The State of Medicine in Addiction Recovery

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Addiction is a serious, chronic and relapsing disorder, use multiple evidence based treatments.

Medications should be considered as part of a comprehensive treatment plan, addressing both disordered physiology and disrupted lives.

Medications should be considered for treatment of: psychiatric sx’s, addictive d/o’s, and co-occurring d/o’s.

Emerging literature supports use of meds in youth with SUDs and psychiatric comorbidity.
Addiction is a brain disease
ASAM “Short” Definition of Addiction

...A Primary, chronic, RELAPSING disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursing reward and/or relief by substance use and other behaviors. -ASAM
Does Abstinence-Based Treatment Work?

National Treatment Outcome Research Data on Opioid Addiction Patients

242 patients in residential treatment:

- 34% relapse w/in 3 days
- 45% relapse w/in 7 days
- 50% relapse w/in 14 days
- 60% relapse w/in 90 days

Multiple “Studies consistently show 2/3 of patients in abstinence-based programs relapse”. Dr Batki, MD Prof of Psy, Upstate Med Center Syracuse
Does Abstinence-Based Treatment Work?

• Studies: Of patients who complete abstinence-based treatment only 36% are sober at one year.

• Why? Multiple reasons – Hypodopaminergic brain, Post-Acute Withdrawal discomfort, Denial, Minimization, Lack of Support, Co-occurring Illness, No meetings, No sponsor, no Monitoring, Not followed medically like other chronic illnesses....
Why do people relapse?

Reasons for Relapse

- 62% mood was bad
- 39% wanted to try opioid drugs once more
- 48% ease of access to opioids
- 62% cravings were too much
- 37% someone offered them opioids
- 43% missed the support of the treatment center
Success rates vary

- Depending on
  - The Individual
  - The Addiction
  - Co Morbid conditions
  - Psychosocial/Family
Relapsing Disease

- Medical relapse
  - Blame the medication or the disease
  - Aggressive work up to find treatments to protect patient from the disease

- Addiction relapse
  - Blame the patient
Medication Assisted Treatment/Recovery

• Use sparingly and only when needed

• Treat symptoms to help patient stay in recovery and learn tools for long term wellness

• Some meds may be long term, but most will be short term while neurogenesis and synaptogeneiss and neural repair occur, especially in the first 3-6 months of recovery.

• My whole philosophy is stabilizing until the foundation is built, then moving away from medications when possible.
Medication Assisted Treatment/Recovery

Medication Assisted Treatment/Recovery: Alcohol Dependence

FDA-Approved:

- Disulfuram (Antabuse)
- PO naltrexone (Revia)
- IM naltrexone (Vivitrol)
- Acamprosate (Campral)

Non-FDA-approved:

- Topiramate (Topamax)
- Ondansetron (Zofran)
- Baclofen
Medication Assisted Treatment/Recovery: Opioid Dependence

Detoxification:
  • Opioid-based agonist (methadone, buprenorphine)
  • Non-opioid based (clonidine, supportive meds)
  • Antagonist-based (naltrexone: “rapid”)

Relapse prevention:
  • Agonist maintenance (methadone)
  • Partial agonist maintenance (buprenorphine)
  • Antagonist maintenance (naltrexone)

Overdose reversal:
  Naloxone (Narcan nasal, Auto-injector)
Medication Assisted Treatment/Recovery: Opiate Receptor Activation
Medication Assisted Treatment/Recovery: Opioid Substitution Goals

- Reduce symptoms & signs of withdrawal
- Reduce or eliminate craving
- Block effects of illicit opioids
- Restore normal physiology
- Promote psychosocial rehabilitation and non-drug lifestyle
Maintenance Medication - Reduce Relapse Rates

40 Heroin Addicts randomized to:

- 1 week detox followed by placebo and counseling
- 1 year BUP maintenance and counseling

Heroin use:

- Buprenorphine detox, placebo maintenance = 100% relapsed - 4/20 died!!
- Buprenorphine maintenance = 75% (SD 60%) opioid negative urine drug screens. 0/20 deaths
Maintenance Medication - Reduce Relapse Rates

In one study, all patients who were detoxed and counseled relapsed with about 50 days. Those receiving maintenance medication with counseling demonstrated a lower rate of relapse.

