Behavioral Health is Essential To Health

Prevention Works

Treatment is Effective

People Recover
Serious Mental Illness and Opioid Use Disorder
Serious Mental Illness and Opioid Use Disorders

Arthur Robin Williams, MD MBE
Columbia University, Department of Psychiatry

Nick Szubiak, MSW, LCSW
Director, Clinical Excellence in Addictions
National Council for Behavioral Health
Teaching Points

- Over half of patients with SMI (bipolar disorder, schizophrenia) have a co-occurring SUD
- Care outcomes respond best to comprehensive treatment with culturally competent practices
- However treatment programs are often bifurcated between treating mental illness OR substance use
- Like all individuals with an opioid use disorder (OUD), those with SMI benefit from MAT
Dually Diagnosed Care

• Individualized treatment should be the goal:

“Co-occurring disorders are not a single entity with a single best practice intervention.”

- Minkoff et al 2014
Diagnosis

• Can be hard to attribute psychosis, mood, and anxiety symptoms during active use
• Collateral history is key
• Be open to re-evaluating diagnosis and treatment planning
Help the patient explore:

- How are your substance use problems and mental health problems defined by your parents? Peers? Other patients?
- What do they think you should be doing to remedy these problems?
- How do you decide which suggestions to follow?
- In what kinds of treatment settings do you feel most comfortable?
- What do you think I (the clinician) should be doing to help you improve your situation?

- CSAT TIP #42
Diagnosis of Substance Use Disorder

- DSM-5 released May 2013
- “Substance Use Disorder” terminology
- 11 diagnostic criteria over 12-months:
  - Mild: 2-3 symptoms
  - Moderate: 4-5 symptoms
  - Severe: 6 or more symptoms
11 Symptoms of SUDs

- Excessive amounts used
  - Excessive time spent using/obtaining

- Craving or urges to use
  - Unsuccessful attempts to cut down

- Tolerance
  - Withdrawal

- Hazardous use despite
  - Health problems
  - Missed obligations
    - Interference with activities
  - Personal problems
Symptoms Among SMI Patients

- Cravings expressed as other symptoms
- Excessive amounts used
  - Excessive time spent using/obtaining
- Craving or urges to use
  - Unsuccessful attempts to cut down
- Tolerance
- Withdrawal
- Hazardous use despite
  - Health problems
  - Missed obligations
    - Interference with activities
  - Personal problems

11 Symptoms of SUDs

- Excessive amounts used
  - Excessive time spent using/obtaining

- Craving or urges to use
  - Unsuccessful attempts to cut down

- Tolerance
  - Withdrawal

- Hazardous use despite
  - Health problems
  - Missed obligations
    - Interference with activities
  - Personal problems

Drug use interfering with response to medications

11 Symptoms of SUDs

- Excessive amounts used
  - Excessive time spent using/obtaining

- Craving or urges to use
  - Unsuccessful attempts to cut down

- Tolerance
  - Withdrawal

- Hazardous use despite
  - Health problems
  - Missed obligations
    - Interference with activities
  - Personal problems

Use that interferes with treatment adherence

The FDA has approved medications for:

- Alcohol: Antabuse, naltrexone, acamprosate
- Nicotine: NRT, bupropion, varenicline
- Opioids: methadone, buprenorphine, extended-release injectable naltrexone (XR-naltrexone)
Opioid Use Disorder Neurochemistry

- Opioids activate opioid receptors in the brain
- Without opioids, unstable receptors lead to:
  - Withdrawal symptoms
  - Intense cravings
- Receptors are stabilized with MAT medications
- Patients on MAT:
  - Experience fewer and less intense cravings
  - Use drugs at much lower rates
• “Opioids” include synthetic pain pills and heroin in addition to opiates
• “Opiates” are naturally occurring opioids like opium and morphine
• Unlike other addictive drugs, opioids carry greater risks, such as overdose death
• Injection drug use adds risks such as infectious disease (HIV, Hepatitis C) and injuries
Background: MAT for OUD

