

Medications for Substance Use Disorder Treatment

Alcohol Use Disorder Treatment Medications

FDA-Approved

Naltrexone is effective in reducing heavy drinking when used in the oral form (50mg/day) or the long-acting injectable form (Vivitrol®, 380 mg monthly). It reduces craving for alcohol and makes drinking alcohol less pleasurable. It is a mu-opioid antagonist which precludes its use in patients who take opioids. It can occasionally cause hepatic impairment and should be used cautiously in patients with liver disease.

Acamprosate (Campral®) is administered as an oral medication (666 mg TID), and acts at the GABA and glutamate receptors. It appears to be most effective for maintaining abstinence, rather than decreasing heavy drinking. It decreases post-withdrawal anxiety. It can be used in patients with significant liver disease but is renally excreted and contraindicated in renal failure.

Disulfiram (Antabuse®) acts by causing unpleasant symptoms when alcohol is consumed. The medication interrupts the normal metabolism of alcohol and causes a build-up of acetaldehyde, which produces symptoms of nausea, vomiting, flushing, dyspnea, among others. A typical dose is 250 mg daily. Care must be taken to avoid all forms of alcohol (e.g. in mouthwash) in order to avoid symptoms. It is contraindicated in patients with severe coronary disease or psychosis. It works best when supervised daily administration of the medication is provided, in order to avoid nonadherence.

Off-label

Topiramate acts at both GABA and glutamate receptors and is associated with both a decrease in heavy drinking days and an increase in the number of days abstinent. The dose is slowly titrated up from 25 mg per day to a maximum of 150 mg po BID. It may be started while patients are still drinking and can cause a gradual reduction in intake. Side effects include mental slowing, weight loss and paresthesia.

Gabapentin is thought to act as a calcium modulator at presynaptic terminals inhibiting the release of glutamate. Its use is associated with increased rates of abstinence and a decrease in heavy drinking. The preferred dose is 1800 mg/day. Side effects include sedation and dizziness. Some evidence suggests that combining naltrexone and gabapentin is helpful in improving naltrexone adherence and decreasing insomnia and may be more effective than either medication alone.

Opioid Use Disorder Treatment Medications

FDA-Approved

Methadone is a mu-opioid agonist and is an effective medication for OUD. Its use is associated with a reduction in injection drug use, mortality, costs of care, crime, and risk of HIV and hepatitis C transmission. In the US methadone must be dispensed from an Opioid Treatment Program

(OTP) approved by the federal government; it is illegal for office-based providers to prescribe methadone for treatment of OUD. Canadian physicians can take additional training and gain the ability to prescribe methadone for OUD from their offices. Other countries have varying regulations regarding methadone. The starting dose is up to 30 mg per day which is gradually increased to the effective dose of typically 60-120 mg per day. The medication is dispensed daily and under direct observation, but eventually patients may qualify for “take-homes.” There is a risk of overdose if the dose is raised too quickly or if the medication is diverted and taken in large doses, especially when combined with other opioids or sedative-hypnotics. Side effects include sedation, constipation, and (rarely) prolongation of the QT interval leading to an increased risk of torsades de pointes ventricular tachycardia.

Buprenorphine is also a mu-opioid agonist and an effective medication for OUD. It is available in several formulations and includes combination products (buprenorphine and naloxone) and monoproducts (buprenorphine alone). The combination forms are oral transmucosal products and are available as generic and proprietary formulations (Suboxone®, Zubsolv®, and Bunavail®). Monoproducts are available as a generic taken sublingually, subdermal implantable rods which last six months (Probuphine®), and a monthly injectable (Sublocade®).

Treatment with buprenorphine is also associated with a reduction in injection drug use, mortality, costs of care, crime, and risk of HIV and hepatitis C transmission. Buprenorphine has a very low risk of respiratory depression unless combined with sedative/hypnotic agents.

Naltrexone is an opioid antagonist that is largely ineffective for OUD in the oral form, but there is evidence for its use to decrease relapse in OUD when administered as a long-acting intramuscular injection (Vivitrol®). Each injection is effective for 4 weeks, and acts by blocking the effect of other opioids during that period. Starting patients on naltrexone can be challenging because they must be abstinent from opioids between 7-10 days prior to starting the medication in order to avoid precipitated withdrawal. Once a patient is receiving naltrexone, they appear to have a relapse rate that is similar to that of patients treated with buprenorphine or methadone. However, unlike these two medications, naltrexone does not appear to be associated with decreased mortality, and patients typically continue naltrexone for a much shorter time.

Tobacco Use Disorder Treatment Medications

FDA-Approved

Combined Nicotine replacement therapies (NRT) are available in many forms including a longacting daily patch and several short-acting options. These are most effective when used in combination, with the patch providing baseline control of nicotine withdrawal symptoms and the short-acting agents addressing craving and breakthrough withdrawal symptoms. Patches, gum, and lozenges are available over the counter, while the nasal spray and oral inhaler require prescription. People who smoke > 10 cigarettes (1/2 pack) per day should start with the highest dose patch (21 mg) and taper the dose over 10 weeks. Those who smoke less should start with the 14 mg patch. Patients should also use a short acting form of NRT concurrently. Starting treatment with more than one daily patch (plus a short acting agent such as gum or lozenges) may be appropriate for patients who smoke more than 1 pack per day.

