

Managing Common Psychiatric Conditions in Patients with Substance Use Disorders

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John A. Renner Disclosures

- John A. Renner, Jr., M.D. has no financial relationships to disclose

The contents of this activity may include discussion of off label or investigative drug uses. The faculty is aware that is their responsibility to disclose this information.

Target Audience

- The overarching goal of PCSS is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.

Educational Objectives

- At the conclusion of this activity participants should be able to:
 - Identify the most common psychiatric disorders seen in individuals with substance use disorders
 - Discuss the impact of co-occurring psychiatric conditions on the course of substance use disorders
 - Describe procedures for screening individuals with substance use disorders for common psychiatric disorders
 - Explain the management of substance use disorders and co-occurring psychiatric disorders in the primary care setting

Outline

- **Case presentation**
- The epidemiology of alcohol/drug disorders and other common psychiatric disorders
- Screening for suicidal and homicidal risk
- Substance-induced vs. independent psychiatric disorders
- Screening for common psychiatric disorders
- Management of common co-occurring conditions:
 - Depression
 - Anxiety Disorders including PTSD
 - Bipolar Disorder
 - ADHD
- Treatment recommendations and the importance of integrated care

Case: Anna is a 25 yo Army veteran who overdosed on heroin

- Anna returned from Iraq 20 months ago.
- Her boyfriend brought her to the emergency room after she overdosed on heroin. She was breathing but unconscious.
- How should she be managed?
- What are your questions?



