Help! My Patient’s on Buprenorphine: Co-managing Pharmacotherapy in Patients with Opioid Use Disorder

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Maine Chapter ACP
Sept 30, 2016

Image: drugabuse.gov (NIDA)
Disclosures

• Drs. Truncali and Nichols have no conflicts of interest in relation to this presentation.
Agenda

• Outline the neurobiology of addiction
• Describe evidence based medical treatments for opioid dependence
• Work through short answer cases that highlight clinical pearls about medical treatments of OUD
WHY MEDICALLY ASSISTED TREATMENT?
Addiction

A chronic, relapsing brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences

- National Institute on Drug Abuse
The natural history of narcotics addiction among a male sample (N=581).

Hser, Archives of Genl Psych, 2001
# Experience of Addiction

**Progression from experimentation to addiction**

<table>
<thead>
<tr>
<th>Behaviors</th>
<th>Experimentation / Controlled Use</th>
<th>Some Overuse</th>
<th>Uncontrolled Use / Addiction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Voluntary action</td>
<td>Sometimes taking when not intending, having trouble stopping or taking more than intended</td>
<td>- Impulsive action</td>
</tr>
<tr>
<td></td>
<td>- Abstinence</td>
<td></td>
<td>- Compulsive consumption</td>
</tr>
<tr>
<td></td>
<td>- Constrained drug taking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Binge or Intoxication Experience</td>
<td>Euphoria</td>
<td>Feeling good</td>
<td>Escape of dysphoria</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>Low energy</td>
<td>Anhedonia</td>
<td>Depression, anxiety, restless</td>
</tr>
<tr>
<td>Anticipation</td>
<td>Looking forward</td>
<td>Desire for drug</td>
<td>Obsession with getting drug</td>
</tr>
</tbody>
</table>

1 Modified graphic from Volkow, Koob, McLellan NEJM, 2016
Help! It’s 1980 and I can’t get out!

Partnership for a Drug-Free America

NIDA, www.drugabuse.gov
The New Millennium
Toward an understanding of the brain and drugs

3. Prefrontal cortex notes importance of the stimulus

1. Dopamine surge in NAc → Pleasure

2. Memories laid down about the experience

Adapted from NIDA
Dopamine in the Nucleus Accumbens with Survival-Related Activities

Blum et al., J Genet Syndr Gene Ther 2012
Drugs release dopamine in concentrations 2-10x that of natural rewards

Blum et al., J Genet Syndr Gene Ther 2012
1. Dysphoria—reward center less affected by dopamine

2. Triggers created due to enhanced learning that pairs environmental stimuli or emotional states with drug induced reward

3. Executive dysfunction—prioritizing drugs over natural rewards

Changes in reward circuitry with addiction

Adapted from NIDA
Neurometabolic effects of chronic cocaine use are at least partially reversible.
Addiction: Repeated drug use necessary but not sufficient

- Genes and Biology
- Repeated Drug Taking
- Environment
- Brain Changes
- Addiction

Adapted from Nora Volkow, NIDA. Addiction as a Brain Disease: What every PCP Should Know About SUDs
Treating addiction as a chronic disease

• If viewed as a chronic disease
  • Identification is done early, in primary care
  • Condition is not cured, but managed
  • When symptoms can’t be managed they may be referred
  • Relapse is reduced but not eliminated

• Ideal treatment for addiction (like DM) is multi-faceted - involves behavioral intervention, social services and medication assisted therapy (MAT)

Adapted from Tom McLellan, NIDA. Acute vs Chronic Care Models in Addiction Treatment
Medications for OUD: Overview

• Relapse after “detox” alone is extremely high\textsuperscript{1-4}

75\% of urine screens were negative for illicit drugs among those retained in treatment

BPN 16mg daily vs 6day “detox”

- 6 day bpn taper, 4/20 deaths
- 75\% of urine screens were negative for illicit drugs among those retained in treatment

1. Vaillant, Br J Addiction, 1988
Medications for OUD: Overview

• How long must treatment last?

