Examining All The Treatment Options for Opioid Use Disorder (OUD): Doing the Same Thing Expecting Different Results

ED JOHNSON, M.ED. MAC, LPC, CCS
THE CAROLINAS & KENTUCKY PROGRAM MANAGER,
SOUTHEAST ATTC
EDJOHNSON@MSM.EDU
WWW.ATTCNETWORK.ORG/SOUTHEAST
Goals for the Training

- Understand the neurobiology of opioid use disorder (OUD) and treatment.
- Become familiar with the various medications used to treat OUD.
- 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%

NSDUH 2014
Average Annual Drug Overdose Death Rate Based on Decedent’s County of Residence 2012 - 2015

Death Rate (per 100,000 residents)

- 6 - 16
- 17 - 20
- 21 - 25
- 26 - 38
- 39 - 69

Appalachian Counties
* Unreliable
+ Suppressed

* Rates based on counts less than 20 are unreliable, and should be interpreted with caution.
+ Rates based on counts less than 5 were suppressed according to the state data release policy.

Note: Produced by the Kentucky Injury Prevention and Research Center (http://www.mc.uky.edu/kiprc/), May 31, 2016. Data are provisional and subject to change. Numbers between 0 and 5 were suppressed according to state data release policy.
Kentucky Resident Drug Overdose Deaths Involving Fentanyl, by County of Residence, 2014-2015 Combined

Fentanyl

Death count
- 0
- <5
- 5 - 50
- 51 - 100
- 101 - 200

Appalachian Counties

Note: Produced by the Kentucky Injury Prevention and Research Center (http://www.mc.uky.edu/kiprc/), May 31, 2016. Data are provisional and subject to change. Numbers between 0 and 5 were suppressed according to state data release policy. When a drug overdose episode involves two or more drugs, the case is counted under each relevant drug category.
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.
“We Can’t Fight This Epidemic Without Removing Stigma”

President Barack Obama
Charleston, West Virginia
October 21, 2015
Levels of Stigma

- Legal vs. Illicit
- Type of illicit substance used
- Method of Use
## The Power Of Words To Hurt Or Heal

<table>
<thead>
<tr>
<th>Stigmatizing Words</th>
<th>Alternative Terminology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addict, Abuser, Junkie, User</td>
<td>Person in active addiction, person with a substance use disorder, person experiencing an alcohol/drug problem, patient /client, person served</td>
</tr>
<tr>
<td>Relapse</td>
<td>Recurrence / return to use</td>
</tr>
<tr>
<td>Substance Abuse / Prescription Drug Abuse</td>
<td>Substance Use Disorder, Prescription Drug Misuse</td>
</tr>
<tr>
<td>Clean, Dirty</td>
<td>Negative, positive/ Drug free, Free from illicit and non-prescribed medication</td>
</tr>
<tr>
<td>Replacement or Substitution Therapy</td>
<td>Treatment, medication-assisted treatment, medication</td>
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</tbody>
</table>
“Recovery is a process of change whereby individuals improve their health and wellness, to live a self-directed life, and strive to reach their full potential.”

SAMHSA/CSAT 2011
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
The Acute Care Model

- Encapsulated set of service activities (assess, admit, treat, discharge, termination of service relationship).
- Professional expert drives the process.
- Services transpire over a short (and ever-shorter) period of time.
- Individual/family/community is given impression at discharge (“graduation”) that recovery is now self-sustainable without ongoing professional assistance.
Types of Chronic Diseases

- Hypertension
- Asthma
- Diabetes
- Addiction
The Chronic Care Model

- Initial triage and stabilization, support services are varied and open ended most concentrated early on.
- Professionals serve as consultants. Goal is for course of treatment to be patient driven to achieve highest level of adherence.
- Services are open ended, routine follow-up the norm.
- Individual/family/community educated on the “process” nature of “treatment”. Goal is to facilitate improved quality of life and wellness for the patient in whatever way works best for the patient.
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?

- Disulfram (Antibuse)
- Naltrexone (Vivitrol, Revia)
- Acamprosate (Campral)
- Buprenorphine (Suboxone, Subutex)
- SSRI Antidepressants
- Trazedone, Serax
What are some of the medications used to assist recovery from Opioid Use Disorders?