* Kakko J. et al., Lancet. 2003;361:66*
Medication Assisted Treatment/Recovery: Buprenorphine

- Suboxone, Subutex, Zubsolv, Bunavail
- FDA approved 2002, age 16+
- Mandatory certification from DEA (100 pt. limit)
- Office-based, expands availability
- Analgesic properties
- Ceiling effect
- Mechanism: \( \mu \)-opioid PARTIAL agonist
Studies of MAT with Suboxone – How long should it be used?

MAT with Suboxone for 7 days vs 28 days in 990 pts with Opioid SUD

• Similar relapse rates either way - about 87% at three months (Ling 2009)

• MAT with Suboxone for 3 mo...
  60% opioid free at 1 year (Katz 2009/Galanter 2003)

• MAT with Suboxone for 6 – 9 mo
  90% opioid free after one year (did not look at other drugs) (Badgaiyan 2015)
Naltrexone/Vivitrol

- For opioids and alcohol dependence
- Daily oral or 1x monthly injectable
- Covered by Medicaid/Medicare (LA)
Cost effectiveness of treatment

• Cost to society of drug abuse is $200 BILLION/year

• Treatment is less expensive than incarceration
  • Methadone Maintenance = $4700/year
  • Imprisonment = $18400/year

• Other studies show that every $1 invested in treatment can yield up to $7 in savings
Patients treated with VIVITROL and counseling had a SIGNIFICANTLY HIGHER PERCENTAGE OF OPIOID-FREE WEEKS

• During weeks 5–24

Confirmed abstinence = negative urine drug test and no self-reported opioid use

<table>
<thead>
<tr>
<th></th>
<th>PLACEBO</th>
<th>VIVITROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median patients (with psychosocial support) had</td>
<td>35% cumulative opioid-free weeks</td>
<td>90% cumulative opioid-free weeks</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0002</td>
<td></td>
</tr>
</tbody>
</table>

In the prespecified subset (n=53, 8% of the total study population) patients who abstained for 7 days prior to the first injection had

**92% FEWER HEAVY-DRINKING DAYS**

- Median heavy-drinking days per month
- The same treatment effects were not evident among the subset of patients (n=571, 92% of the total study population) who were actively drinking at the time of treatment initiation
- Baseline for both VIVITROL 380 mg and placebo was 15.2 heavy-drinking days per month


Please see Important Safety Information throughout this presentation. Prescribing Information and Medication Guide will be furnished during this program.
Current Opioid MAT Controversies

• Which patients should be offered MAT and when in their treatment course should they be offered it?
• How long do you continue MAT?
• How to change someone from Methadone or Buprenorphine to Vivitrol?
• Long-term side effects of all?
• MAT vs Abstinence and is there a happy medium?
• Is a patient who uses medication to maintain sobriety in “real recovery” (and does it matter)?
• Lawsuits alleging failure to meet the standard of care/ best practices???
Choosing Agonist vs. Antagonist Based Treatment

<table>
<thead>
<tr>
<th></th>
<th>AGONIST</th>
<th>ANTAGONIST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintain physiological dependence and potential for withdrawal</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Potential for tolerance development</td>
<td>+/-</td>
<td>-</td>
</tr>
<tr>
<td>Euphoric effects/abuse/diversion</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Compatible with ongoing illicit opioid use</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>May alter use of other drugs</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Extinction of heroin-reinforced behaviors/reversal of underlying neurobiology</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>Indefinite?</td>
<td>?</td>
</tr>
<tr>
<td>Cultural/ideological barriers to availability</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Professional/public opposition</td>
<td>++</td>
<td>+</td>
</tr>
</tbody>
</table>

Not offering medication after they stop drug use puts patients at increased risk of overdose and death.
Using Blockers to Treat Opiate Dependence

- The concept developed in parallel to methadone, in part fueled by the controversies in response to methadone.
- In 1960s studies by Martin on various opiates in humans discovered opiate blockers, naltrexone was well tolerated and had a long duration of action.
  - Subjects maintained on the blocker did not feel effects of morphine and it was impossible to induce physical dependence.
- Wikler suggested that opiate blockers are used for treatment of heroin addiction.
  - Based on the behavioral/learning model of addiction, attempts at re-addiction while on the blocker will lead to the extinction of drug seeking.
Improving Treatment Retention Using Long-Acting Preparations

- **Injections**
  - 1\textsuperscript{st} gen: oil suspension (Wedgewood)
  - 2\textsuperscript{nd} gen: microspheres with NTX in suspension
    Vivitrol licensed in 2007