- MAT is an effective response to OUD treatment:
  - Reduces drug use
  - Protects against overdoses
  - Prevents injection behaviors
  - Reduces criminal behavior
  - Increases treatment retention

• MAT includes 3 pharmacotherapies:
  ✓ **Methadone** (schedule II)
  ✓ **Buprenorphine** (schedule III)
  ✓ **Naltrexone** (not controlled)

• Each pharmacotherapy should be provided in addition to psychosocial services and behavioral therapy

• Patients may require pharmacotherapy for OUD for extended periods, sometimes years. The duration of therapy, when, and how to taper medications should be individualized based on the needs and function of the patient.
Background: MAT for OUD

- Each MAT pharmacotherapy requires a different induction process for stabilizing the patient
- Each modality has different logistical and financial requirements
- Each modality has different pros and cons
- Patients may respond better to one modality
- As a result, all three should be available to every patient
- SAMHSA has an online decision support tool, “Decisions in Recovery”, available at this link: http://archive.samhsa.gov/MAT-Decisions-in-Recovery/

Longer Retention = Better Outcomes
Co-occurring Treatment

• Effective treatment requires:
  ✓ Integrated approach
  ✓ Stage based care
  ✓ Attention to both disorders
Methadone

- Provided only at SAMHSA certified opioid treatment programs that initially require daily attendance
- Methadone fully activates the opioid receptor but lasts for 24 hours, smoothing out highs and lows
- Methadone, at appropriate dosing, relieves withdrawal and prevents euphoria
- Doses >60mg increase retention. Typically effective doses range between 80 and 120 mg.

CSAT TIP #43
Methadone: Pros and Cons

• Pros
  ✓ Induction from active use
  ✓ Lower medication costs but program fees vary
  ✓ Best medication for retaining patients in treatment at 12 months (~80%)
  ✓ Lowers drug use and criminal activity
  ✓ Decrease in all cause mortality and HIV seroconversion
  ✓ Treatment option for pregnant women

Friedman et al 1994; Lund et al 2013
Methadone: Pros and Cons

• Cons
  ✓ Requires daily dosing on site initially
  ✓ Many states and rural areas have limited access
  ✓ Can cause medical complications (drug/drug interactions for patients with serious mental illness)
  ✓ Patients can intentionally space out doses and use opioids in between
  ✓ Has street value and can be sold or diverted
  ✓ Patients face more stigma
Buprenorphine (approved 2002)

- Used since 1970s for pain
- Developed for addiction treatment more recently
- DATA 2000 Act allows buprenorphine to be provided by prescription opposed to only directly administered or dispensed by a program
- Physicians must complete 8-hour training and get “waivered” with a DEA “X number” to prescribe
- CARA Act now also allows NPs/PAs to train and prescribe
- Can be prescribed with multiple refills
- Often sold as a combo product with naloxone to deter misuse
Buprenorphine: Pros and Cons

- **Pros**
  - Greatly reduces overdose risk
  - Reduces cravings
  - Flexible dosing
  - Providers are relatively easier to find
  - Safe and effective for pregnancy, newborn outcomes
Buprenorphine: Pros and Cons

- **Cons**
  - Patients must be in mild withdrawal to take first dose
    - Can precipitate withdrawal if taken too soon
    - As a result, some patients struggle to start
  - Physicians need DEA waiver, few prescribe it
  - Similar to methadone, buprenorphine has street value and can be sold/diverted
  - Patients can intentionally space out doses and use opioids in between
  - Some people inject it (despite naloxone)
Buprenorphine: Monitoring

