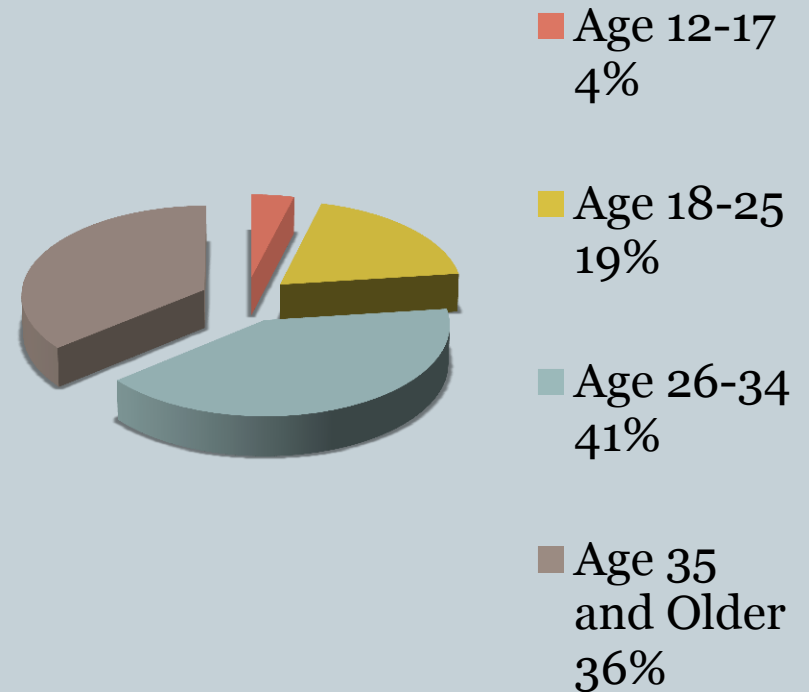
- In 2013 1.9 million Americans aged 12 or older used opioid pain relievers non-medically.
- In 2014 the average age at first use for opioid pain relievers was 21.7 years.
- 53% obtained the pain relievers from a family member or friend
- 21% from one doctor
- Between 2000 and 2012 admissions to treatment for opioid pain relievers increased 500%