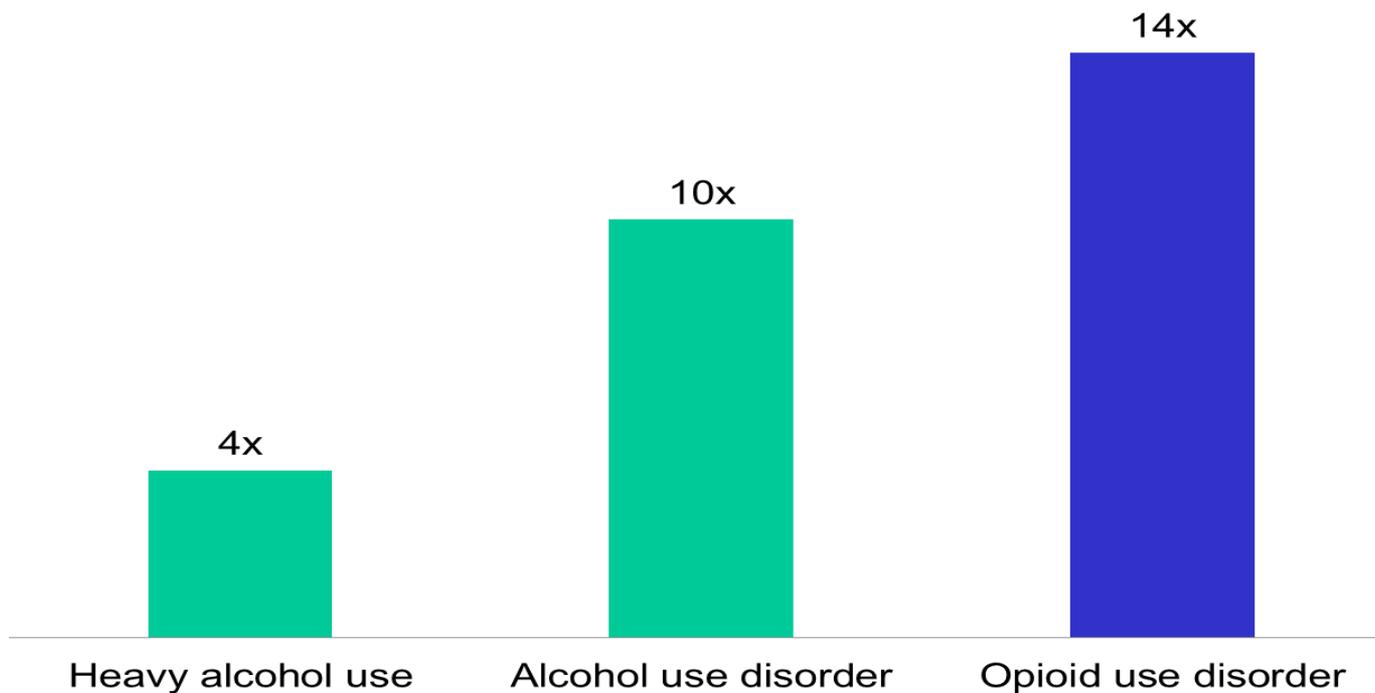
Case: Anna 25 yo Veteran

- Anna was successfully revived after multiple doses of naloxone (narcan). History reveals opioid treatment for combat injuries. She now snorts heroin on a daily basis; her boyfriend thinks she may have gotten some heroin laced with fentanyl.
- How likely is this a suicide attempt? Or an accident?
- What diagnoses should be considered?
- What is your initial treatment plan?

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Risk of Completed Suicide Higher Among Patients with Substance Use Disorder



Prescription Opioid Deaths and Suicide

- Sixty-five percent of 184,136 calls to Poison Control Centers (2006-2013) for any prescription opioid misuse documented suicide intent
 - 75% of prescription opioid deaths were suicide
 - 86% of prescription opioid deaths age 60+ were suicides

Case: Anna 25 yo Veteran

Treatment issues:

- Suicide assessment
- Motivation for treatment
- Prior substance use history; medical history, **psychiatric history**
- Pain – requirements for ongoing care?
- Depression?
- PTSD?

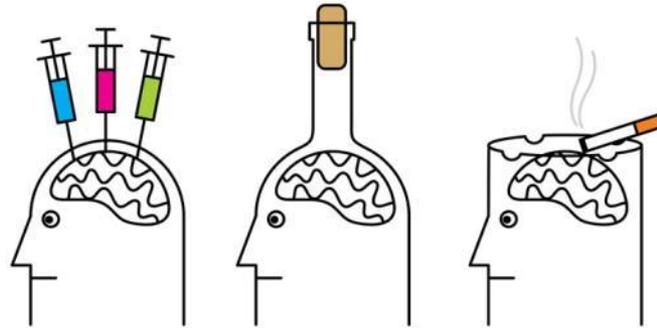
Odds Ratios for Alcohol Use Disorders and other Psychiatric Disorders

DSM-IV DISORDER	12 MONTH O.R.	LIFETIME O.R.
Drug Use Disorder	9.0	10.4
Drug Abuse	6.4	7.5
Drug Dependence	15.0	15.9
Nicotine Dependence	3.5	4.9
Any Mood Disorder	2.2	2.4
Bipolar I	2.7	3.5
Bipolar II	2.1	2.6
Any Anxiety Disorder	1.9	2.3
Panic with Agoraphobia	2.7	2.5
Panic without Agoraphobia	2.1	2.3
GAD	2.1	2.2
Antisocial Personality Disorder	2.9	6.5

Odds Ratios for Drug Use Disorders and other Psychiatric Disorders

DSM-IV DISORDER	12 MONTH O.R.	LIFETIME O.R.
Alcohol Use Disorder	9.0	10.4
Alcohol Abuse	2.7	1.9
Alcohol Dependence	9.7	7.6
Nicotine Dependence	5.8	5.5
Any Mood Disorder	3.5	3.2
Bipolar I	5.1	4.8
Bipolar II	2.4	2.4
Any Anxiety Disorder	2.7	2.6
Panic with Agoraphobia	5.8	4.5
Panic with out Agoraphobia	3.1	2.9
GAD	4.5	2.8
Antisocial Personality Disorder	6.4	7.8

Lifetime Prevalence in Bipolar I Patients



- Any alcohol use disorder 58.0%
- Any drug use disorder 37.5%
- Nicotine use disorder 44.4%

No differences noted between men and women

The most common co-occurring psychiatric disorders in substance use disorder patients

- Alcohol use disorder or another drug disorder
- Nicotine use disorder
- Bipolar I disorder
- Mood disorders
- Panic with agoraphobia
- Antisocial personality disorder

What about PTSD and SUD?