• Recommended practice is to check prescription drug monitoring programs (PMP/PDMP) if available
• Routine urine testing
  ✓ Urine positive for buprenorphine (if negative, suggests diversion)
  ✓ Urine should be negative for opioids and benzodiazepines
• Monitor for:
  ✓ “Losing” prescriptions and/or running out early
    ▪ May need dose increase
    ▪ Prescribe for shorter intervals, can observe ingestion
  ✓ Requesting dose > 16-24mg (may suggest diversion)
    ▪ Use in-office medication counts
Naltrexone (1984, 2010)

- Naltrexone binds tightly to opioid receptors, pushing off all other opioids (whether used before or after)
- Available as a daily pill or as a monthly injection, “the blocker shot,” called xr-naltrexone
- May reduce cravings for patients who maintain treatment due to activity at opioid receptor
- Does not cause physical dependence and patients lose their opioid tolerance while taking
  - May increase overdose risk if return to active use
XR-Naltrexone (Vivitrol is brand)

Monthly injection is an extended release form of naltrexone, enhancing outcomes

Krupitsky, et al.
Naltrexone: Oral vs. Injection

- Retention in treatment is used as a primary outcome of treatment with naltrexone
- Great majority of patients on XR-naltrexone remain abstinent
- Retention rate in groups treated with injection preparations is twice that of the oral pill group, approximating 50-70% at 6 months

(Sullivan et al., 2015)
XR-Naltrexone: Pros and Cons

- Pros
  - Naltrexone does not cause withdrawal when patients stop taking it
  - Blocks opioid effects
    - ~50% of patients “test” the blockade initially and quickly extinguish use
    - This effect wanes after ~3 weeks
  - Injection has 2x retention as oral treatment
  - Patients often face less stigma
XR-Naltrexone: Pros and Cons

- **Cons**
  - Most difficult induction, requires ~7-10 days of abstinence: Patients must fully detox to start, often drop out
    - Risk of severe precipitated withdrawal that may require hospitalization if administered too early
  - As with other pharmacotherapies, hard to find providers and some insurers don’t reimburse (costs $1,500/mo)
  - If patients stop medication they could overdose if/when returning to use due to loss of tolerance
  - Blocks the effects of opioid analgesia, therefore contraindicated among patients who require opioids
XR-Naltrexone: Monitoring

- Least likelihood of misuse/diversion (no misuse potential)
- Injection is directly administered by clinician
- Frequent urine testing remains vital to treatment
- Patients with protracted withdrawal may require additional treatment
  - Insomnia common for 1-2 months
  - Anxiety and gastrointestinal distress also common
XR-Naltrexone: Induction

- Vivitrol induction
  - Patient selection
    - Indications and Contraindications
  - Induction procedures
    - Systems design, pre-medicate, side effects
  - Anticipatory guidance
- Logistical challenges
• Often protracted withdrawal affects insomnia and anxiety
  ✓ Treat aggressively with comfort medications
  ✓ Schedule frequent follow up visits
• Monitor for patients “testing the blockade”
• Also monitor for new and unprecedented drug use or activity
• Monitor for emergence of new symptoms
XR-Naltrexone: Indications for Use

• Patients unable/unwilling to attempt agonist maintenance
• Prevent relapse after agonist treatment
• Less addiction severity/brief history
  ✓ Consider additional drug and alcohol involvement
• Already fully detoxified (i.e. post release/discharge)
• Higher level of resources and coping skills
• Patients in monitoring programs (i.e. clinicians or pilots who have already completed agonist tapers)
XR-Naltrexone: Contraindications

- Patients with chronic or severe pain requiring opioids
  ✓ Patients with SMI may report pain differently
- Patients with frequent relapse or overdose history
- Patients with unstable mood, anxiety disorders
- Patients with poorer coping skills and mood reactivity
  ✓ Always consider comorbid mental illness
XR-Naltrexone: Resources

- Providers’ Clinical Support System (PCSS)
  - PCSS-O: [http://pcss-o.org/](http://pcss-o.org/)

- SAMHSA
  - [http://www.samhsa.gov/medication-assisted-treatment/treatment/naltrexone](http://www.samhsa.gov/medication-assisted-treatment/treatment/naltrexone)
  - Brief Guide: Clinical Use of Extended-Release Injectable Naltrexone in the Treatment of Opioid Use Disorder
Duration of Treatment

- The duration of therapy, when, and how to taper medications should be individualized based on the needs and function of the patient.