Abstinence for 3 of the past 4wks
653 Patients with Prescription Opiate Dependence

% Successful Outcome

<table>
<thead>
<tr>
<th></th>
<th>%</th>
<th></th>
<th></th>
<th></th>
<th>%</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>WK 12 End of BUP</td>
<td>49</td>
<td></td>
<td></td>
<td></td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>WK 16 End of Taper</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>WK 24 Post Taper</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

Weiss RD et al. *Arch Gen Psychiatry*. 2011;68
Medications for OUD: Overview

• How long?

In a group of 350 methadone maintenance patients who were tapered off, 35% were opiate free at 6yrs. Of those who relapsed 35% did so after three years of sobriety.¹

¹ Stimmel, Jama, 1977
## Medications for OUD: Overview

- Maintenance treatment (MAT) reduces mortality, drug use and other negative outcomes *

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Opioid Use</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2/100p-yrs(^1), or 13x gen pop(^2))</td>
<td>RR = 0.66(^4)</td>
<td>↓HIV Risk (0.46)(^6)</td>
</tr>
<tr>
<td>RR = 0.36(^3)</td>
<td>29-&gt; 26 vs 4d use/mo(^5)</td>
<td>↓Hep C risk (0.47)(^7)</td>
</tr>
<tr>
<td></td>
<td>$ on drugs $883-&gt;$755(^5)</td>
<td>Illegal income $450-$36/mo (vs $412)(^5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Preg outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ rx retention(^8)</td>
</tr>
</tbody>
</table>

*Data for methadone. Effect of buprenorphine similar in non head to head comparisons*

1. Degenhart, Addiction, 2010 (meta analysis, obs)
2. Hulse, Addiction, 1999
3. WHO, 2009
4. Mattick, Cochrane, 2009, RCT
5. Schwartz, Arch Gen Psych, 2006
Medications for OUD: Overview

- Maintenance treatment (MAT) has mortality benefit above that of psychosocial treatment alone

<table>
<thead>
<tr>
<th></th>
<th>Mortality at 6 months OR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine (BPN)</td>
<td>1.0</td>
</tr>
<tr>
<td>Methadone (MMT)</td>
<td>0.91 (0.6-1.4)</td>
</tr>
<tr>
<td>Non-pharm treatment</td>
<td>1.75 (1.1-2.7)</td>
</tr>
<tr>
<td>No treatment</td>
<td>2.25 (1.1-4.5)</td>
</tr>
</tbody>
</table>

1. Clark, Health Affairs, 2011 (observational)
Medications for OUD: Overview Essentials

• Medication Assisted Treatment (MAT) …
  • Should continue well beyond the period of withdrawal, likely for years, and possibly lifelong
  • Is superior to psychosocial treatment alone
  • Reduces mortality, frequency of drug use and other associated outcomes
Time for a break
MEDICATIONS FOR OUD
Medications for Opioid Dependance

- Three FDA approved medication options for management of opioid use disorder

- Methadone
- Buprenorphine
- Naltrexone
Which of these medications would have the lowest risk of respiratory depression?

- Naltrexone
- Methadone
- Buprenorphine
Methadone: Pharmacology

- Full opioid agonist
- Reduced peak effects and "smoother" pharmacokinetics
Methadone Maintenance: Overview

- Federally licensed programs – methadone clinics
  - Observed administration → reduce diversion & ensure adherence
- Dosing 60-120mg/day
  - High dose 85mg+
  - Cravings versus withdrawal
- Adverse Effects:
  - sedation, respiratory depression, hypogonadism, QTc prolongation, dental decay
- Very complex pharmacokinetics
  - DDIs
  - Non linear MME conversions
Methadone Drug-Drug Interactions

• Caution with:
  • Benzodiazepines (esp. diazepam) and other sedatives
  • QT prolonging medications
    • Antiarrhythmics, antimicrobials, antiemetics, antipsychotics, citalopram…

• Metabolized mostly by 3A4 and 2B6;

• Drug Interactions with many drugs:
  • Diltiazem, verapamil, ketoconazole, erythromycin, clarithromycin, nefazodone, fluvoxamine, ritonavir…
3A4, 2B6, GABAergics... Oh my!