- 34% of PTSD co-occurs with SUD
- 5-12 x more PTSD in women who misuse drugs
- Suicide attempts in 20% of patients with PTSD; risk is double in PTSD + SUD
- US Iraq veterans – 50% binge alcohol & tobacco use

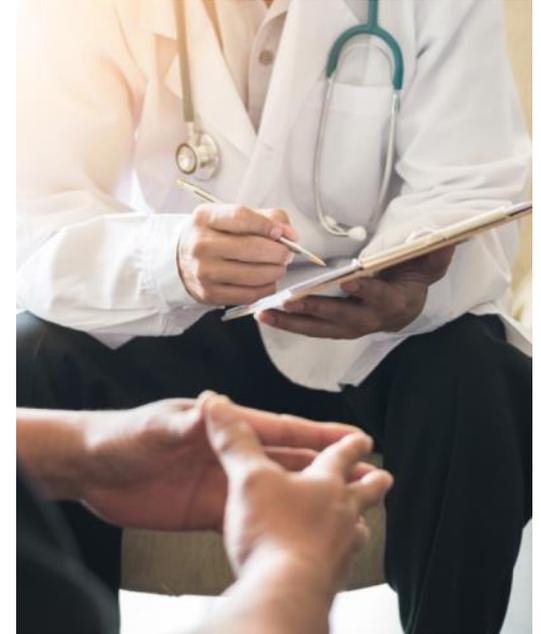


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Principles of Assessment: Initial Screening

- **SCREEN FOR SUICIDALITY**
 - Current suicidal ideation and specific plan
 - Previous suicide attempts or plans
 - Access to weapons or other means
 - Family history
- **SCREEN FOR HOMICIDALITY**
 - Identified victim and specific plan/intent
 - History of violence
 - Access to weapons or other means
- **OBTAIN IMMEDIATE ASSISTANCE IF SCREENS ARE POSITIVE**
- **DO NOT LEAVE PATIENTS ALONE WHO ARE AT RISK**



Principles of Assessment: Caring for Intoxicated Patients

- Screen for suicidality and homicidality
- Inquire about interest in inpatient medication withdrawal treatment
- Review vital signs / attend to acute medical needs and hospitalize if required
- **DO NOT CONTINUE A PROBING PSYCHIATRIC EVALUATION OF ANY INTOXICATED PATIENT, EVEN IF ONLY MILDLY INTOXICATED**
 - Reschedule for an appointment when sober
 - Explain need for sobriety for a psychiatric assessment

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Establish the Diagnosis of an Independent Psychiatric Disorder

- Do not attempt to confirm the psychiatric diagnosis while patient is intoxicated or within 3-4 weeks of substance use or withdrawal management
- Verify drug-free state with laboratory tests and assess psychiatric status when sober
- Obtain a careful longitudinal history tracking both substance use and psychiatric symptoms – track parallel symptom courses
- Confirm history with relatives
- Review family history for psychiatric disorders

Clarify the Diagnosis: Substance-Induced Psychiatric Disorder

- Occur during or within 30 DAYS of intoxication or withdrawal
- Symptoms are associated with substance use
- Can mimic:
 - PSYCHOTIC DISORDERS
 - MOOD DISORDERS
 - ANXIETY DISORDERS
 - PERSONALITY DISORDERS

*Mark Your
Calendar*



Case: Anna 25 yo Veteran

Initial Diagnoses:

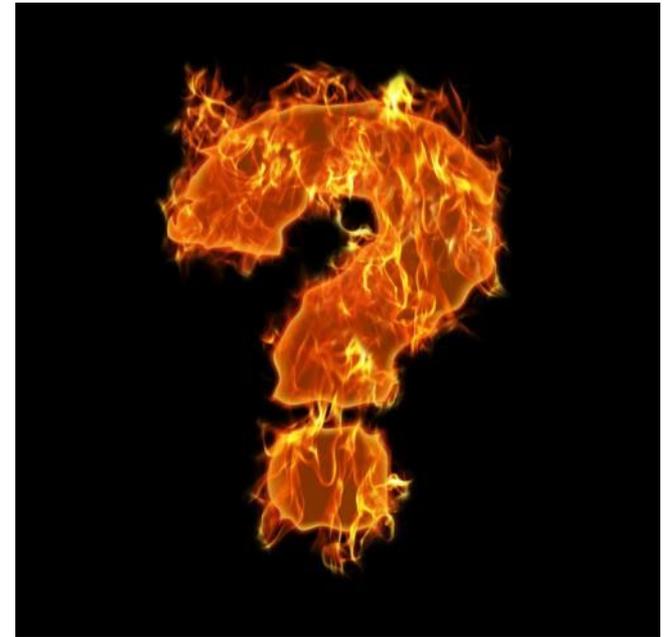
- Opioid Use Disorder
- Posttraumatic Stress Disorder
 - Independent or Substance-Induced?
 - Combat related; single incident or complex?
- Major Depressive Disorder
 - Independent or Substance-Induced?
 - Need to reassess after sobriety