# By Age

## Non-Medical Users of Opioid Pain Relievers

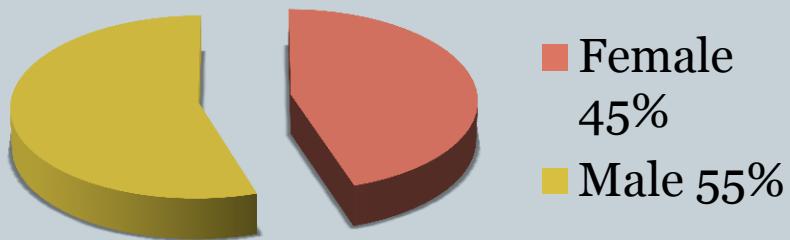


## Heroin Use

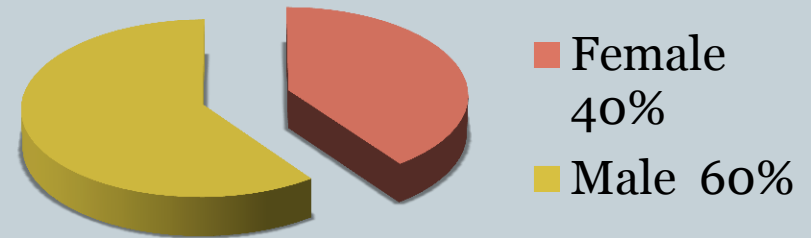


# By Gender

## Non Medical Users of Opioid Pain Relievers

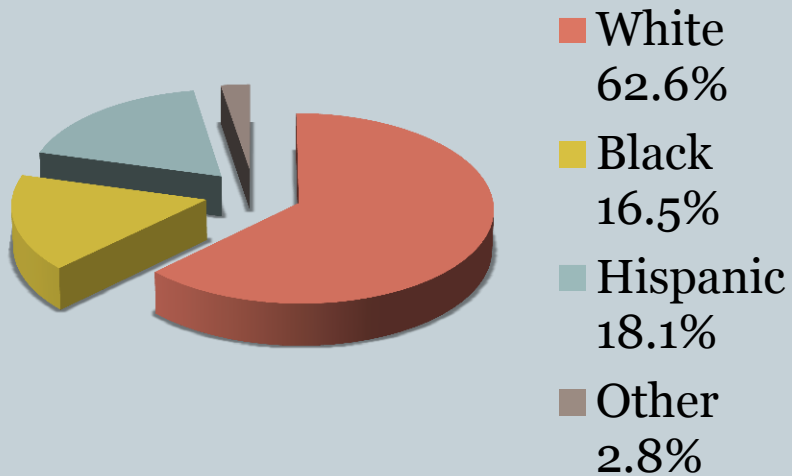


## Heroin Users

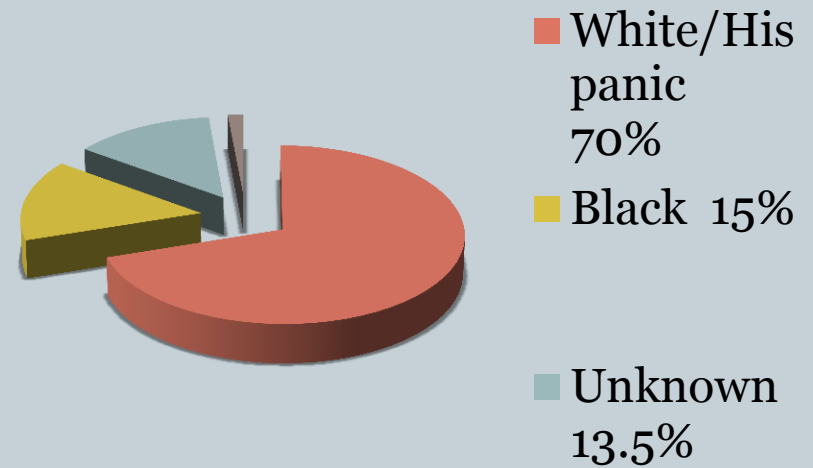


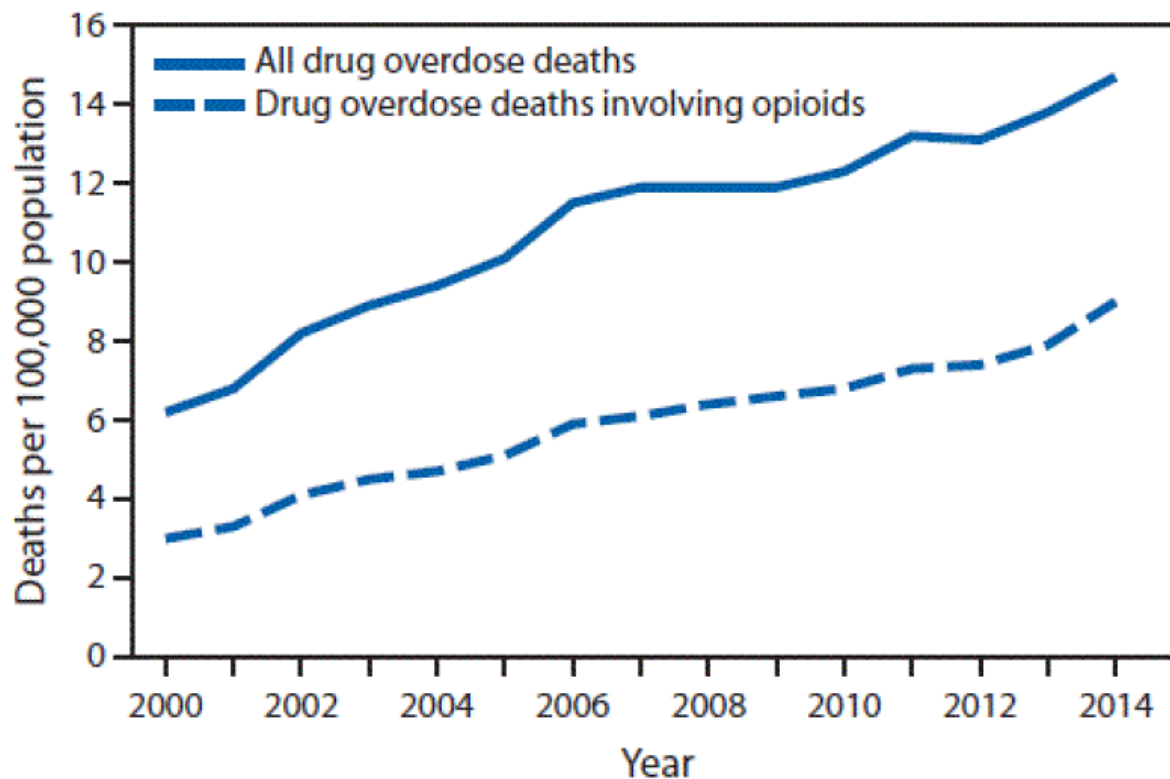
# By Race / Ethnicity

## Non Medical Users of Opioid Pain Relievers



## Heroin Users (by Treatment Admission)





## Drug Overdose Deaths and Drug Overdose Deaths Involving Opioids in the United States 2000-2014

**Source:** National Vital Statistics System, Mortality file.

\* Age-adjusted death rates were calculated by applying age-specific death rates to the 2000 U.S. standard population age distribution.

† Drug overdose deaths are identified using *International Classification of Diseases, Tenth Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14.

§ Drug overdose deaths involving opioids are drug overdose deaths with a multiple cause-of-death code of T40.0, T40.1, T40.2, T40.3, T40.4, or T40.6. Approximately one fifth of drug overdose deaths lack information on the specific drugs involved. Some of these deaths might involve opioids.

¶ Opioids include drugs such as morphine, oxycodone, hydrocodone, heroin, methadone, fentanyl, and tramadol.

# Opioid Use and Overdose Deaths



- Between 1999 and 2010 deaths from pain medication overdoses increased five fold among women while only increasing 3.6 times for men.
- Between 2010 and 2012 Heroin deaths doubled
- Women are more likely than men to be prescribed opioid pain medications and at higher doses
- Of the 15,323 overdose deaths among women in 2010, 71% involved opioid pain medications and 85% involved opioid pain medications and another drug



# Guiding Vision



The guiding vision of our work must be to create a world in which people with:

- a history of alcohol and/or drug problems
- people in recovery
- people at risk for these problems

are valued and treated with dignity, and where stigma, accompanying attitudes, discrimination and other barriers to recovery are eliminated

# Stigma



Depictions of substance use disorders seem to contain two main fallacies that can taint reputability and reinforce stigma:

- (1) inaccurate representations of the illness
- (2) frequent depiction of mainly negative symptomology