Methadone-Drug* Interactions
(*Medications, illicit drugs, & other substances)

Researcher/Writer:  Stewart B. Leavitt, PhD, Editor, Addiction Treatment Forum

Table 1: Drugs That Are CONTRAINDIATED with Methadone (May Precipitate Opioid Withdrawal)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Table</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimetidine</td>
<td></td>
<td>Tagamet</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td></td>
<td>Quinolone antibiotic</td>
</tr>
<tr>
<td>Fluconazole</td>
<td></td>
<td>Anti-fungal antibiotic</td>
</tr>
<tr>
<td>Grapefruit</td>
<td></td>
<td>Juice or whole fruit</td>
</tr>
</tbody>
</table>

Table 2: Drugs That May Result in Altered Metabolism or Unpredictable Interactions with Methadone

Table 3: Drugs That May LOWER SML and/or DECREASE Methadone Effects

Table 4: Drugs That May RAISE SML and/or INCREASE Methadone Effects

Table 5: CYP450 Enzyme Inhibitors

Table 6: CYP450 Enzyme Inducers

Table 7: Other Interactions

Methadone doses don’t correlate linearly with MME

Selected EDRs (Equianalgesic Dose Ratios): Morphine-to-Methadone Conversion

<table>
<thead>
<tr>
<th>Morphine Dose (mg/d)</th>
<th>30-90</th>
<th>90-300</th>
<th>300+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine:Methadone EDR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ripamonti et al., 1998</td>
<td>4:1</td>
<td>6:1</td>
<td>8:1</td>
</tr>
<tr>
<td>Mercadante et al., 2001</td>
<td>4:1</td>
<td>8:1</td>
<td>12:1</td>
</tr>
</tbody>
</table>

Morphine Dose (mg/d) | <100 | 101-300 | 301-600 | 601-800 | 801-1000 | >1001 |
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Morphine:Methadone EDR</td>
<td>3:1</td>
<td>5:1</td>
<td>10:1</td>
<td>12:1</td>
<td>15:1</td>
<td>20:1</td>
</tr>
</tbody>
</table>

Ayonrinde, 2000

Methadone’s Pharmacokinetics

- Non-linear MME
- Long $T_{1/2}$ (~30 hours)
- Very large $V_d$ (~7.5 L/kg)

**Clinical significance:**

1. Wait 7-10 days between dose increases
2. It will take about 7 days for DDIs to present themselves – *not as overt and apparent to patients due to the delay in effect*
3. Most iatrogenic methadone ODs are in patients being treated with tablets for chronic pain
Methadone Cost

• $407/month
  Waterville, Maine

• $510/month
  Bangor, Maine
Buprenorphine: Pharmacology

- Partial agonist
  - Very high affinity for mu
  - Added to a full agonist = withdrawal
  - Added to a naïve person = analgesia
  - Full agonist added to it = mixed results

- Usually w/ naloxone
  - Injection deterrent
Buprenorphine: Overview

Pros

• Prescribed in office (“X”) and dispensed at a pharmacy
• Few drug-drug interactions
• Lack of QT prolongation
• Reduced overdose risk

Cons

• Complicates management of acute pain
• Abuse potential/Street Value
  • Causes euphoria and sedation for those without tolerance
  • Often purchased to self treat opioid withdrawal
Buprenorphine and Acute Pain

- Moderate pain:
  - Split the dose 3-4x daily (16mg/day = 4mg q6h)
  - Option to add a full agonist with possibly higher doses

- Severe, or post-op pain – 2 possible options:
  1) Treat through the buprenorphine with possibly higher doses of full agonists
  2) Hold the buprenorphine and treat the acute pain (*likely need higher doses due to tolerance*) –
     - Very Risky: Monitor RR closely x72 hrs after last buprenorphine dose
     - Buprenorphine can be reintroduced after the full agonist is gone (~12-18h for short acting)

Since we can’t get a mu occupancy level...
...what’s the easy way to assess if a patient on chronic buprenorphine is free of opioids?