- Naltrexone (Vivitrol)
- Methadone
- Buprenorphine (Suboxone, Subutex, Zubsolv, Bunavail)
- 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.
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

<table>
<thead>
<tr>
<th>Level</th>
<th>Symptoms Presence</th>
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<tbody>
<tr>
<td><strong>Mild</strong></td>
<td>Presence of 2-3 symptoms</td>
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<tr>
<td><strong>Moderate</strong></td>
<td>Presence of 4-5 symptoms</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td>Presence of 6 or more</td>
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</table>

- **Tolerance** (not met if taking opioids solely under appropriate medical supervision.)
- **Withdrawal** (not met if taking opioids solely under appropriate medical supervision.)
Opiate/Opioid: What’s the Difference?

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

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

- 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
- Thebaine
Opioid Agonists

- Semisynthetics: Derived from chemicals in opium
  - Diacetylmorphine – Heroin
  - Hydromorphone – Dilaudid®
  - Oxycodone – Percodan®, Oxycontin®
  - Hydrocodone – Vicodin®
Opioid Agonists

- **Synthetics**
  - Propoxyphene – Darvon®, Darvocet®
  - Meperidine – Demerol®
  - Fentanyl citrate – Fentanyl®
  - Methadone – Dolophine®
  - Levo-alpha-acetylmethadol – ORLAAM®
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®, Suboxone®, Zubsolv®, Subutex®, Bunavail®
- Pentazocine – Talwin®
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

Opioid Effect

Dose of Opioid

Full Agonist
(e.g., methadone)

Partial Agonist
(e.g. buprenorphine)

(e.g. naloxone)
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).
A Brief History of Opioid Treatment


- **2002**: Tablet formulations of buprenorphine (Subutex®) and buprenorphine/naloxone (Suboxone®) were approved by the Food and Drug Administration (FDA).

- **2011**: Injectable Naltrexone (Vivitrol®) is approved for treatment of opioid use disorder.
Purpose Behind Using Medication with Opioid Use Disorder:

- Manage physical withdrawal symptoms
- Reduce risk of drug overdose
- Block any euphoric effect
- Facilitate therapeutic engagement
- Achieve long-term changes and prevent return to use
Behavioral treatments educate patients about the conditioning process and teach recovery management 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.
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
- Short term

(National Institute on Drug Abuse, 2009)
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 treatment programs include individual and/or group counseling, as well as provision of, or referral to other needed medical, psychological, and social services.

(National Institute on Drug Abuse, 2009)
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)
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**

**Medication Pathways**

**Week 1**
- Suboxone® for withdrawal (if medically indicated)

**Weeks 2–3**
- No medication
- Suboxone®
- Optimize dose
- Suboxone® taper; low-dose oral naltrexone

**Week 4**
- No medication
- Suboxone®
- ER naltrexone injection
## 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

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Suppresses opioid withdrawal for 24-36 hours</td>
<td>With long half life can result in respiratory suppression if combined with other opioids or benzodiazepines.</td>
</tr>
<tr>
<td>Full agonist can achieve blocking effect</td>
<td>With longer half life patients experience withdrawal symptoms for longer period of time.</td>
</tr>
<tr>
<td>Relatively inexpensive</td>
<td></td>
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<tr>
<td>Safe for pregnant women</td>
<td></td>
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</tbody>
</table>
Advantages and Disadvantages of Methadone

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<tr>
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<tbody>
<tr>
<td>• At appropriate dose, patients experience slight “effect”</td>
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</tr>
<tr>
<td>• Patients can remain on Methadone for surgery and other medical procedures.</td>
<td>• Being clinic based, during initial stabilization, patient remains in “culture of addiction”</td>
</tr>
<tr>
<td>• “Counseling” required</td>
<td></td>
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</tbody>
</table>
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®, which is just buprenorphine and Suboxone®, which is a combination of buprenorphine and nalaxone. Two new formulation are Zubsolv® and Bunavail®
- Suboxone was designed to discourage injection. If tablet is ground, naloxone is released precipitating withdrawal when injected or snorted
## Buprenorphine: Subutex®