# The Power Of Words To Hurt Or Heal

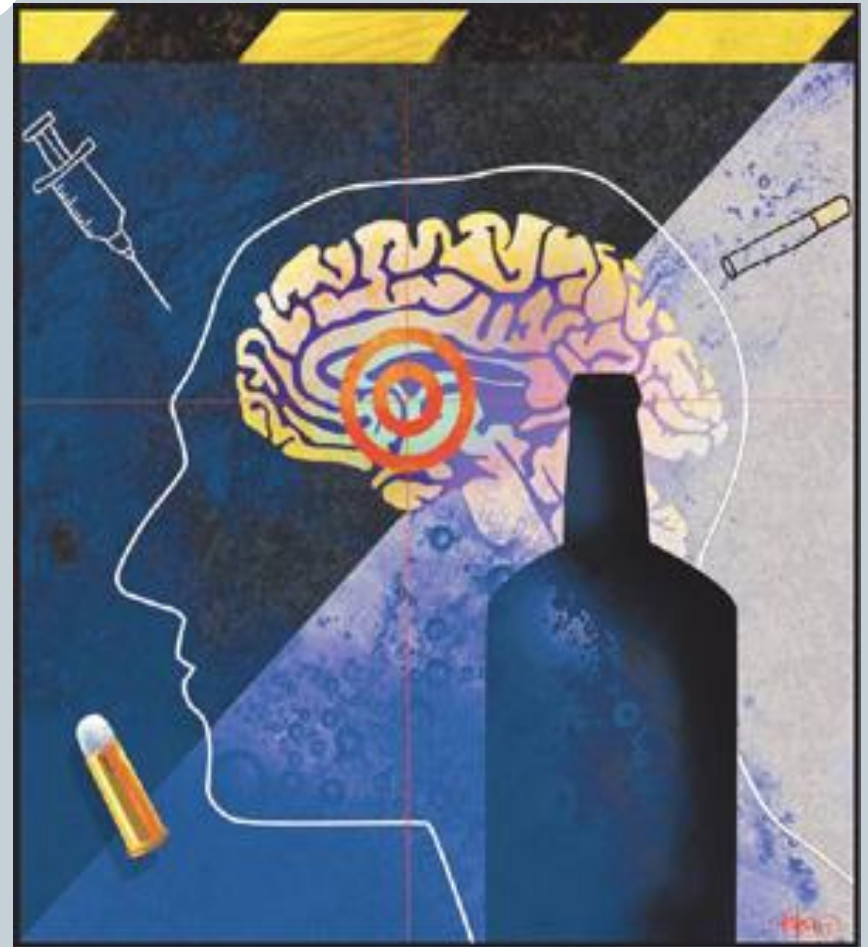
<b>Stigmatizing Words</b>	<b>Alternative Terminology</b>
<b>Addict, Abuser, Junkie, User</b>	<b>Person in active addiction, person with a substance use disorder, person experiencing an alcohol/drug problem, patient /client, person served</b>
<b>Relapse</b>	<b>Recurrence / return to use</b>
<b>Substance Abuse / Prescription Drug Abuse</b>	<b>Substance Use Disorder, Prescription Drug Misuse</b>
<b>Clean, Dirty</b>	<b>Negative, positive/ Drug free, Free from illicit and non-prescribed medication</b>
<b>Replacement or Substitution Therapy</b>	<b>Treatment, medication-assisted treatment, medication</b>



**ADDICTION AS A  
CHRONIC MEDICAL  
CONDITION**

# Medical Conditions

- Affect specific organs or parts of the body
- Have identifiable causes
- Have identifiable signs and symptoms
- Are treatable/curable (or not)
- Are either acute or chronic



# Acute vs. Chronic

- An “Acute” Condition has:

- Rapid onset
- Short course
- May be severe

- A “Chronic” Condition has:

- Gradual onset
- Lifetime course
- May have “acute” episodes
- Multi-modal Treatments
- Variable response rates depending on patient, treatment and outside factors

# Types of Chronic Diseases



- Hypertension
- Asthma
- Diabetes
- Addiction

# Medication Assisted Recovery

The use of medication as prescribed and overseen by a physician knowledgeable about addiction care to support recovery from Substance Use Disorders (SUD).





# Medication Assisted Recovery



What are some of the medications used to assist recovery from Substance Use Disorders in general?

- Disulfiram (Antibuse)
- Naltrexone (Vivitrol, Revia)
- Acamprosate (Campral)
- Buprenorphine (Suboxone, Subutex)
- SSRI Antidepressants
- Trazedone, Serax

# Medication Assisted Recovery



What are some of the medications used to assist recovery from Opioid Use Disorders?

- Naltrexone (Vivitrol)
- Methadone
- Buprenorphine (Suboxone, Subutex, Zubsolv)
- Clonidine

# Terminology



## Dependence versus Substance Use Disorder (SUD)

- An SUD 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

# Terminology



## **Tolerance**

- the loss of or reduction in the normal response to a drug or other agent, following use or exposure over a prolonged period a higher dose is required to achieve the same effect.

## **Dependence**

- A state in which an organism functions normally in the presence of a drug. It is manifested as a disturbance when the drug is removed (withdrawal).

# Terminology



## Withdrawal

- a period during which somebody addicted to a drug or using certain medications as prescribed stops taking it, causing the person to experience **painful or uncomfortable symptoms**

OR

- a person **takes a similar substance** in order to avoid experiencing the effects described above.


# DSM 5 Criteria for Opioid Use Disorder

Two or more of the following occurring at any time during the same 12 month period:

- Substance taken in larger amounts over time
- Persistent desire or unsuccessful efforts to cut down or stop
- A lot of time and activities spent getting, using or recovering
- Craving
- Recurrent use resulting in failure to fulfill major roles
- Continued use despite persistent social problems
- Important activities given up or reduced because of use
- Recurrent use in physically hazardous situations
- Continued use in spite of knowledge of the damage it is doing to the self

# DSM 5 Criteria for Opioid Use Disorder

- Tolerance (not met if taking opioids solely under appropriate medical supervision.)
- Withdrawal (not met if taking opioids solely under appropriate medical supervision.)
- Mild – Presence of 2-3 symptoms
- Moderate – Presence of 4-5 symptoms
- Severe – Presence of 6 or more



**OPIOIDS AND  
THE BRAIN:  
PHARMACOLOGY  
AND HALF-LIFE**



# Opiate/Opioid : What's the Difference?



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## Opiate

- A term that refers to drugs or medications that are derived from the opium poppy, such as heroin, morphine and codeine.

## Opioid

- A more general term that includes opiates as well as the synthetic drugs or medications, such as buprenorphine, methadone, meperidine (Demerol<sup>®</sup>), fentanyl—that produce analgesia and other effects similar to morphine.

# Terminology



## Half life:

The amount of time it takes for the body to get rid of half of the dose of a medication. When a patient is taking a medication on a regular basis there is an ongoing process of drug absorption and drug removal based on metabolism and clearance

# Terminology



## Steady State:

The point when the amount of drug going in is the same as the amount of drug getting taken out. It takes between 5-6 half lives for a medication to reach steady state. Medications with short half lives reach steady state relatively quickly while long half lives take a long time to reach steady state.