Longer retention = Better outcomes
Clinical considerations before tapering:
- Treatment history (i.e. prior relapse after taper)
- Addiction history (length/severity)
- Family history
- Resilience and personality traits
- Life stressors, loss, and transitions
- Patient motivations for tapering

-Alford et al., 2011; Stimmel et al., 1977
Long-term Recovery

Can you be in recovery while on medications?
Can you be in recovery while on medications?

YES!
Long-term Recovery

Can you be in recovery while on medications?

YES!

ASAM, AAAP, NIDA, SAMHSA, FDA, CDC, AMA, ONDCP...
Recovery

- SAMHSA: “A process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential.”

http://store.samhsa.gov/shin/content/PEP12-RECDEF/PEP12-RECDEF.pdf
Recovery

- ASAM: “In most cases of addiction, the integration of psychosocial rehabilitation and ongoing care with evidence-based pharmacological therapy provides the best results. Chronic disease management is important for minimization of episodes of relapse and their impact.”
Recovery

- NIDA: “Recovery from drug addiction is a long-term process and frequently requires multiple episodes of treatment. As with other chronic illnesses, relapse to drug abuse can occur and should signal a need for treatment to be reinstated or adjusted. Because individuals often leave treatment prematurely, programs should include strategies to engage and keep patients in treatment.”
Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program


Objective: The primary aim of this study was to compare the impact of NAVIGATE, a comprehensive, multidisciplinary, team-based treatment approach for first-episode psychosis designed for implementation in the U.S. health care system, with community care on quality of life.

Method: Thirty-four clinics in 21 states were randomly assigned to NAVIGATE or community care. Diagnosis, duration of untreated psychosis, and clinical outcomes were assessed via live, two-way video by remote, centralized raters masked to study design and treatment. Participants (mean age, 23) with schizophrenia and related disorders and ≤6 months of antipsychotic treatment (N=404) were enrolled and followed for ≥2 years. The primary outcome was the total score of the Heinrichs-Carpenter Quality of Life Scale, a measure that includes sense of purpose, motivation, emotional and social interactions, role functioning, and engagement in regular activities.

Results: The 223 recipients of NAVIGATE remained in treatment longer, experienced greater improvement in quality of life and psychopathology, and experienced greater involvement in work and school compared with 181 participants in community care. The median duration of untreated psychosis was 74 weeks. NAVIGATE participants with duration of untreated psychosis of <74 weeks had greater improvement in quality of life and psychopathology compared with those with longer duration of untreated psychosis and those in community care. Rates of hospitalization were relatively low compared with other first-episode psychosis clinical trials and did not differ between groups.

Conclusions: Comprehensive care for first-episode psychosis can be implemented in U.S. community clinics and improves functional and clinical outcomes. Effects are more pronounced for those with shorter duration of untreated psychosis.

AJP in Advance (doi: 10.1176/appi.ajp.2015.15050632)
Symptomatic and functional outcomes of substance use disorder persistence 2 years after admission to a first-episode psychosis program
Examples of drug drug interactions (SAMHSA 2016)