Buprenorphine Formulations & Doses

- Buprenorphine SL tabs (Subutex)
- Buprenorphine/naloxone SL tabs (Suboxone, Zubsolv)
- Buprenorphine/naloxone SL films (Suboxone)
- Buprenorphine/naloxone buccal films (Bunavail)
- Subcutaneous 6 month implant (Probuphine)

- Not bio-equivalent:

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Equivalent Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suboxone or generic tablets or film</td>
<td>8mg/2mg</td>
</tr>
<tr>
<td>Bunavail® buccal film</td>
<td>4.2mg/0.7mg</td>
</tr>
<tr>
<td>Zubsolv® sublingual tablet</td>
<td>5.7mg/1.4mg</td>
</tr>
</tbody>
</table>
Buprenorphine Monthly Cost
(for 16mg/day or equivalent)

• Buprenorphine SL tabs
  • Generic - $179

• Buprenorphine/naloxone SL tabs
  • Generic - $346
  • Zubsolv - $478
    • ↑ bioavail = smaller dose = smaller tab = faster dissolve time

• Buprenorphine/naloxone SL films
  • Suboxone - $478
  • Bunavail - $493
    • ↑ bioavail = smaller dose = ability to absorb via buccal mucosa

• Buprenorphine Implant
  • $825 (upfront as $4950 for 6 months)
Naltrexone Pharmacology, IM Dose and Cost

- 380mg IM injection
  - every 28 days
- $1100 per 28 days
Extended-Release Naltrexone IM Injection

- **Office Injection**
- **Pros:**
  - Zero abuse potential
  - No tolerance
  - No special provider licensing
  - No PK interactions
- **Cons:**
  - Opioid overdose potential @ trough
  - Injection site reactions
  - Pain control with opioids
  - No opioids for 7 days before initiation
Injection Site Reactions

- Gluteal injection
  - Use 2 inch needle in patients who are obese
- Reaction can be very severe
  - some require surgery
  - permanent damage
- Pain, swelling, tenderness, induration, bruising, pruritus, or redness
- FDA warning:
  - 196 reports including cellulitis, induration, hematoma, abscess, sterile abscess, necrosis
  - 16 required surgical intervention ranging from I&D to extensive surgical debridement
XR-Naltrexone: Efficacy

- **RCTs**, n=60, 8wks duration$^1$ and n=250, 6m duration$^2$
  - **Opiate free urine**: 62-90% NTX vs 25-50% placebo, but 50-56% lost to f/u
    - 50% abstinence maintained in 1yr follow up
  - **Retention**: 68% NTX vs 39% placebo
    - 62% retention in 1yr follow up
  - **Heroin craving**:
    - no differences in “wanting heroin”, but reduced “needing heroin” with NTX
    - significantly reduced over time: -10.1 in NTX vs 0.7 control
- **Overall Adverse Effects**: fatigue, injection site induration and pain
  - 1 yr follow up AEs: 21% - 6% injection site reactions and 17% mild LFT elevations
- **Role in criminal justice patients$^3,4,5$**

Which medication to use?