# Terminology



## Receptor:

Specific cell binding site or molecule: a molecule, group, or site that is in a cell or on a cell surface and binds with a specific molecule, antigen, hormone, or antibody

# Terminology



## Receptor Affinity:

The preference for specific molecules, antigens, hormones or antibodies by receptor sites. A molecule with a higher affinity will replace other substances on the site and will bind more tightly to the site.

## Opiates Act on Many Places in the Brain and Nervous System

Opiates can change the brain stem, an area that controls automatic body functions, and depress breathing

Opiates can change the limbic system, which controls emotions to increase feelings of pleasure.

Opiates can block pain messages transmitted by the spinal cord from the body

# What Do Opioids Do?



- Stimulate opioid receptors in central nervous system & gastrointestinal tract
- Analgesia – pain relief (somatic & psychological)
- Antitussive action – cough suppression
- Antidiarrheal
- Euphoria,
- Respiratory depression



# How Do Opioids Affect the Body?



- Pupillary constriction (Pinpoint Pupils)
- Constipation
- Histamine release (itching, bronchial constriction)
- Reduce libido
- Tolerance, cross-tolerance
- Withdrawal: acute & protracted



# How Are Opioids Used?



- Intravenously injected
- Smoked
- Snorted
- Orally administered

# Possible Acute Effects of Opioid Use



- Surge of pleasurable sensation = “rush”
- Warm flushing of skin
- Dry mouth
- Heavy feeling in extremities
- Drowsiness
- Clouding of mental function
- Slowing of heart rate and breathing
- Nausea, vomiting, and severe itching

# Consequences of Opioid Use



- Addiction
- Overdose
- Death
- Use related negative consequences
- (e.g., HIV infection, malnutrition)
- Negative consequences from injection:
  - Infectious diseases (e.g., HIV/AIDS, Hepatitis B and C)
  - Collapsed veins
  - Bacterial infections
  - Abscesses
  - Infection of heart lining and valves
  - Arthritis and other rheumatologic problems

# Opioid Withdrawal Syndrome



- Intensity varies with level & chronicity of use
- First signs occur shortly before next scheduled dose
- Duration of withdrawal is dependent upon the half-life of the drug used:
  - Peak of withdrawal occurs 36 to 72 hours after last dose
  - Acute symptoms subside over 3 to 7 days
  - Protracted symptoms may linger for weeks or months

# *Opioid* Withdrawal Syndrome


## Acute Symptoms

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- Pupillary dilation
- Lacrimation (watery eyes)
- Rhinorrhea (runny nose)
- Muscle spasms (“kicking”)
- Yawning, sweating, chills, gooseflesh
- Stomach cramps, diarrhea, vomiting
- Restlessness, anxiety, irritability

# *Opioid* Withdrawal Syndrome

## Protracted Symptoms



- Deep muscle aches and pains
- Insomnia, disturbed sleep
- Poor appetite
- Reduced libido, impotence, anorgasmia
- Depressed mood, anhedonia
- Drug craving and obsession

# Terminology



## Agonist:

A chemical that binds to a receptor site and triggers a response by the cell. They mimic the action of naturally occurring substances.

# Opioid Agonists



Natural derivatives of opium poppy

- Opium
- Morphine
- Codeine



# Opioid Agonists



- Semisynthetics: Derived from chemicals in opium
  - Diacetylmorphine – Heroin
  - Hydromorphone – Dilaudid<sup>®</sup>
  - Oxycodone – Percodan<sup>®</sup>, Percocet<sup>®</sup>
  - Hydrocodone – Vicodin<sup>®</sup>

# BAYER

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# Opioid Agonists



- Synthetics

- Propoxyphene – Darvon<sup>®</sup>, Darvocet<sup>®</sup>
- Meperidine – Demerol<sup>®</sup>
- Fentanyl citrate – Fentanyl<sup>®</sup>
- Methadone – Dolophine<sup>®</sup>
- Levo-alpha-acetylmethadol –  
ORLAAM<sup>®</sup>

# Opioid Partial Agonists



## Partial Agonist:

A chemical that binds and activates to a given receptor site but has only partial efficacy at the site relative to a full agonist.

- Buprenorphine – Buprenex<sup>®</sup>, Suboxone<sup>®</sup>, Zubsolv<sup>®</sup>, Subutex<sup>®</sup>
- Pentazocine – Talwin<sup>®</sup>