Substance-Induced Psychiatric Disorders

- Substance intoxication and withdrawal can mimic almost any psychiatric disorder
 - Stimulants / cannabinoids / hallucinogens: can mimic mania and schizophrenia
 - Alcohol / opioid / sedative-hypnotic withdrawal: can mimic depression and anxiety disorders

Clarify the Diagnosis: Independent Psychiatric Disorder

- Symptoms may antedate drug use
- Symptoms don't diminish post withdrawal
- Symptoms continue during extended periods of sobriety: > 3 months
- Positive family history



Case: Anna 25 yo Veteran

Follow-up Interview reveals:

- No suicidal ideation
- Sad, increased social isolation for the last 3 months
- Does not want to leave her apartment unless she takes extra opioids
- Insomnia, frequent nightmares
- Jumpy; panic with loud noises
- Diagnosis?

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Screening for Depressive Disorders

- Comorbid depressive symptoms are common among substance users
- **PHQ-9** is a free, widely-used screening test, may be completed by patient in the waiting room
- PHQ-9 scores **under 10** → 99% negative predictive value
- PHQ-9 scores ≥ 10 should prompt further evaluation, but **NOT** diagnosis

PATIENT HEALTH QUESTIONNAIRE -9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems?
(Use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____
=Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all <input type="checkbox"/>	Somewhat difficult <input type="checkbox"/>	Very difficult <input type="checkbox"/>	Extremely difficult <input type="checkbox"/>
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INCLUDES THE FIRST TWO QUESTIONS OF PHQ-9, MAY BE ANSWERED YES/NO

Screening for Anxiety Disorders

- Comorbid anxiety symptoms are common among substance users
- **GAD-7** is a free, widely-used method for *screening* and *following* anxiety symptom severity over time
- GAD-7 score ≥ 10 suggests moderate-severe anxiety
- **DSM 5** criteria still used for *diagnosis*

GAD-7				
Over the <u>last 2 weeks</u> , how often have you been bothered by the following problems? <i>(Use "✓" to indicate your answer)</i>	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.

(For office coding: Total Score T ___ = ___ + ___ + ___)

Screening for Obsessive Compulsive Disorders

- **Obsessions** are persistent/repetitive:
 - **Thoughts**
 - **Images**
 - **Urges** (e.g. to wash hands)
- **Compulsions** are repetitive:
 - **Behaviors** (e.g. washing hands)
 - **Mental acts / rituals**
- For DSM 5 OCD diagnosis, symptoms must be *either*.
 - **Impairing /distressing**
 - **Time consuming** (e.g. >1 hr daily)



Yale-Brown Obsessive Compulsive Scale ([Y-BOCS](#)) is the standard screening tool for OCD, but may be complicated and time-consuming to use

Clinical Implications

- **SUBSTANCE-INDUCED PSYCHIATRIC DISORDERS**
 - Symptoms will clear with sobriety but may require initial hospitalization or psychiatric treatment
 - Additional psychiatric treatment is not required, treatment should be focused on the SUD
- **INDEPENDENT PSYCHIATRIC DISORDERS**
 - Requires specific psychiatric treatment
 - Should be integrated with the SUD treatment
 - Both SUD and symptoms of the co-occurring disorder will be more severe, there are higher levels of disability and treatment is more complicated

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- **Management of common co-occurring conditions:**
 - **Depression**
 - **Anxiety Disorders including PTSD**
 - **Bipolar Disorder**
 - **ADHD**
- Treatment recommendations and the importance of integrated care

General Principles: Managing SUDs and Co-Occurring Disorders

- Evaluate when sober
- Integrate psychiatric and SUD treatment
- Sobriety is the first priority
- MAT where appropriate
- Psychopharmacology when indicated
 - Avoid habit-forming medications if possible
- Psychotherapy interventions if applicable
- Specialized AA/NA groups