Varenicline (Chantix®) is a partial agonist at the nicotinic acetylcholine receptor. It is initiated at a dose of 0.5 mg/day and rapidly titrated to the effective dose of 1 mg BID. It should be started at least one week before the planned quit date and continued for 12 weeks or longer.

Administration

with food and water reduces the risk of nausea. There is some mixed evidence that it is associated with neuropsychiatric symptoms, although the FDA has removed the boxed warning with regards to serious neuropsychiatric events. Its use is not recommended in patients who are psychotic or markedly mentally unstable. Recent data also suggest that use of varenicline may intensify the intoxicating effects of alcohol. Follow up monitoring should be arranged for all patients within one week of starting treatment.

Bupropion (Zyban®) is also used as an anti-depressant that works by enhancing noradrenergic and dopaminergic release. Compared with other medications used for smoking cessation, bupropion is associated with less short-term weight gain; however, this appears to be a temporary effect. Treatment is initiated at dose of 150 mg daily for the first three days and then increased to 150 mg BID. Although usually treatment lasts for 4 weeks, treatment may be continued for up to a year. Bupropion decreases the seizure threshold and may also be associated with neuropsychiatric symptoms. Follow up monitoring should be arranged for all patients within one week of starting treatment.

Off-label

Nortriptyline is a tricyclic antidepressant but the exact mechanism of action for smoking cessation is unknown. Nevertheless, it has been effective regardless of comorbid depression. The dosing is similar to that for the treatment of depression and blood levels should be checked when a steady state has been reached. The initial dose is 25 mg/day initiated between 10-28 days before quit date with a gradual increase to 75-100 mg/day over 10 days to 5 weeks. The course of treatment is 12 weeks. The medication should then be gradually tapered to prevent discontinuation side effects. Due to the anticholinergic effects, exercise caution in the elderly and those with cardiovascular disease.

Clonidine is a centrally acting alpha-agonist hypotensive agent that is effective in smoking cessation. The exact mechanism of action is unknown. The dose ranges from 0.15-0.75 mg/day by mouth and from 0.10-0.20 mg/day transdermal (TTS). There is no clear dose response relationship. Initial dosing is typically 0.10 mg BID orally or 0.10 mg/day TTS, increasing by 0.10 mg/day per week if needed. The treatment duration ranges from 3-10 weeks. Smoking cessation should be initiated between 0 to 3 days after starting the medication. Patients should be cautioned not to stop the medication abruptly due to rebound hypertension. The most significant side effects include dry mouth, sedation, dizziness, and constipation.

Behavioral Health Interventions for Substance Use Disorder Treatment

Behavioral Interventions and Approaches	Substance Use Disorder(s)	Mental Health Condition(s)	Availability by Profession and Training
<p>Motivational Enhancement Therapy (MET): is a counseling approach that helps individuals resolve their ambivalence about engaging in treatment and stopping their drug use.</p>	<ul style="list-style-type: none"> • Alcohol, marijuana, and nicotine. • Mixed results for heroin, cocaine, and nicotine <p>*Effective at engaging all individuals in treatment</p>	<ul style="list-style-type: none"> • Mental health • Chronic conditions such as diabetes, cardiovascular conditions, and asthma • Making positive behavioral changes to support better health 	<p>MINT Training is available across multiple professions.</p>
<p>Cognitive Behavioral Therapy (CBT): is designed to modify harmful beliefs and maladaptive behaviors.</p>	<p>Substance use disorders:</p> <ul style="list-style-type: none"> • Alcohol • Cocaine • Nicotine • Marijuana • Methamphetamines 	<ul style="list-style-type: none"> • Depression • Anxiety disorders • Adjustment disorders • mood disorders 	<p>LPC, LCSW, LMFT, Psychologists, some Licensed Alcohol and Drug Abuse Counselors</p>
<p>Dialectical Behavioral Therapy (DBT): is designed specifically to reduce self-harm behaviors, including suicidal attempts, thoughts, or urges; cutting; and drug use</p>	<p>Substance Use Disorders (all)</p>	<ul style="list-style-type: none"> • Borderline personality disorder • Depression • Bipolar • PTSD • Bulimia • Binge eating 	<ul style="list-style-type: none"> • LPC, LCSW, LMFT, and Psychologists • The Linehan Board of Certification has developed certification standards for clinicians.
<p>Seeking Safety (SS): A present-focused therapy where patients learn behavioral skills for coping with trauma/post-traumatic stress disorder and substance use disorder.</p>	<p>Substance Use Disorders (all)</p>	<p>Trauma and PTSD</p>	<ul style="list-style-type: none"> • Anyone can conduct Seeking Safety. It does not require any specific degree, licensure, or Certification. • Manualized Training is available
<p>Contingency Management Interventions/Motivational Incentives: Involves giving patients tangible rewards to reinforce positive behaviors such as abstinence</p>	<ul style="list-style-type: none"> • Alcohol • Stimulants • Marijuana • Opiates • Nicotine 	<p>None</p>	<ul style="list-style-type: none"> • Program progress tracked by the team • Voucher-based reinforcement or prize incentives