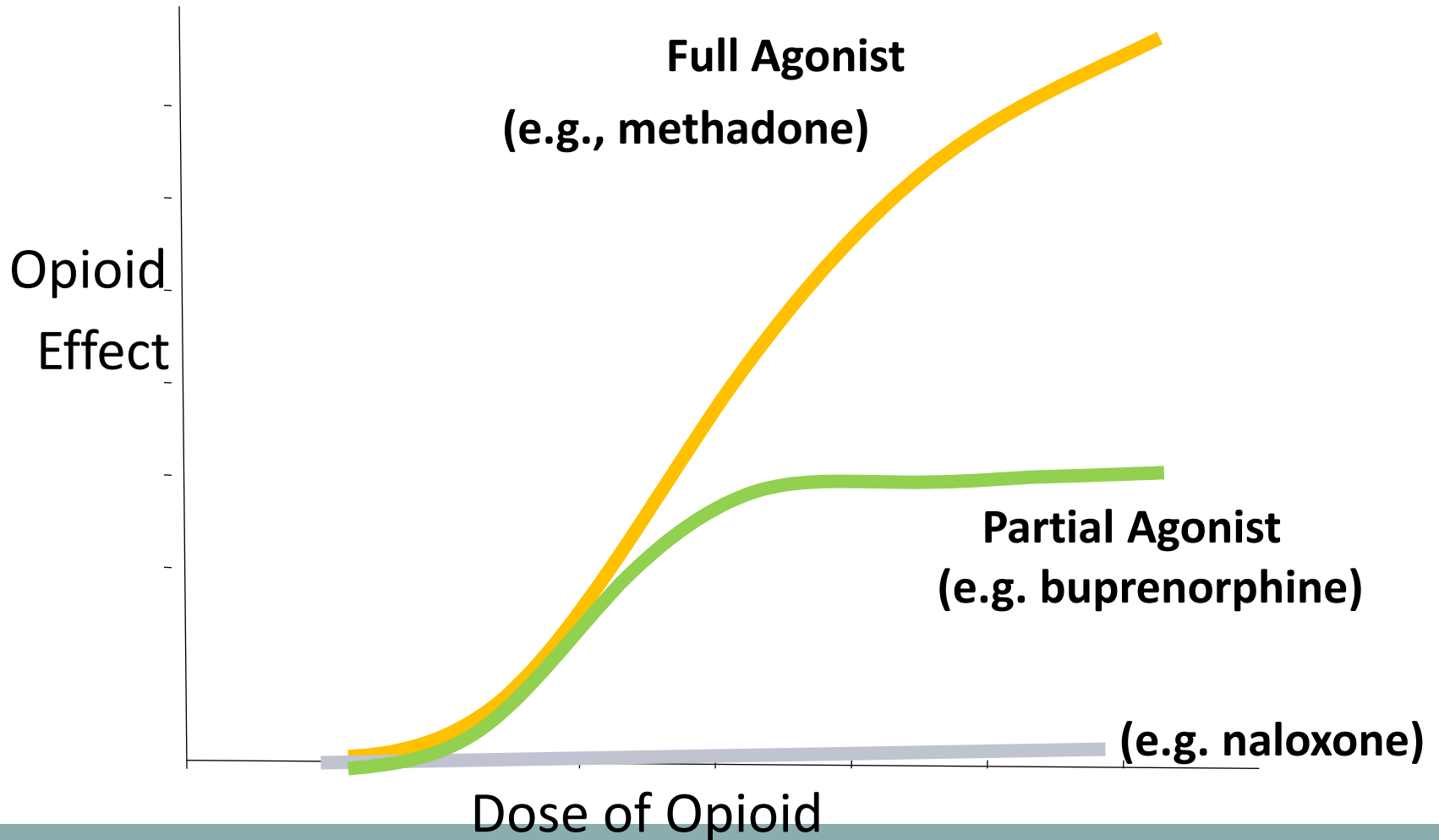
# Opioid Antagonists



## Antagonist:

Type of receptor ligand that does not provoke a biological response upon binding to a receptor but blocks agonist response.

# Partial vs. Full Opioid Agonist and Antagonist





**TREATMENT  
FOR OPIOID USE  
DISORDERS**

# A Brief History of Opioid Treatment



- 1964: Methadone is approved.
- 1974: Narcotic Treatment Act limits methadone treatment to specifically licensed Opioid Treatment Programs (OTPs).
- 1984: Naltrexone is approved, but has continued to be rarely used (approved in 1994 for alcohol addiction).
- 1993: LAAM is approved (for non-pregnant patients only), but is underutilized.



# A Brief History of Opioid Treatment



- 2000: Drug Addiction Treatment Act of 2000 (DATA 2000) expands the clinical context of medication-assisted opioid treatment.
- 2002: Tablet formulations of buprenorphine (Subutex<sup>®</sup>) and buprenorphine/naloxone (Suboxone<sup>®</sup>) were approved by the Food and Drug Administration (FDA).
- 2004: Sale and distribution of ORLAAM<sup>®</sup> is discontinued.
- 2011: Injectable Naltrexone (Vivitrol<sup>®</sup>) is approved for treatment of opioid use disorder

Effective treatment generally requires many facets. Treatment providers are important in helping the patients to:

- Manage physical withdrawal symptoms
- Understand the behavioral and cognitive changes resulting from drug use
- Achieve long-term changes and prevent return to use
- Establish ongoing communication between physician and community provider to ensure coordinated care
- Engage in a flexible treatment plan to help them achieve recovery

# Treatment Options for Individuals with Opioid Use Disorder

- Behavioral treatments educate patients about the conditioning process and teach relapse prevention strategies.
- Medications such as methadone and suboxone operate on the opioid receptors to relieve craving. Medications such as naltrexone block opioid receptor sites
- ***Combining the two types of treatment enables patients to stop using opioids and return to more stable and productive lives.***

# Treatment Options for OUD - MAW



## Medically-Assisted Withdrawal (Detox)

- Relieves withdrawal symptoms while patients adjust to a drug-free state
- Can occur in an inpatient or outpatient setting
- Typically occurs under the care of a physician or medical provider
- Serves as a precursor to behavioral treatment, because it is designed to treat the acute physiological effects of stopping drug use

# Treatment Options for OUD - MAW



## Long-Term Residential Treatment

- Provides care 24 hours per day
- Planned lengths of stay of 6 to 12 months
- Models of treatment include Therapeutic Community (TC), Cognitive Behavioral Therapy.

## Outpatient Psychosocial Treatment

- Less costly than residential treatment
- Varies in types and intensity of services offered
- Group counseling is emphasized
- Medically-assisted withdrawal is offered generally done with clonidine and other non-narcotic medications.

# Treatment Options for OUD - MAW



## Behavioral Therapies

### Motivational Interviewing

- Since most patients are Pre-Contemplation, this modality is very effective with individuals early in treatment.
- Cognitive-behavioral interventions
  - Modify patient's thinking, expectancies, and behaviors
  - Increase skills in coping with various life stressors

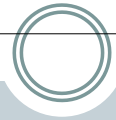
# Treatment Options for OUD



## Comprehensive Opioid Recovery (COR) 12

- Treatment Modality developed by Hazelden for individuals with OUD
- After initial stabilization, based on individual situations, Treatment Team recommends one of three options for patients. If necessary a person in any of the tracks will receive Buprenorphine / Naloxone for detoxification.
- All tracks receive the same comprehensive treatment services.

# Treatment Options for OUD





# Treatment Options for OUD – Medication Assisted Treatment (MAT)

## Agonist Maintenance Treatment

- Usually conducted in outpatient settings
- Treatment provided in opioid treatment programs traditionally using methadone or suboxone, now with suboxone in office-based settings
- Patients stabilized on adequate, sustained dosages of these medications can function normally.
- Can engage more readily in counseling and other behavioral interventions essential to recovery and rehabilitation
- The best, most effective opioid agonist maintenance programs include individual and/or group counseling, as well as provision of, or referral to other needed medical, psychological, and social services.