- Similar doses of buprenorphine and methadone are no different with regard to retention and suppression of illicit opioid use
  - Bup 8mg/day is similar to methadone 40-84mg/day
  - Bup 16–32mg/day is similar to methadone 85mg/day or greater

- In practice = patient preference and availability
  - Daily administration, cognitive effects, agonist effects, cost

- Other considerations
  - Medication interactions
  - Need for acute pain control
  - Diversion concerns
  - Provider licensing or clinic availability
  - Pregnancy

CO-MANAGING PATIENTS ON MAT: CLINICAL PEARLS
Case 1: Blue and Burning

• 26 y/o woman
• **PMH:** diabetes, anxiety, depression, and a stable OUD
• **Meds:** metformin 1000mg BID, sertraline 100mg/day, diazepam 5mg q6h prn, and methadone 90mg/day.
• Her depression is not responding to sertraline and diarrhea limits further dose increases. She is switched to fluoxetine 60mg/day.
• At the same visit, she complains of signs of a UTI and is started on ciprofloxacin.

• Which of the following medication combinations could be problematic? (select all that apply)
Case 1: Methadone and DDIs

• Which of the following medication combinations could be problematic? (select all that apply)
  A. Fluoxetine and methadone
  B. Methadone and diazepam
  C. Ciprofloxacin and methadone
  D. Fluoxetine and diazepam

Take 1-2 minutes to discuss your thoughts with your neighbor
Case 1: Answer

- Fluoxetine and methadone
  - Fluoxetine mediated 3A4 inhibition increases methadone concentrations. Interaction is not as predictable at doses of 20mg.day but becomes more significant at 40-80mg/day dosing or with other 3A4 inhibiting medications
Case 1: Answer

• Methadone and diazepam
  • Methadone is a full agonist and can cause fatal respiratory depression with monotherapy. This is magnified when GABA agonists are co-administered such as diazepam
Case 1: Answer

• Ciprofloxacin and methadone
  • Ciprofloxacin is a weak 3A4 inhibitor, but can increase levels of methadone in combination with other 3A4 inhibitors
  • Methadone causes QT prolongation at doses >40mg/day and cipro can also prolong the QT, resulting in TdP in some instances
Case 1: Answer

- **Fluoxetine and diazepam**
  - Fluoxetine mediated 3A4 inhibition increases diazepam concentrations. Interaction is not as predictable at doses of 20mg/day but becomes more significant at 40-80mg/day dosing or with other 3A4 inhibiting medications

- A, B, C, and D were all potential DDIs in this case!
Case 2: “It worked amazingly!”

- 35 y/o woman presents with worsening panic attacks
- PMH: Generalized Anxiety Disorder, Panic Disorder, OUD stable x 7yrs
- Meds/Treatments: escitalopram 20mg daily, buprenorphine/naloxone SL tabs 16mg/4mg daily, and counselling once weekly.
- Thyroid and cardiac etiologies were ruled out and propranolol was initiated. Patient re-presents with inadequate response to propranolol and asks specifically for a benzodiazepine.
- The patient’s friend gave her a Xanax to try and “it worked amazingly!” - she is requesting a prescription for this medication too.
Case 2: “It worked amazingly!”

- What of the following are you concerned about? (Select all that apply)
  A. Respiratory depression and overdose risk due to combined alprazolam and buprenorphine
  B. Increased propranolol levels due to interaction with alprazolam
  C. Anxiety may be a symptom of relapse or ongoing substance use
  D. Patient is taking a medication that is not prescribed to her

Take 1-2 minutes to discuss your thoughts with your neighbor
Case 2 Answer: Benzodiazepines and MAT

- Respiratory depression and overdose risk due to combined alprazolam and buprenorphine
- SAMHSA DAWN report\(^1\):
  - Benzodiazepines + opioid pain relievers or alcohol = 24-55% increase in risk compared with benzodiazepines alone
  - Increasing age increased predicted risk
- New FDA warning about the combination and serious risks and death

<table>
<thead>
<tr>
<th></th>
<th>Age: 12-34</th>
<th>35-44</th>
<th>45-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzo only vs.</td>
<td>NS</td>
<td>1.43</td>
<td>1.27</td>
<td>1.54</td>
</tr>
<tr>
<td>Benzo + Opioid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Case 2 Answer:
Benzodiazepines and MAT