Exhibit 4. Potential Interactions Between Buprenorphine and Other Drug Classes

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Potential Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td>Some reports of coma and death associated with misuse of the combination of buprenorphine (particularly via injection) and benzodiazepines. Decreased ceiling effects on buprenorphine-induced respiratory depression, making the respiratory effects similar to those of full mu opioid agonists. Dose reduction of the benzodiazepine, of buprenorphine, or both may be necessary. Patients should be warned to use these medications only as directed.</td>
</tr>
<tr>
<td>Other central nervous system depressants (e.g., sedatives, hypnotics, general anesthetics, tranquilizers, other opioids, alcohol)</td>
<td>Increased risk of respiratory depression, profound sedation, hypotension, coma, and death.</td>
</tr>
<tr>
<td>CYP3A4 inducers (e.g., phenobarbital, carbamazepine, phenytoin, rifampicin)</td>
<td>May cause increased clearance of buprenorphine, which could lead to decreased plasma concentrations, lack of efficacy, or possibly abstinence syndrome.</td>
</tr>
<tr>
<td>CYP3A4 inhibitors (e.g., azole antifungals such as ketoconazole; macrolide antibiotics such as erythromycin; HIV protease inhibitors; antidepressants such as fluoxetine, fluvoxamine, amitriptyline)</td>
<td>May cause decreased clearance of buprenorphine, leading to increased buprenorphine plasma concentrations and resulting in increased or prolonged opioid effects. Patients should be monitored for respiratory depression and sedation. Dose reduction of either medication may be necessary.</td>
</tr>
</tbody>
</table>
Insight Across Diagnoses

- Insight and denial used differentially (*PubAtlas, 2014)
  - “Lack of Insight” term used in psychosis
  - “Denial” term used in addiction
  - Stigmatized diagnoses more associated with denial
  - Implications for systems of care

<table>
<thead>
<tr>
<th></th>
<th>Schizophrenia (N=103,512)</th>
<th>Bipolar Disorder (33,504)</th>
<th>Addiction or SUDs (40,867)</th>
<th>Eating Disorders (15,183)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denial [MeSH] (2,380)</td>
<td>61</td>
<td>24</td>
<td>38</td>
<td>16</td>
</tr>
<tr>
<td>“Lack of Insight” or “Impaired Insight” (454)</td>
<td>199</td>
<td>35</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Ratio of Denial:Insight</td>
<td>0.31</td>
<td>0.69</td>
<td>3.45</td>
<td>3.2</td>
</tr>
</tbody>
</table>
Cultural Stigma

• Providers also need to be attuned to potential disparities in access.
• Recently, when we provided a grant to engage communities of color around their preferences for and experiences with substance use treatment, we discovered fears of discrimination.
• Communities expressed concern that disclosing substance use or enrolling in treatment could impact their ability to receive other needed supports, like housing or food subsidies.
• They also cautioned against treating addiction without also developing better prevention strategies that could halt substance use from occurring in the first place.

Methadone and Buprenorphine: Disparities

Methadone Patients* and BUP Patient Study
Sample: Demographic Differences

- Methadone Admissions to TEDS Sites
- BUP Patient Study (N=433)

Percent of Patients Treated

<table>
<thead>
<tr>
<th>Category</th>
<th>Methadone</th>
<th>BUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>35%</td>
<td>42%</td>
</tr>
<tr>
<td>White</td>
<td>53%</td>
<td>91%</td>
</tr>
<tr>
<td>Employed</td>
<td>29%</td>
<td>58%</td>
</tr>
<tr>
<td>Some Post-Secondary Education</td>
<td>19%</td>
<td>56%</td>
</tr>
</tbody>
</table>

* TEDS varies in its coverage of admissions by state. In some states, admissions to private facilities are underrepresented.

SAMHSA/OSAT's Evaluation of the Buprenorphine Waiver Program 2002-2005
Further Reading

• SAMHSA Report to Congress on Co-occurring Disorders

• CSAT TIP #42 on Persons with Co-occurring disorders

• CSAT TIP #43: Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs
This webinar/paper/report/product/etc. was developed [in part] under contract number HHSS283201200021I/HHS28342003T from the Substance Abuse and Mental Health Services Administration (SAMHSA), U.S. Department of Health and Human Services (HHS). The views, policies and opinions expressed are those of the authors and do not necessarily reflect those of SAMHSA or HHS.