# Treatment Options for OUD – MAT



## Antagonist Maintenance Treatment

- Usually conducted in outpatient setting
- Initiation of naltrexone often begins after medically supervised withdrawal in a residential setting
- Repeated lack of desired opioid effects will gradually over time result in breaking the habit of opiate addiction.
- Patient noncompliance is a common problem. A favorable treatment outcome requires a positive therapeutic relationship, effective counseling or therapy, and careful monitoring of medication compliance.

(National Institute on Drug Abuse, 2009)

# Myths and Stigma of Medication

## Myths

- Methadone and buprenorphine are addicting
- Methadone and buprenorphine are legal highs
- Medication is “liquid handcuffs”

## Facts

- Physical dependence is different from addiction
- When used correctly, there is no intoxication
- Medication is an individual decision; it is possible to discontinue medication with strong social supports – discontinuing medication is not right for everyone

# Advantages and Disadvantages of Methadone

## Advantages

- Used effectively and safely for over 40 years
- Extensively researched
- Not intoxicating or sedating, if prescribed properly
- Effects do not interfere with ordinary activities

## Disadvantages

- Huge stigma
- Highly regulated
- Only Clinic Based
- OTPs can only dispense liquid form
- Pill form (used by Pain Clinics) highly divertable.

# Advantages and Disadvantages of Methadone

## Advantages

- Suppresses opioid withdrawal for 24-36 hours
- Full agonist can achieve blocking effect
- Relatively inexpensive
- Safe for pregnant women

## Disadvantages

- With long half life can result in respiratory suppression if combined with other opioids or benzodiazepines.
- With longer half life patients experience withdrawal symptoms for longer period of time.

# Advantages and Disadvantages of Methadone

## Advantages

- At appropriate dose, patients experience slight “effect”
- Patients can remain on Methadone for surgery and other medical procedures.
- Counseling required

## Disadvantages

- At appropriate dose patients experience slight “effect”
- Being clinic based, during initial stabilization, patient remains in “culture of addiction”

# Buprenorphine



- Partial Opioid Agonist Medication.
- Currently, comes in tablet or film, both of which are used sublingually. An Implantable formulation Probuphine was recently approved by the FDA. There are ongoing clinical trials on a patch formulation.
- Can be prescribed by an office-based physician (with specialized training and DEA License) and medication can be purchased from a commercial pharmacy.
- Two formulations: Subutex<sup>®</sup>, which is just buprenorphine and Suboxone<sup>®</sup>, which is a combination of buprenorphine and naloxone. New formulation Zubsolv<sup>®</sup>
- Suboxone was designed to discourage injection. If tablet is ground, naloxone is released precipitating withdrawal when injected or snorted

# Buprenorphine: Subutex®

## Advantages

- Comes in generic form so is less expensive
- Office-based, patients can receive 30 day prescription
- Most insurance companies will pay (patient has co-pay)
- Counseling encouraged but not required.

## Disadvantages

- Highly divertible
- Lack of “counseling” component contributes to active addiction mentality “script and go”
- No “effect”, suboptimal results with heroin users
- Due to strong binding at receptor sites, patients cannot remain on subutex for surgery and other medical procedures.



# Buprenorphine: Subutex®

## Advantages

- Off Label use for pregnant women
- No “effect”
- More effective with short term prescription medication addicts
- Due to “ceiling effect”, very limited respiratory suppression potential

## Disadvantages

- Because of higher diversion potential, less widely used.
- Possible respiratory suppression with high doses of Subutex® combined with high doses of benzodiazepines.

# Buprenorphine: Suboxone<sup>®</sup>

## Advantages

- No “effect”
- More effective with short term prescription medication addicts
- Due to “ceiling effect”, very limited respiratory suppression potential

## Disadvantages

- Significant ER overdose problems.
- Possible respiratory suppression with high doses of Suboxone<sup>®</sup> combined with high doses of benzodiazepines.

# Buprenorphine: Suboxone®

## Advantages

- Office-based, patients can receive 30 day prescription
- Most insurance companies will pay (patient has co-pay)
- Counseling encouraged but not required.

## Disadvantages

- Highly divertible
- Lack of “counseling” component contributes to active addiction mentality “script and go”
- No “effect”, suboptimal results with heroin users

# Buprenorphine: Suboxone®

## Advantages

- Due to receptor binding, withdrawal symptoms are less severe than with methadone.

## Disadvantages

- Can't be prescribed for women who are pregnant.
- Self-pay much more expensive than methadone.
- Due to strong binding at receptor sites, patients cannot remain on suboxone for surgery and/or other medical procedures.

# Vivitrol®



Vivitrol®, or Injectable Naltrexone (Depot Naltrexone), received initial approval for use with individuals diagnosed with alcohol dependence to reduce cravings. It received FDA approval in 2011 for use with opioid dependence.

- ✓ Naltrexone is an opioid antagonist, therefore it blocks the effects of opioid use.
- ✓ One injection lasts 25-30 days

# Vivitrol®



## Advantages

- Injectable formulation removes the need for daily dosing
- Blocks opioid effects thus supporting recovery
- Very effective as a follow-on to completion of Medically Supervised Withdrawal.

## Disadvantages

- Extremely expensive.
- An individual needs to be free from opioid for 5-7 days prior to first injection.
- Possible reaction at injection site.