- **Implants**
  - 1\textsuperscript{st} gen: compressed NTX c. 1996, now licensed in Russia (Prodetozone)
  - 2\textsuperscript{nd} gen: NTX mixed with polymer matrix c.2001, Australia
Naltrexone Initiation During Detoxification: Rapid Naltrexone Induction Procedure

Columbia Rapid Naltrexone Induction Protocol

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>admission</td>
<td>4 mg bid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naltrexone</td>
<td></td>
<td></td>
<td>3 mg</td>
<td>6 mg</td>
<td>25 mg</td>
<td>50 mg</td>
<td>380 mg po</td>
</tr>
<tr>
<td>Supportive medications</td>
<td>clonidine 0.1-0.2 mg qid, clonazepam 0.5-1.0 mg qid, toradol, ranitidine, zolpidem, trazodone</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- Approximately 70% of patients complete inpatient rapid naltrexone induction procedure and accept long-acting naltrexone (NTX-XR)
- Modification of the algorithm depending on the level of physiological dependence
# Rapid Naltrexone Induction Algorithm

(Sigmon et al., 2012)

<table>
<thead>
<tr>
<th>Severity (physical dependence/anticipated withdrawal)</th>
<th>Setting</th>
<th>Outpatient</th>
<th>Outpatient or partial hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NONE</strong></td>
<td>Already abstinent (completed buprenorphine taper and has abstained for 7-10 days, exiting controlled environment)</td>
<td>Buprenorphine Dose</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clonidine</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clonazepam</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ancillary medications</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hydration</td>
<td>Routine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time to first NTX dose</td>
<td>Day 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Initial oral NTX dose</td>
<td>25-50 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Time to Vivitrol injection</td>
<td>Days 1-2</td>
</tr>
</tbody>
</table>
## Transition from Buprenorphine Maintenance to Naltrexone

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Buprenorphine</strong></td>
<td>2 mg qd</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Naltrexone</strong></td>
<td></td>
<td></td>
<td></td>
<td>1-3 mg</td>
<td>6 mg</td>
<td>25 mg</td>
<td>50 mg po 380 mg im</td>
</tr>
<tr>
<td><strong>Supportive medications</strong></td>
<td>clonidine 0.1-0.2 mg qid, clonazepam 0.5-1.0 mg qid, toradol, ranitidine, zolpidem, trazodone, d-amphetamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Many people who are unable to taper off buprenorphine have anxiety disorder, which can benefit from SSRI or an anticonvulsant (gabapentin, pregabalin)
- People who stop buprenorphine maintenance are either anxious or sedated, treat symptomatically accordingly (e.g., clonazepam, stimulant)
Protracted Withdrawal: Naltrexone Flu

- Patients who start naltrexone right after detoxification commonly experience a “flu-like” sign and symptoms
  - Somatic complaints: insomnia, GI distress, hyperalgesia, anergia
  - Anxiety, irritability, dysphoria, anhedonia
  - Severity may be lower if naltrexone is started 10-14 days after completion of detoxification (but many relapse by then)

- Partially alleviated with aggressive symptomatic treatment,
  - Insomnia (v. frequent, often severe): zolpidem, trazodone, quetiapine
  - GI distress: H2 blockers
  - Anxiety/hyperarousal: clonazepam, clonidine

- Most of these symptoms remit by 2-4 weeks
  - True prolonged symptoms are rare and likely reflect additional psychopathology

- Persistent/protracted withdrawal vs. acute effects of naltrexone (?)
  - Negative mood and vegetative symptoms are significantly higher in participants who are receiving higher dose of naltrexone
Naloxone – Expanded Access is Recommended

Many organizations strongly recommend that naloxone be readily accessible to individuals likely to witness a life-threatening opioid emergency

- World, Federal, State, Medical Organizations –
Available Naloxone Formulations

• Naloxone for Medical Settings
  • Vial and syringe for Injection
  • Prefilled Glass Cartridges for Injection

• Take-Home Naloxone
  • Naloxone Auto-injector
  • Naloxone Nasal Spray

• Other Naloxone Option
  • Intranasal (IN) Delivery Kit - Prefilled Cartridge for Injection adapted for IN Administration with Mucosal Atomizer
Dr. Arwen Podesta, NPI-1194914598
2238 1st St., Slidell, LA 70458

Naloxone Standing Order Prescriptions

Date: 11-8-16 MD: [Signature]

This prescription is for patients with any of the following:
1) With a history of opioid overdose.
2) With a history of substance use disorder.
3) Taking benzodiazepines with opioids.
4) At risk for returning to a high dose usage and has a low tolerance to opioids (e.g., recently released from prison with an opioid addiction history, or a period of abstinence).
5) Taking higher dosages of opioids (≥50 MME/day).
6) **ANYONE**, including a pregnant woman, self reporting illicit opioid usage (e.g. Heroin, OxyContin, Hydromorphone or Hydrocodone)
7) **ANYONE** who might be in a position to **assist or provide** a person warranting emergent management of an opioid-related drug overdose.