• Increased propranolol levels due to interaction with alprazolam
  • No interaction here.
Case 2 Answer:
Benzodiazepines and MAT

• Anxiety may be a symptom of relapse or ongoing substance use
  • Ongoing ethanol, marijuana, or opioid use?
  • Withdrawal syndromes associated with the above
Case 2 Answer: 
Benzodiazepines and MAT

- Patient is taking a medication that is not prescribed to her
  - Controlled substance - felony
  - Risk of overdose
  - Risk of other DDIs, allergy, etc.
  - Need for patient education around these dangers

A, C, and D were all potential DDIs in this case!
Case 3: The Trouble with Stones

- Christa is an otherwise healthy 25 yo mother of two with OUD on buprenorphine maintenance. She used to use oxycodone, obtained primarily through prescriptions from her primary provider at the time.
- You are called by the emergency room that Christa has moderate to severe R flank pain due to a ureteral stone. They want to coordinate with you about pain management. While very uncomfortable and anxious about pain, Christa has also expressed the concern that taking an prescription opioid will trigger relapse, and that she will get ‘in trouble’ with her SUD treatment provider.
Case 3: The Trouble with Stones

In addition to reassurance to the patient and maximizing NSAIDs, you advise:

a) stop buprenorphine as it will block pain control and provide replacement with 3-5 days worth of hydrocodone

b) continue buprenorphine and recommend 3-5 days of prn hydrocodone

c) divide buprenorphine to TID and provide 3-5 days of prn hydrocodone

d) change buprenorphine to methadone 30mg daily for 3-5 days

Take 1-2 minutes to discuss your thoughts with your neighbor
Case 3: Stones / Acute Pain

Answer: C  Divide maintenance dose and add agonist pain control as needed

- Patients with OUD commonly have anxiety about untreated pain, being seen as drug seeking, and loss of addiction treatment and relapse ¹
- There is no evidence that treating acute pain with opiates increases relapse rates. Theory supports the opposite – the stressor of acute pain may increase relapse ¹

Case 3: Stones / Acute Pain, cntd

Answer: C  Divide maintenance dose and add agonist pain control as needed

• BPN appears to have incomplete blockade of pain receptors such that additional opioids can provide analgesia $^{2,3}$ with low risk of respiratory depression $^{4,5}$.
• Stopping BPN for short duration pain is riskier and more complicated than continuing it. BPN cessation leads to opiate withdrawal which creates anxiety and worsens the experience of pain $^1$
• BPN for addiction is once daily dosing but analgesic properties last 8 hours$^3$ so dividing the usual dose into TID is also recommended

Case 3: Stones / Acute Pain, cntd

Answer: C  Divide maintenance dose and add agonist pain control as needed

- Transition back to buprenorphine after use of methadone is not straightforward and may be complicated by relapse\(^6\)
- The following may limit the risk of relapse during acute pain treatment: early follow up, no phone-refills policy, enlisting help of a trusted recovery support and coordination with buprenorphine provider

Thank you

Questions?

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EXTRA SLIDES
DSM V: Substance Use Disorder

- Taking more or for longer than intended
- Spending a lot of time obtaining, using, or recovering from use
- Giving up or reducing important social, occupational, or recreational activities
- Persistent desire for or being unable to cut down
- Craving, or a strong desire to use (new)
- Failure to fulfill major role obligations at work, school, or home
- Continued use despite social or interpersonal problems related to use
- Continued use in physically hazardous situations
- Continued use despite knowledge of physical or psychological problems related to use
- Tolerance - need more to achieve same effect or less effect from a given amount*
- Withdrawal, or use to avoid withdrawal*  
  2-3= mild, 4-5=moderate, 6+ severe

*not considered met if taking medication under appropriate medical supervision
Prevalence of Drug or Alcohol Addiction

- 23 million Americans (8.9% population) needed treatment for a drug or alcohol use problem in 2013 -- likely an underestimate\(^1\)
- About 2/3 of this are due to alcohol
- 19% received treatment in 2010; half of that was self help \(^2\)