**THE IMPORTANCE OF  
THE ATTITUDE OF  
TREATMENT STAFF TO  
PATIENT SUCCESS**

# Classic Research



*In 1974:*

Sampled opinions of:

- “ex-addict” counselors maintained with methadone
- “ex-addict” counselors who were abstinent
- “non-addict” counselors
- administrative and supervisory staff

▲ *The staff uniformly viewed methadone maintenance as preferable to the use of heroin – but as significantly less desirable than the person's functioning without drugs*



# Later Research



- Subsequent research in the 1980s and 1990s examined the relationship between attitudes of staff in methadone maintenance programs and patient retention in treatment
- The general finding of this line of research indicated that, compared to patients treated in methadone maintenance programs that emphasized indefinite maintenance, patients treated in programs that were abstinence-oriented
  - were more likely to use heroin while in treatment
  - leave treatment earlier
  - more likely to return to maintenance after discharge

# The Quiz

- 1. Methadone/buprenorphine maintenance patients who continue to use illicit opiates should have their medication dose reduced.**
- 2. Patients who ignore repeated warnings to stop using illicit opiates should be gradually withdrawn off methadone/buprenorphine.**
- 3. No limits should be set on the duration of methadone/buprenorphine maintenance.**
- 4. Methadone/buprenorphine should be gradually withdrawn once a maintenance patient has ceased using illicit opiates.**
- 5. Methadone/buprenorphine services should be expanded so that all opioid dependent patients who want medication can receive it.**
- 6. Methadone/buprenorphine maintenance patients who continue to abuse non-opioid drugs (e.g. benzodiazepines) should have their dose of methadone/buprenorphine reduced.**
- 7. Abstinence from all opioids (including methadone/buprenorphine) should be the principal goal of methadone maintenance.**
- 8. Left to themselves, most methadone/buprenorphine patients would stay on methadone for life.**
- 9. Maintenance patients should only be given enough methadone/buprenorphine to prevent the onset of withdrawals.**
- 10. It is unethical to maintain individuals on methadone/buprenorphine indefinitely.**
- 11. The clinician's principal role is to prepare methadone/buprenorphine maintenance patients for drug-free living.**
- 12. It is unethical to deny an individual methadone/buprenorphine.**
- 13. Confrontation is necessary in treating drug addiction.**
- 14. Patients should remain in methadone/buprenorphine maintenance for at least three to four years.**

# Scoring The Quiz

Score 1 for each “yes” to question 1, 2, 4, 6, 7, 8, 9, 10, 11, and 13.

Score 1 for each “no” to questions 3, 5, 12, and 14.

# Staff Attitudes Toward Methadone

- Caplehorn and colleagues reported in 1998 that the Median Abstinence Orientation Scale was strongly related to patient time in treatment.
- A 1-unit increase in scores was related to a more than threefold risk of discharge.
- Estimates suggest that approximately 60% of patients would have left an abstinence-oriented program in the first year of treatment, while only approximately 20% would have left an indefinite maintenance program.

# Therapeutic Challenges with Individuals with OUD

- Rarely have only one Substance Use Disorder
- Opioid Withdrawal is the overwhelming motivation for entering Treatment.
- Once at steady state of medication decreased motivation for treatment involvement.
- While individuals might be at a “Contemplation” or “Action” Stage related to opioids routinely the individuals are “Pre-contemplation” with other Substance Use Disorders.

# So Who Benefits Most From What?



- **MSW or Short Term Taper**
  - Individuals with strong support and high motivation or who are immediately going into long term treatment

## Methadone

Individuals with longer opioid use history or history of injection

# So Who Benefits Most From What?



- **Buprenorphine**

- Only used Pain Meds, no other SUD,  
Individuals with OUD – Mild

## **Vivitrol**

Individuals with high motivation;  
individuals who have completed a taper

But, first and foremost,  
what Treatment Modality  
does the patient want!



# Therapeutic Interventions



## Motivational Interviewing

- Since most patients are Pre-Contemplation, this modality is very effective with individuals early in treatment.

## Cognitive Behavioral Therapy (CBT)

Once individuals enter the “Contemplation”, “Action” or “Maintenance” Stage, most effective.

## Contingency Management

- Based on principles of operant conditioning
- Uses reinforcement (e.g., vouchers) of positive behaviors in order to facilitate change

# Levels of Care



MAR for OUD is a Level 1 (Outpatient) treatment.

Since Individuals with OUD routinely have other SUD, other levels of care could be beneficial for those.

If MAR is effective for OUD, it would be counter productive to remove the patient from that modality in order to enter a higher level of care

# Treatment and Overdose



- Abstinence based treatments for OUD (and Incarceration) result in an individuals tolerance being lowered
- The majority of overdose deaths are from individuals returning to use within 90 days of leaving treatment or detention
- Availability of Naloxone



# Opioid Dependence and Pregnancy

“These ladies are not those who would consider going to prenatal care. These are ladies who are strung out on heroin and cocaine and their only next decision is how to get their next fix,” she said on the House floor. “These ladies are the worst of the worst. Again, I want to emphasize what they are thinking about, and that is just money for the next high.”

*Tennessee State Rep. Teri Lynn Weaver (R-Lancaster)*

*April 14, 2014*

*speaking in support of her bill SB 1391*

# Consequences of OUD During Pregnancy

- Poor nutritional status
- Intrauterine growth restriction
- Maternal and/or fetal death from opioid overdose
- Preterm birth
- Placental abruption
- Poor fetal heart patterns
- Fetal death

# Goals of Treatment



- Improve outcomes for mother and newborn
  - Minimize prenatal risks
  - Increase participation in prenatal care
  - Minimize opioid withdrawal symptoms
  - Decrease illicit drug use and risk of overdose
  - Assist mother to transition to a safe and stable lifestyle

# Treatment of Opioid Use Disorder



- **FDA approved medications**
  - Methadone
  - Buprenorphine (with and without naloxone)
  - Naltrexone (oral and long-acting injection)
- **All have improved substance use outcomes, and helped stabilize lifestyles**



# Maintenance v. Medication-assisted Withdrawal

- WHO 2014 Guidelines: “Pregnant women dependent on opioids should be encouraged to use opioid maintenance treatment whenever available rather than to attempt opioid detoxification. Opioid maintenance treatment in this context refers to either methadone maintenance treatment or buprenorphine maintenance treatment.”
- Guidance regarding maintenance versus medication-assisted withdrawal has traditionally been based largely on good clinical judgment
- Medication followed by no medication treatment has frequently been found to be unsuccessful, with relatively high attrition and a rapid return to illicit opioid use
- Maintenance medication facilitates retention of patients and reduces substance use compared to no medication
- Biggest concern with opioid agonist medication during pregnancy is the potential for occurrence of neonatal abstinence syndrome (NAS)- a treatable condition

