Use of Suboxone and Other Treatment Modalities: Myths, Facts & Tips for Better Outcomes

MPHP Prescribers Summit 2018
Gulfport, MS
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Mississippi Physician Health Program
No Disclosures

• Todays speaker has no disclosure of real or apparent conflict related to the content of this presentation.
1. Discuss factors which have contributed to the U.S. prescription drug crisis.
2. Describe medication assisted treatment and other treatment modalities.
3. Describe buprenorphine for opioid replacement therapy.
Opioid Epidemic: Economic Impact

- 2015: $504 billion; 2.8% GDP
- “Previous studies and estimates fail to fully account for the lives lost to overdose.”

The Underestimated Cost of the Opioid Crisis

The Council of Economic Advisers
November 2017

(https://www.whitehouse.gov/)
The Comprehensive Addiction & Recovery Act (CARA)

- Passed on March 11, 2016
- First major legislation since the Controlled Substances Act of 1970
- Expand education and prevention
- Make naloxone available to first responders
- Provide resources to treat incarcerated individuals
Opioid Trends: 2010-2016

Dispensed Opioid Prescriptions in Millions
12.4% Decline

Current Prescription Opioid Misusers in Millions
35% Decline

Current Heroin Users in Thousands
99% Increase

© www.MSPHP.com
What is Driving the Increase in Heroin Use & Deaths?

• “A key factor is… low cost and high purity of heroin.”
• Cost of one gram:
  ▪ 1982: $2,690
  ▪ 2012: $465
Fentanyl: Game Changer

- 20,000 deaths in 2016
  - 540% increase in 3 years
- 50X potency heroin
- 100X potency morphine
- Carfentanil = 10,000X potency morphine

Drugs Involved in U.S. Overdose Deaths, 2000 to 2016

- Synthetic Opioids other than Methadone, 20,145
- Heroin, 15,446
- Natural and semi-synthetic opioids, 14,427
- Cocaine, 10,619
- Methamphetamine, 7,663
- Methadone, 3,314

Adverse Selection: Opioid Use

- Patients with mental health and substance abuse co-morbidities are more likely to receive chronic opioid therapy than patients who lack these risk factors.

  (Sullivan, *Pain*, 2010)
Addiction: Primary, Chronic Brain Disease

• “Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.”

(ASAM Public Policy Statement, 2011)
Screening: General Tips

- Identify high risk patients
- Eliminate harmful/ineffective therapy
- Avoid controlled substances for chronic conditions
  - Opioids
  - Benzodiazepines

(CDC Guidelines, 2016)
Screening for SUD: Single Question

- “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons, or for the way it made you feel?”
- 100% sensitive
- 73.5% Specific

(Smith PC, et al., 2010)
Use PDMP to Identify:

- MME/day
- “Doctor shoppers”: treatment first, if possible
- Dangerous combinations
- Those at highest risk of overdose

https://mississippi.pmpaware.net/login
Log in page
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**I agree to the terms of the acknowledgement.**

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* Pharmacy is created using a combination of pharmacy name and the last four digits of the pharmacy license number.

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- **5 different prescribers in 3 months**
- **3 months**
- **Date filled**
- **Prescriber(s)**
- **MME/day**
Urine Drug Testing (UDT): Negative Results

• Negative test does NOT:
  ➢ R/O substance use
  ➢ R/O out SUD

• Negative test DOES mean:
  ➢ Targeted substance has not been used in detection window
  ➢ Possible use below cut off level

(ASAM Consensus Document, 2017)
Point of Service UDT

- 12 panel + Temperature
- Cost: $2.50 per cup
Abbreviations

- OTP = opioid treatment program
- ORT = opioid replacement therapy
- MAT = medication assisted treatment
MAT: Medication Assisted Treatment

• FDA approved medications for:
  ➢ Tobacco Use Disorder:
    OTC nicotine replacement formulations; Varenicline; Bupropion.
  ➢ Alcohol Use Disorder:
    Acamprosate, Naltrexone; Disulfuram.
  ➢ Opioid Use Disorder:
    buprenorphine; methadone; Naltrexone.