\(^1\) NSDUH, 2010
\(^2\) Nora Volkow, Quantimed, 2012
Drug Abuse or Dependence, Ages 12+

- Marijuana: 4,304
- Pain Relievers: 2,056
- Cocaine: 1,119
- Tranquilizers: 629
- Stimulants: 535
- Heroin: 467
- Hallucinogens: 331
- Inhalants: 164
- Sedatives: 135

SAMHSA. NSDUH, 2012
Overdose Deaths

Figure: Brandeis University, PDMP, accessed 2/2014
Past One Month Use in Maine Teens

Teens use when:
- Perceived harm is low
- Availability is high

<table>
<thead>
<tr>
<th>Past month use</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>28%</td>
</tr>
<tr>
<td>Marijuana</td>
<td>22%</td>
</tr>
<tr>
<td>Prescription Drugs</td>
<td>7%</td>
</tr>
</tbody>
</table>

OSA, Annual Report 2011-2012 (Data from MIYHS)
Alcohol Abuse or Dependence by Age of Initiation, Ages 12+

SAMHSA. NSDUH,
Amount of prescription painkillers sold by state per 10,000 people (2010)

Kilograms of prescription painkillers per 10,000 people

- 3.7 - 5.9
- 6.0 - 7.2
- 7.3 - 8.4
- 8.5 - 12.6

SOURCE: Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 2010
• Relapse: “recurrence of symptoms requiring medical attention”

McLellan et al, JAMA 2000,
Image: Insynergy
Acute Pain Management - Pearls

• Must make up the opioid ‘debt’
  I.e., usual methadone/BUP dose plus short acting opiate
• BUP blocks most agonists may require regional analgesics or high potency opioid (i.e., fentanyl) vs switching to full agonist until pain condition stops
• Limit prescriptions and coordinate care
Prescription Opiate Abuse

- Non medical prescription opiate use increasing in the last decade
- Rate of opiate prescribing for pain visits increased from 11% in 2000 to 20% in 2010
- The US is 4.6% of world population but consumes 80% of global opiate supply

1: Daubresse et al, Medical Care, 2013
2: Manchikanti, Pain Physician 2010
Psychosocial Treatments: Evidence

- Data on effectiveness of psychosocial treatment vary, reviews being a challenge
  - Cochrane, 2011 no effect of additional psychosocial rx for those in standard methadone mtc (MMT)
  - McLellan, 1993 – 3 levels of care added to methadone 69% of lowest level required ‘protective transfer’ vs 41 and 19% for higher
- Studies in patients not seeking treatment for drug use show benefit (potential for ‘anytime interventions’) ¹

¹ McLellan et al., JAMA 2000
Psychosocial Treatments: Evidence

- Pregnant women cocaine+ at early prenatal visit assigned to Usual care vs 1wk residential care & 2x/wk counseling ¹

- At delivery, treated vs untreated
  - Cocaine+ urine: 37 vs 63%
  - Birth wt (2934 v 2539g) and Gestation (39 v 34 wks)
  - 10 v 26% ICU care with LOS 7 vs 39 days
  - Costs 15K vs 47 K

- IV drug using pts seeking HIV testing assigned to Test or Test + 3 sessions motivational counseling ²

- At 6 months, treated vs untreated:
  - Drug injection 20 v 45%
  - Abstinence 4x more likely
  - Arrests 14 vs 24%

1: Sivkis, Drug Alc Dep, 1997
2: Booth, Drug Alc Dep, 1996
What can a generalist do?
Prescription Opiate Abuse Treatment Study (POATS)

- N=653, US patients with prescription opiate dependence, 50% had chronic pain
- Designed to assess effect of counseling but we’re looking at the effect of taper
- All received 12wks BUP and 4wks taper
- Outcome: Success vs No success
  - Success= abstinence for at least 3 of the final 4 weeks
- Results – no difference for counseling