Managing Co-Occurring Depressive Disorders

First confirm the diagnosis:

- Wait 2 to 3 weeks for withdrawal symptoms to clear
- Positive family history
- +/- Symptoms antedate drug or alcohol use
- Monitor patient for suicidal ideation, changes in mood, affect, appetite or sleep pattern

Consider pharmacotherapy if the patient refuses or has not responded to psychotherapy alone

Initial Stabilization

- Medication withdrawal treatment may be required for alcohol use disorder or benzodiazepine use disorder
- For opioid use disorder: initial stabilization on methadone or buprenorphine; if starting XR- naltrexone, medication withdrawal treatment may be required first
- No other treatment may be possible until the patient is stable

Case: Anna 25 yo Veteran

- After initial stabilization on buprenorphine/naloxone, her depressive symptoms began to clear. This suggests that her depression was substance-induced.



- Her clinician decided to focus treatment on her opioid use disorder and combat-related PTSD.
- Anna agrees to participate in an intensive outpatient “Dual Diagnosis” program for women veterans.

Managing Co-Occurring Disorders

TREATMENT # 1: PSYCHOTHERAPY:

- Once stable, consider psychotherapy options first for patients with a substance use disorder and less severe depressions or anxiety disorders:
 - CBT
 - The “Seeking Safety” Protocol

What is the role of Cognitive-Behavioral Therapy?

- CBT is well established as an effective evidence-based therapy for substance use disorders, depression, anxiety, PTSD and chronic pain.
- CBT typically includes skill acquisition:
 - Relaxation therapy
 - Cognitive restructuring
 - Effective communication
 - Stress management
- This is followed by skill consolidation and rehearsal:
 - Training to generalize new skills
 - Maintenance of behavioral change
 - Strategies to avoid relapse

CBT / Relapse Prevention

The “Seeking Safety” Protocol

- Manualized Group Therapy
- 25 sessions
- Integrated PTSD and Subst. Abuse Treatment
- Focuses on “Safety”
 - No Acting Out
 - No Substance Use
- Combines Cognitive Behavioral approaches to both disorders
- Useful for a variety of Dual Diagnosis Patients



Managing Co-Occurring Disorders

- TREATMENT # 2: PHARMACOTHERAPY:
 - May be the initial option for most patients; generally medications should not be started until the patient is sober
- Standard pharmacotherapy for psychiatric disorders
 - Most options will work, but
 - Avoid habit-forming medications
 - Caution with benzodiazepines and gabapentin
- Add medications if symptoms fail to respond to psychotherapy alone

How to Manage the Pharmacotherapy of Psychiatric Disorders in SUD Patients

- Begin with non-dependence producing medications - the selective serotonin reuptake inhibitors (SSRI's) are a good choice to treat BOTH depression and anxiety
- Adequate doses for an adequate time (6 to 8 weeks)
- If no response consider serotonin-norepinephrine reuptake inhibitors (SNRI's), or dual action agents
- CBT will improve the response to medications
- Benzodiazepines have no role as a primary treatment for depression, anxiety or PTSD in patients with a substance use disorder
- Benzodiazepines can be used with caution for some anxiety disorders if the patient has not responded to CBT and/or antidepressant medications and has no history of misuse of benzodiazepines

Antidepressants in the Treatment of Co- Occurring Depression & Alcohol Dependence

Double-Blind Studies	Medication	Depression Med vs. Placebo	Drinking Med vs. Placebo
Mason '96	Desipramine	M > P	M > P
McGrath '96	Imipramine	M > P	M = P
Cornelius '97	Fluoxetine	M > P	M > P
Roy '98	Sertraline	M > P	M = P
Roy-Byrne '20	Nefazodone	M > P	M = P
Pettinati '01	Sertraline	M = P	M = P
Moak '03	Sertraline	M > P	M = P
Hernandez '04	Nefazodone	M = P	M > P

Managing Co-Occurring Depressive Disorders

- Most standard pharmacotherapies for depression are effective in patients with substance use disorders
- The majority of well done trials are for SSRIs in individuals with Alcohol Use Disorder
 - Relatively few trials on opioid or stimulant use disorder
 - Few trials with other classes of antidepressants
 - Most trials show improvement in depression; results on SUD symptoms are mixed
- SSRI's are considered the first line medications