(https://www.samhsa.gov/medication-assisted-treatment)
Meds for Opioid Withdrawal

- **Clonidine**
  - PO or transdermal
  - 0.1–0.3mg every 6–8 hours
  - Maximum dose of 1.2mg/day
- **Benzodiazepines for anxiety (inpatient)**
- **Loperamide for diarrhea**
- **Acetaminophen/NSAIDS for pain**
- **Ondansetron or other agents for nausea**

(ASAM National Practice Guideline, 2015)
Naloxone (Narcan)

- Opioid receptor antagonist
- Temporarily reverses an opioid overdose
- Effects last 30-60 minutes
- Many formulations;
  - Injectable 1mg/mL ($)
  - Narcan Nasal Spray ($$)
  - Evzio 2mg auto-injector ($$$)
- Indicated for: h/o OD, SUD, >50MME, or concurrent BZOs

(CDC Guidelines, 2016)
## Naltrexone versus Naloxone

<table>
<thead>
<tr>
<th>Naloxone:</th>
<th>Naltrexone:</th>
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<tbody>
<tr>
<td><strong>IV/IM/intranasal</strong></td>
<td><strong>PO/IM</strong></td>
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<tr>
<td><strong>Onset: IV = 1-2 minutes</strong></td>
<td><strong>Onset: 30-60 minutes</strong></td>
</tr>
<tr>
<td><strong>Duration: 30-60 minutes</strong></td>
<td><strong>Duration:</strong></td>
</tr>
<tr>
<td><strong>Uses:</strong></td>
<td>✓ Oral: 24-48 hrs</td>
</tr>
<tr>
<td>✓ Emergent OD reversal</td>
<td>✓ IM: 30 days</td>
</tr>
<tr>
<td>✓ Buprenorphine preps.</td>
<td><strong>Uses:</strong></td>
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<tr>
<td></td>
<td>Addiction(opioids/EtOH)</td>
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</tbody>
</table>

(SAMHSA)
Naltrexone

- To treat alcohol/opioid addiction
- Blocks effects of opioids
- Lasts:
  - 1-2 days (PO)
  - 30 days (IM)
- Formulations:
  - Vivitrol (360mg IM)
  - Revia (50 mg PO)

(SAMHSA)
Effectiveness of MAT

- The CDC Guideline for Prescribing Opioids for Chronic Pain (March 2016): [https://www.cdc.gov/drugoverdose/prescribing/guideline.html](https://www.cdc.gov/drugoverdose/prescribing/guideline.html)
Drug Addiction Treatment Act of 2000
Qualified physicians may prescribe/dispense FDA approved Schedule III, IV, and V opioid medications for the treatment of opioid addiction
- Methadone is Schedule II
- Buprenorphine is Schedule III
(SAMHSA)
Physician & Program Data

Total: 47312
275 Patient Certified
8.4%

30 Patient Certified
72.3%

9,129
19.3%

34,191
100 Patient Certified

Mississippi Physicians with DATA 2000 Waiver: 184

(https://www.samhsa.gov/)
Buprenorphine Waiver

- Multiple online courses
• Opioid binding sites (green)

• Reward Pathway (orange)
Buprenorphine Pharmacology

• Semisynthetic, partial \( \mu \)-opioid agonist
• Partial agonists activate receptors, but not to the same degree as full agonists.
  ➢ less euphoria
  ➢ less respiratory depression
  ➢ less sedation
• \( k \)-receptor antagonist (blocks dysphoria)
  (ASAM National Practice Guideline, 2015)
Buprenorphine Ceiling Effect

Full agonist (methadone)

Partial agonist (buprenorphine)

Antagonist (naloxone)

(SAMHSA, TIP 40)

*Conceptual representation only, not to be used for dosing purposes.
Buprenorphine Pharmacology