Weiss RD et al. Arch Gen Psychiatry. 2011;68
POATS Successful Outcomes

Weiss RD et al. *Arch Gen Psychiatry.* 2011 68

<table>
<thead>
<tr>
<th></th>
<th>% Successful Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>WK 12 End of BUP</td>
<td>49</td>
</tr>
<tr>
<td>WK 16 End of Taper</td>
<td>27</td>
</tr>
<tr>
<td>WK 24 Post Taper</td>
<td>9</td>
</tr>
</tbody>
</table>
The State of Present Treatment

- Splintered, hard to navigate
- Inaccessible because of lack of coverage and availability
- Models of care not evidence based
  - Medication management often absent from treatment
  - Little quality control
- Addiction provider training is lacking
Addiction Treatment: Who is Doing It?

- Largely addiction counselors, started as peer support
- Training for addiction counseling licensure is short, largely apprenticeship model, often 12step based; EBM not part of training
- Among physicians, required addiction training is barebones
  - 2% of IM, 1.5% pediatrics and 0% family practice boards is substance abuse focused
Need for Higher Quality Treatment

“Of [the 1 in 10 people with addiction] who do receive treatment, few receive anything that approximates evidence-based care. [...] most medical professionals who should be providing addiction treatment are not sufficiently trained to diagnose or treat the disease, and most of those providing addiction care are not medical professionals and are not equipped [...] to provide the full range of effective treatments. Misunderstandings about the nature of addiction and the best ways to address it, as well as the disconnection of addiction medicine from mainstream medical practice, have undermined

National Center on Addiction and Substance Abuse
Columbia University, June 2012
MAT is under-used

<table>
<thead>
<tr>
<th>Medication</th>
<th>% addiction facilities providing medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>14%</td>
</tr>
<tr>
<td>Methadone</td>
<td>11%</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>15%</td>
</tr>
</tbody>
</table>

Methadone Maintenance: Benefits

- **all cause mortality** 0.51 per 100 person years on treatment vs 1.57 off treatment (aRR= 3.64)
- **heroin use** (RR= 0.66) - from 30 days use/month to 4
- **risk of HIV** (RR= 0.46)
- **illegal income** from $459/month to $36
- **treatment retention** (4.8x w/ 60-80mg vs <60mg)
- **function:** 26% to 60% **employment** after 12 months
- **Very cost effective** ($8,200 – $10,900 per QALY)

Methadone reduces heroin use.

Relapse to IV drug use after methadone maintenance in 105 males who left treatment

Adapted from Ball & Ross - *The Effectiveness of Methadone Maintenance Treatment, 1991* and *Diagnosis and Treatment of Opioid Dependence*, M Torrington, MD PPT

Naltrexone in Criminal Justice Patients

• Randomized trial$^2$, N=34 within one week of jail release
  - **Opioid relapse**: 38% NTX vs 88% placebo (p<0.01)
  - **Opiate free urine**: 59% NTX vs 29% placebo (p<0.01)

• Open label, randomized trial$^3$
  - N=298 criminal justice offenders in the community, 24 wks duration
    - Naltrexone versus usual treatment
    - **Time to relapse**: 10.5 wks NTX vs 5 wks (HR 0.49)
    - **Relapse rate**: 43% NTX vs 63% (OR 0.43)
    - **Opiate free urine**: 75% NLX vs 56%
    - **Overdoses**: 0% NLX vs 4.5%

Buprenorphine: Evidence

- Multicenter US RCT\(^1\), n=326
  - Buprenorphine vs placebo x 4wks
  - TIW urine testing
  - Stopped early
    - Opiate free urine: 18-21% medication vs 6% placebo, \(p<0.001\)
    - Reduced cravings, \(p<0.001\)
- Meta-analysis\(^2\) of 31 trials with 5430 people
  - Retention in treatment: doses 2-16mg/day (RR= 1.5, 1.74, & 1.82)
  - Doses 16mg/day suppressed heroin use