# Treatment of OUD During Pregnancy

- No medications currently approved for treatment of pregnant opioid-dependent women
- Methadone is considered standard of care
- Buprenorphine has shown promise
- Opioid antagonists are not recommended
- Pharmacotherapy should be used in conjunction with psychosocial support



# Methadone Maintenance as Standard of Care During Pregnancy



- Accepted since the late 1970s to treat opioid addiction during pregnancy
- Methadone maintenance recommended as standard of care by NIH consensus panel
- Has same benefits for pregnant patients as for patients in general
- Reduces fluctuations in maternal serum opioid levels, protecting fetus from withdrawal
- Associated with significant neonatal abstinence syndrome (NAS)

# Neonatal Abstinence Syndrome



- **Neurologic Excitability**
  - Hyperactivity
  - Irritability
  - Sleep disturbance
- **Gastrointestinal Dysfunction**
  - Uncoordinated sucking/swallowing
  - Vomiting
- **Autonomic Dysregulation**
  - Fever
  - Sweating
  - Nasal stuffiness

# Other Causes of NAS-like Symptoms



- **Maternal use of the following:**
  - Nicotine
  - Alcohol
  - Cocaine
  - Antidepressants
  - Benzodiazepines
  - Antipsychotics

# Neonatal Abstinence Syndrome (NAS)

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- Typically occurs within 72 hours and may last several weeks
- Occurs in 60-80% of babies born to methadone-maintained mothers
- Rates are similar or slightly less for buprenorphine
- Approximately 50% will require pharmacotherapy
- Buprenorphine exposed infants appear to have attenuated symptoms associated with NAS

# Methadone in Pregnancy



- Methadone maintenance in conjunction with comprehensive prenatal care is associated with:
  - Reduction in illicit substance use by mother
  - Reduction in exposure to other risky behaviors
  - Improves adherence to prenatal care
  - Improved maternal health
  - Longer duration of gestation
  - Increased birth weight

# Methadone in Pregnancy



- Accelerated clearance in 3<sup>rd</sup> trimester
  - Larger maternal blood volume
  - Increased metabolism due to rising progestins
- Increased doses are often required as gestation nears term
- Divided daily doses may keep maternal plasma levels more stable
- Enhanced fetal growth and head circumference when maternal dose is increased in third trimester



# Methadone in Pregnancy



- Prevents erratic maternal opioid levels that occurs with use of illicit opioids, and so lessens fetal exposure to repeated withdrawal episodes
- Reduces the likelihood of complications with fetal development, labor, and delivery.

# Candidates for Buprenorphine Treatment



- Those for whom benefits clearly outweigh risks
- Lack of access to a methadone clinic
- Women who cannot tolerate methadone
- Those who refuse methadone treatment
- Women who become pregnant while maintained on buprenorphine should stay on it
- Women on combination product should be switched to buprenorphine alone

# Maternal Opioid Treatment: Human Experimental Research (MOTHER) study (N=175)



- Multi-site, double-blind, double-dummy, flexible-dose, randomized clinical trial
- Women were randomized to buprenorphine sublingual tablets or methadone liquid
- Pregnant participants and their newborns underwent comprehensive assessment
- Participants received observed medications daily
- Monetary vouchers were given for negative urine drug screens (UDS)

# MOTHER Outcomes



- **Neonatal outcomes**
  - Percentage treated for NAS
  - NAS peak score
  - Total amount (mg) of morphine for NAS
  - Days in hospital for infant
- **Maternal outcomes**
  - Complications at delivery
  - Amount of voucher money earned
  - Analgesia during delivery (%)
  - Retention

# MOTHER Study Results

	<b>Methadone</b>	<b>Buprenorphine</b>	<b>P-value</b>
% Treated for NAS	57 (n=41)	47 (n=27)	NS
NAS Peak score	12.8 (0.6)	11.0 (0.6)	p=0.04
Morphine needed	10.4 (2.6)	1.1 (0.7)	p<0.009
Hospital days	17.5 (1.5)	10.0 (1.2)	p<0.009
% Complications	51 (n=37)	31 (n=18)	p=0.03
Did not complete	18 (n=16)	33 (n=28)	p=0.02
# Prenatal visits	8.8 (0.5)	8.7 (0.4)	NS
Analgesia	82 (n=60)	85 (n=49)	NS
Voucher \$ earned	1570 (121)	1391 (123)	NS

Adapted from Jones HE, Kaltenbach K, Heil SH, et al. *N Engl J Med* 2010;363:2320-31.

# Conclusions from the MOTHER Study



- Methadone and buprenorphine improved substance use outcomes
- No difference in the occurrence of NAS between treatment groups
- Infants of mothers treated with buprenorphine had less severe NAS and required less medication and less duration of treatment for NAS
- Buprenorphine treatment may be preferable given its attenuation of NAS symptoms
- More women treated with buprenorphine dropped out of treatment, which is consistent with other studies

# Buprenorphine Use in Pregnancy



- More women in the MOTHER trial dropped out of the buprenorphine group because of dissatisfaction with medication
- Splitting the dose into smaller increments given throughout the day may give better opioid coverage
- The improvement in the severity of NAS suggests significant benefit over methadone
- Women must be willing to take buprenorphine

# Breast Feeding on Methadone



- Small amounts of methadone found in breast milk (not related to maternal methadone dose)
- Limited data suggest breastfeeding may decrease NAS symptoms
- Gradual weaning from breast is recommended to prevent NAS
- Women HIV positive and/or continuing to use illicit drugs should not breast feed



# Breast Feeding with Buprenorphine



- Excreted in breast milk with plasma to milk ratio of 1
- Given low bioavailability of buprenorphine, infant exposure is approximately 1/5-1/10 of total buprenorphine available
- Buprenorphine levels in breast milk may have little effect on NAS

# MAW During Pregnancy



- Safest time is during the 2<sup>nd</sup> Trimester.
- 1<sup>st</sup> and 3<sup>rd</sup> Trimester have increased risk of miscarriage
- Significant stress to fetus
- Academy of Obstetricians and Gynecologists