New Strategy: Combining SSRI and Naltrexone for Alcohol Use Disorder

- Double-blind placebo controlled trial in 170 depressed patients with AUD:
 - Sertraline up to 200mg/day + Naltrexone up to 100mg/day
 - All patient received CBT
 - Patients receiving combination achieved more abstinence and had lower likelihood of being depressed compared to those receiving placebo or either drug alone
 - Study needs to be replicated (Pettinati, 2010)

Managing Co-Occurring Anxiety Disorders

- First confirm the diagnosis:
 - Wait 4 to 6 weeks for withdrawal symptoms to clear (or for the patient to stabilize on MAT)
- Positive family history
- +/- Symptoms antedate alcohol/drug use
- Begin treatment with behavioral therapies
 - If no response after 2-3 weeks, add pharmacotherapy

What are the Evidence-Based Pharmacotherapies for Anxiety Disorders?

- A systematic review of randomized controlled trials, including the Cochran Database, reported on data from trials demonstrating a $\geq 50\%$ reduction from baseline score on the Hamilton anxiety scale in generalized anxiety disorder:
 - Fluoxetine was ranked first for response and remission
 - Sertraline was ranked first for tolerability
- In a subanalysis for generalized anxiety disorder meds licensed in the UK:
 - Duloxetine was ranked first for response
 - Escitalopram was ranked first for remission
 - Pregabalin was ranked first for tolerability



Evidenced-Based Treatment of Co-Occurring Anxiety and SUD

- There is little research on this topic
- Comprehensive review of studies by McHugh (2015) showed:
 - CBT for SUD generally effective but may be hard to access
 - Medication treatment had some benefits on anxiety but not on SUD
 - Buspirone reduced anxiety and drinking (1 trial). Less clear results in 2 other trials
 - Medication misuse was not seen with benzodiazepines
 - Naltrexone plus exposure therapy had better outcomes for PTSD
 - Integrated treatment for SUD and exposure therapy for anxiety had best outcomes

Managing Co-Occurring Anxiety Disorders

- Pharmacotherapy recommendations:
 - Generalized anxiety disorder: SSRIs, DULOXETINE (first line) BUSPIRONE
 - Panic disorder: ANTIDEPRESSANTS BEHAVIORAL THERAPY
 - Agoraphobia: ANTIDEPRESSANTS BEHAVIORAL THERAPY
 - Social phobia: PROPRANOLOL or CLONIDINE
 - OCD: SSRIs

Benzodiazepines are only recommended if the patient has failed to respond to less dependence producing medications

Managing Co-Occurring Anxiety Disorders

The Role of Benzodiazepines

- Meta-Analysis including Cochrane Library review showed no advantage for antidepressants over benzodiazepines (BDZ) in treating a range of anxiety disorders
- Comprehensive literature review demonstrated efficacy for BDZ for GAD, panic disorder and agoraphobia, and probable efficacy for social phobia & alcohol induced anxiety disorders in patients with a history of SUDs, and little evidence of added risk for BDZ misuse or increased relapse
- Avoid use in individuals with a primary sedative-hypnotic use disorder. Deaths have also been reported with the combination of buprenorphine and BDZ, caution should be used when prescribing. Also see NEJM: Lembke 2/2/18

Managing Co-Occurring Anxiety Disorders

- Treating Posttraumatic Stress Disorder:
 - SSRIs, Venlafaxine ER
 - Specialized psychotherapy:
 - CBT: Cognitive Behavioral Therapy
 - Exposure therapy: a type of CBT, teaches patient to gradually focus on traumatic memories, feelings or situations
 - CPT: Cognitive Processing Therapy
 - EMDR: Eye Movement Desensitization and Reprocessing
 - Prazosin for nightmares
 - Avoid benzodiazepines, marijuana



Bipolar Disorder and Alcohol Use Disorder

- Drinking typically follows onset of mania
- Mixed or dysphoric mania
- Rapid cycling
- Greater severity - suicidality
- Rarely relapse when depressed or euthymic
- Suboptimal response to lithium
- AUD may remit after mood is stabilized