Medication SIG:

Evzio (Naloxone HCL 0.4mg/ml) auto-injector two pack, for suspected opioid overdose, repeat after 2 minutes if no or minimal response. Quantity # 1, 1 refill
Call 911 after 1st auto-injection administration.

If Evzio not covered by insurance

Narcan 4mg/0.1ml single dose Nasal Spray, administer a single spray to a nostril. If in 2 minutes the patient does not respond then give a 2nd dose. Quantity # 2, 1 refill
Call 911 after initial administration.

**OR**

Naloxone 2mg/2ml single dose pre filled syringe, dispense with mucosal atomizer device, spray one-half of syringe (1ml) into each nostril upon signs of opioid overdose, may repeat if no response after 1 min. Quantity # 2, 1 refill

Call 911 after initial administration.

If recipient has questions for Dr. Podesta call her support staff, Call-985-690-6622 or 1-866-825-2238
Naloxone
How to respond to an overdose

How to respond to an overdose

Call 911 Say the person isn’t breathing/is struggling to breathe and provide the exact location of the victim.

Administer naloxone: Intranasal Anyone can safely and legally spray naloxone into the nose. If they do not revive, give a second dose of naloxone. Each kit is one dose.

Stay with the person If you must leave them alone, put them in the “recovery position” by rolling them onto their side. This will keep them from choking if they begin vomiting. They will wake up in withdrawal from opioids due to the naloxone and should not be allowed to re-use opioids. They will probably not realize that they overdosed.

How to administer naloxone

1. Remove yellow cap from top and bottom of the plastic tube.
2. Remove plastic cap from vial of Narcan.
3. Screw the vial into bottom of tube.
4. Screw atomizer on.
5. Spray half the vial into each nostril by pushing the vial up through the tube.

Signs of an overdose

- The person is unresponsive
- Slow heart rate: not breathing or breathing less than 10 breaths a minute
- Muscle twitching
- Blue or gray lips and fingernails
- May be making loud, uneven gurgling sounds

Do not inject the person with anything. Salt, milk, or other drugs do not work against the heroin and can cause more harm.

Do not put them under the shower.

Always call 911 whether you give naloxone or do not.
Naloxone, also known as Narcan, is used to reverse an opioid overdose. When a person overdoses on opioids, their breathing slows down which can lead to death. Naloxone helps the person wake up and continue breathing within 5 minutes. This allows time for EMS to arrive.

**Always call 911** whether you give naloxone or do not.

**Who can pick up naloxone?**

Anyone can get naloxone from University Medical Center or Crescent City Pharmacy.

You do not need to visit a doctor to get a prescription.

You must have your ID with you to pick up naloxone.

**Where can I get naloxone?**

**University Medical Center**

**Outpatient Pharmacy**

2000 Canal Street

Monday-Friday: 9am-5pm

Phone: 504-758-3718

**Crescent City Pharmacy**

2240 Simon Bolivar Ave.

Monitor-Friday: 8am-5:30pm

Saturday: 9am-12 noon

Phone: 504-267-4100

**Where can I go for help?**

For access to current detox services for drug/alcohol problems and for mental health and crisis programs, contact Metropolitan Human Services District (MHSD)

Phone: 504-568-3130

**What are Opioids?**

Opioids include heroin and prescription pain pills like morphine, codeine, oxycodone, methadone and hydrocodone.
NARCAN® (naloxone HCl) NASAL SPRAY 4 mg

DO NOT TEST DEVICES OR OPEN BOX BEFORE USE.

Use for known or suspected opioid overdose in adults and children.

This box contains two (2) 4-mg doses of naloxone HCl in 0.1 mL of nasal spray.

Two Pack

CHECK PRODUCT EXPIRATION DATE BEFORE USE.
In an opioid emergency...

SECONDS COUNT

REACH FOR VOICE GUIDANCE

The first and only intelligent 2 mg take-home naloxone auto-injection system with voice and visual guidance.

Ask your healthcare provider if EVZIO is right for you.
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