- Metabolized by the liver via cytochrome P450
- Slow rate of dissociation from mu opioid receptor
  - Long duration of action
  - Half-life of 24–60 hours (mean 37)
  - Prolonged suppression of opioid withdrawal
- Short duration of analgesia
- Maximal effects at ≤ 24mg (Suboxone)
  (ASAM National Practice Guideline, 2015)
Precipitated Opioid Withdrawal

- Highest affinity of μ-opioid receptor of any opioid
- Occurs with buprenorphine induction prior to onset of mild to moderate opioid withdrawal
- Occurs with naltrexone/naloxone administration during opioid intoxication
- Induction:
  - Short acting opioids: 12-24 hours
  - Long acting opioids: 36-72 hours

(ASAM National Practice Guideline, 2015)
## Buprenorphine Formulations: Treatment of Opioid Use Disorder

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Recommended maintenance dosage</th>
<th>Cost*</th>
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<td><strong>Monotherapy</strong></td>
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</table>
| Buprenorphine (generic)       | 2- and 8-mg sublingual tablets           | Target: 16 mg per day  
Range: 4 to 24 mg per day | $99 for 60 8-mg tablets |
| Probuphine                    | 74.2-mg subdermal implants               | 4 implants for 6 months                            | $863                |
| **Combination medications**   |                                          |                                                     |                     |
| Bunavail                      | 2.1/0.3-, 4.2/0.7-, and 6.3/1-mg buccal films | Target: 8.4/1.4 mg per day  
Range: 2.1/0.3 to 12.6/2.1 mg per day | $486 for 60 4.2/0.7-mg films |
| Buprenorphine/naloxone (generic) | 2/0.5- and 8/2-mg sublingual tablets    | Target: 16/4 mg per day  
Range: 4/1 to 24/6 mg per day | $205 for 60 8/2-mg tablets |
| Suboxone film                 | 2/0.5-, 4/1-, 8/2-, and 12/3-mg sublingual films | Target: 16/4 mg per day  
Range: 4/1 to 24/6 mg per day | $468 for 60 8/2-mg films |
| Zubsolv                       | 1.4/0.36-, 5.7/1.4-, 8.6/2.1-, and 11.4/2.9-mg sublingual tablets  | Target: 11.4/2.9 mg per day  
Range: 2.9/0.71 to 17.2/4.2 mg per day | $494 for 30 11.4/2.9-mg tablets |

“Maintaining short-term opioid abstinence with extended-release naltrexone should be considered an equal treatment alternative to buprenorphine-naloxone as medication-assisted treatment for opioid-dependent individuals.”
MAT: Considerations for Acute Pain

- Buprenorphine:
  - Acute pain: NSAIDS (ketorolac)
  - Moderate pain: divided doses or extra doses of bupe
  - Elective surgery: d/c 24-36 hours before
  - Severe acute pain: high potency opioids/regional anesthesia

- Naltrexone:
  - IM: d/c 30 days before elective surgery
  - PO: d/c 72 hours before elective surgery

(ASAM National Practice Guideline, 2015)
“Replacing One Drug for Another”

• Would you say the same thing about nicotine patches compared to smoking?
Diversion Strategies

- Frequent office visits (weekly in early treatment)
- Urine drug testing
- Recall visits for pill counts
- Use of PDMP
- Limiting use of Subutex (monotherapy):
  - Lactating or pregnant females
  - Naloxone allergies
    (ASAM National Practice Guideline, 2015)
Patient Characteristics Associated with Successful MAT

- Substance-free, safe home environment
- Stable or controlled medical or psychiatric comorbidities
- Sporadic opioid use is not uncommon in the first few months

(ASAM National Practice Guideline, 2015)
Treatment Resources

- www.asam.org
- www.addictionguide.com
- www.drugabuse.gov/publications寻求drug-abuse-treatment-know-what-to-ask/introduction
• Thank You!!!
References:

References:


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