Pharmacotherapy of Bipolar Disorder and Co-Occurring Substance Disorders

- Randomized – double-blind placebo controlled trials
 - 59 Alcohol Dependent Patients – Salloum, 2001
 - 139 Cocaine Dependent Patients – Brady, 2002
- Open Label, Non-Randomized – 6 studies
 - Used Valproate, Lithium, Lamotrigine, Aripiprazole, or Quetiapine
 - Abused drugs included alcohol, cocaine, opiates
 - Number of subjects ranged from 9 to 30
 - Five studies showed improvement in symptoms and drug use
 - One showed improved hypomania, but not in cocaine use

Valproate in Bipolar Alcohol Use Disorder

- Double-blind placebo controlled trial in 59 Bipolar individuals with alcohol use disorder:
 - Valproate + Treatment as usual (TAU) vs. Placebo + TAU
 - TAU = Lithium + psychosocial treatment
 - Results:
 - Valproate group had less heavy drinking days
 - Valproate group had fewer “any” drinking days
 - Both groups had fewer mood swings



Treating ADHD in at Risk Patients

- CBT X 2 weeks without medication
- Then start meds if symptoms persist – medication choices ranked by risk potential
 - Atomoxetine – has no misuse potential
 - Bupropion
 - Methylphenidate ER or amphetamine/dextroamphetamine mixed salts

Managing Insomnia in Patients with Substance Use Disorders

- Substance misuse alters the cycling between NREM and REM sleep
- Insomnia may be prolonged during periods of sobriety and may increase relapse
- Standard medications for insomnia have a high risk for misuse and may cause physiologic dependence



Managing Insomnia in Patients with Substance Use Disorders

- The following medications are not habit forming and have no known misuse potential:
 - Sedating antidepressants: Trazodone (most studied in patients with AUD) & Mirtazapine
 - Melatonin agonists: Melatonin, Ramelteon and Agomelatine
 - Sedating anticonvulsants: Gabapentin* and Topiramate
 - Prazosin (suppresses nightmares in PTSD)

* some patient may misuse gabapentin

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- Psychotherapy interventions if applicable
- Specialized AA/NA groups



General Principles: Managing Pharmacotherapy for Co-Occurring Disorders

- Check State PDMP
- Standard pharmacotherapy for psychiatric disorders
 - First choose non-habit-forming drugs
 - Adequate doses for adequate times
- Caution with habit-forming medications
 - Start low
 - Go slow
 - Non-refillable prescriptions
 - Monitor carefully

Pharmacotherapy Recommendations for Psychiatric Disorders in Primary Care

- Depression – SSRIs; Venlafaxine, Duloxetine, Bupropion
- Generalized Anxiety Disorder – SSRIs; Duloxetine, Buspirone, Escitalopram
- Panic Disorder – SSRIs
- Social Anxiety – Paroxetine
- PTSD – SSRIs, Venlafaxine ER and Prazosin
- Bipolar Disorder – Valproate

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PCSS Mentor Program

- PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid addiction.
- PCSS mentors are a national network of providers with expertise in **addictions, pain, evidence-based treatment including medication-assisted treatment.**
- 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.
- No cost.

For more information visit:

pcssNOW.org/mentoring

PCSS Discussion Forum

Have a clinical question?



Ask a Colleague

A simple and direct way to receive an answer related to medication-assisted treatment. Designed to provide a prompt response to simple practice-related questions.

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PROVIDERS' CLINICAL SUPPORT SYSTEM
For Medication Assisted Treatment

PCSS-MAT is a collaborative effort led by the American Academy of Addiction Psychiatry (AAAP) in partnership with the: Addiction Technology Transfer Center (ATTC); American Academy of Family Physicians (AAFP); American Academy of Neurology (AAN); American Academy of Pain Medicine (AAPM); American Academy of Pediatrics (AAP); American College of Emergency Physicians (ACEP); American College of Physicians (ACP); American Dental Association (ADA); American Medical Association (AMA); American Osteopathic Academy of Addiction Medicine (AOAAM); American Psychiatric Association (APA); American Psychiatric Nurses Association (APNA); American Society of Addiction Medicine (ASAM); American Society for Pain Management Nursing (ASPMN); Association for Medical Education and Research in Substance Abuse (AMERSA); International Nurses Society on Addictions (IntNSA); National Association of Community Health Centers (NACHC); National Association of Drug Court Professionals (NADCP), and the Southeast Consortium for Substance Abuse Training (SECSAT).

For more information: www.pcssNOW.org



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