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Comes in generic form so is less expensive</td>
<td>• Highly divertible</td>
</tr>
<tr>
<td>• Office-based, patients can receive 30 day prescription</td>
<td>• Lack of “counseling” component contributes to active addiction mentality “script and go”</td>
</tr>
<tr>
<td>• Most insurance companies will pay (patient has co-pay)</td>
<td>• No “effect”, suboptimal results with heroin users</td>
</tr>
<tr>
<td>• Counseling encouraged but not required.</td>
<td>• Due to strong binding at receptor sites, patients cannot remain on subutex for surgery and other medical procedures.</td>
</tr>
<tr>
<td>Advantages</td>
<td>Disadvantages</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>• Off Label use for pregnant women</td>
<td>• Because of higher diversion potential, less widely used.</td>
</tr>
<tr>
<td>• No “effect”</td>
<td>• Possible respiratory suppression with high doses of Subutex® combined with</td>
</tr>
<tr>
<td>• More effective with short term prescription</td>
<td>high doses of benzodiazepines.</td>
</tr>
<tr>
<td>medication addicts</td>
<td></td>
</tr>
<tr>
<td>• Due to “ceiling effect”, very limited</td>
<td></td>
</tr>
<tr>
<td>respiratory suppression potential</td>
<td></td>
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<tr>
<td>• No “effect”</td>
<td>• Significant ER overdose problems.</td>
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- Office-based, patients can receive 30 day prescription
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### Disadvantages
- Highly divertible
- Lack of “counseling” component contributes to active addiction mentality “script and go”
- No “effect”, suboptimal results with heroin users
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<tr>
<td>• Due to receptor binding, withdrawal symptoms are less severe than with methadone.</td>
<td>• Can’t be prescribed for women who are pregnant.</td>
</tr>
<tr>
<td></td>
<td>• Self-pay much more expensive than methadone.</td>
</tr>
<tr>
<td></td>
<td>• Due to strong binding at receptor sites, patients cannot remain on suboxone for surgery and/or other medical procedures.</td>
</tr>
</tbody>
</table>
New Treatments for OUD

Probuphine

- Implantable buprenorphine
- Lasts up to six months
- Frequently requires supplemental oral buprenorphine
New Treatments for OUD

The Bridge

- Percutaneous nerve stimulation
- Used for 3-6 days
- Allows patient to participate in an outpatient non-opioid taper to transition to an opioid antagonist
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
<table>
<thead>
<tr>
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<td>• Injectable formulation removes the need for daily dosing</td>
</tr>
<tr>
<td>• Blocks opioid effects thus supporting recovery</td>
</tr>
<tr>
<td>• Very effective as a follow-on to completion of Medically Supervised Withdrawal.</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Extremely expensive.</td>
</tr>
<tr>
<td>• An individual needs to be free from opioid for 5-7 days prior to first injection.</td>
</tr>
<tr>
<td>• No Counseling required</td>
</tr>
</tbody>
</table>
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.

Adapted from Caplehorn et al., Drug Alc Dep, 1998
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.
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 than 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 "recovery capital" 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
  - Patients with high levels of recovery capital

- **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 individual's tolerance being lowered.
- The majority of overdose deaths are from individuals returning to use within 90 days of leaving treatment or detention.
- During induction onto Methadone.
Incorporating OEND Into Addiction Treatment

• When
  ○ Intake and Assessment
  ○ Psychosocial Education Groups
  ○ Individual Counseling
  ○ Recovery Management Discharge Planning
Incorporating OEND Into Addiction Treatment

• How:
  • Ask Questions about overdose “have you ever overdosed” ‘have you ever witnessed an overdose” (be aware of trauma)
  • Approach topic from the perspective of care and safety.
In addition to Medications...

- Calling 911
- Rescue Breathing (CPR)
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_
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

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
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)

- 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\textsuperscript{rd} 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.

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)

<table>
<thead>
<tr>
<th>MOTHER Outcomes</th>
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<tbody>
<tr>
<td><strong>Neonatal outcomes</strong></td>
</tr>
<tr>
<td>- Percentage treated for NAS</td>
</tr>
<tr>
<td>- NAS peak score</td>
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<tr>
<td>- Total amount (mg) of morphine for NAS</td>
</tr>
<tr>
<td>- Days in hospital for infant</td>
</tr>
<tr>
<td><strong>Maternal outcomes</strong></td>
</tr>
<tr>
<td>- Complications at delivery</td>
</tr>
<tr>
<td>- Amount of voucher money earned</td>
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<tr>
<td>- Analgesia during delivery (%)</td>
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<tr>
<td>- Retention</td>
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</tbody>
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# MOTHER Study Results

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

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

Breast Feeding on Methadone

- Small amounts of methadone found in breast milk (amount related to maternal methadone dose but less than used to treat NAS)
- Limited data suggest breastfeeding may decrease NAS symptoms
- Gradual weaning from breast is recommended to prevent NAS
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\textsuperscript{nd} Trimester.
- 1\textsuperscript{st} and 3\textsuperscript{rd} Trimester have increased risk of miscarriage
- Significant stress to fetus
- Academy of Obstetricians and Gynecologists