Behavioral Health Interventions for Substance Use Disorder Treatment *Continued*

Behavioral Interventions and Approaches	Substance Use Disorder(s)	Mental Health Condition(s)	Availability by Profession and Training
<p>Matrix Model (MM): A framework for engaging people with stimulant use disorders in treatment and helping them achieve abstinence. Patients learn about issues critical to addiction and return to use, receive direction and support.</p>	<ul style="list-style-type: none"> • Methamphetamine • Cocaine 	<p>None</p>	<p>LPC, LSW, LMFT, Psychologist and licensed/certified alcohol and drug counselors and case workers</p>
<p>Assertive Community Treatment (ACT): Integrates behavioral treatments for severe mental illnesses co-occurring substance use disorders. ACT has a smaller caseload size, team management, outreach emphasis, a highly individualized approach, and an assertive approach to maintaining contact with patients.</p>	<p>Substance use disorders (co-occurring with other mental illness or problems)</p>	<ul style="list-style-type: none"> • Schizophrenia, Bipolar • Depression • Anxiety • Other: homelessness, criminal justice systems, frequent hospitalizations 	<p>Mobile mental health treatment teams often include a team leader, psychiatrist with a nurse practitioner or physician assistant, substance abuse specialist, vocational specialist, and peer specialist</p>
<p>Exposure Therapy: A behavioral treatment that involves repeated exposure to a feared situation, object, traumatic event, or memory. Exposure can be real, visualized, or simulated, and is always contained in a controlled therapeutic environment. This is treatment for Post-Traumatic Stress Disorder (PTSD) that frequently co-occurs with cocaine use disorder.</p>	<p>Cocaine</p>	<p>Anxiety disorders (phobias and PTSD)</p>	<p>LPCs, MSW, LMFT, psychologist training in exposure therapy is needed for required dosage and experience setup</p>

Peer and Community-Based Supports

Focus	Supports	Details	Resources
Peer-Based	Alcoholics Anonymous and other 12-step groups	<ul style="list-style-type: none"> • Free, peer-led, and available in most communities • Abstinence-focused 	<i>Alcoholics Anonymous (AA):</i> https://www.aa.org/
	Self-Management and Recovery Training (SMART)	<ul style="list-style-type: none"> • Peer-led; available in-person and online • Concepts from cognitive behavioral therapy (CBT) 	<i>Smart Recovery:</i> https://www.smartrecovery.org/
	Peer Recovery Support Specialists	<ul style="list-style-type: none"> • Individuals in long-term recovery • Scope often depends on where they are employed 	<i>SAMHSA Peer Support Role Information:</i> https://www.cdc.gov/ssp/index.html
Community-Based	Community Harm Reduction Programs	<ul style="list-style-type: none"> • Syringe services programs (SSPs) • Naloxone distribution programs • Fentanyl test strip distribution 	<i>The Centers for Disease Control and Prevention Resources on:</i> <ul style="list-style-type: none"> • <i>Syringe Services Programs:</i> https://www.cdc.gov/ssp/index.html • <i>Naloxone Purpose and Program Information:</i> https://www.cdc.gov/stopoverdose/naloxone/index.html • <i>Fentanyl Test Strips:</i> https://www.cdc.gov/stopoverdose/fentanyl/fentanyl-test-strips.html

Alcohol Use Disorder (AUD) Medications

First Line Medications

<i>Medication</i>	<i>Route</i>	<i>FDA</i>	<i>Mechanism</i>
Acamprosate	Oral	Y	Glutamate modulator
Naltrexone	Oral/IM	Y	μ opioid antagonist

Second Line Medications

<i>Medication</i>	<i>Route</i>	<i>FDA</i>	<i>Mechanism</i>
Disulfiram	Oral	Y	Aldehyde dehydrogenase inhibitor
Topiramate	Oral	N	GABA agonist/Glutamate modulator
Gabapentin	Oral	N	Glutamate modulator



Treatment Planning – Medication and Behavioral Health

Ben's Case Information

Ben is a 38-year-old man who is referred by Drug Treatment Court after multiple arrests for disorderly conduct. He has been drinking for many years, and his alcohol use disorder has resulted in his wife leaving him and loss of his job in the film industry.

He has poor social support. He has had multiple attempts at abstinence and has attended AA sporadically as well as having several short stints in counseling.

He knows that he will go to jail if he resumes use, and he is asking for help to control cravings and be able to meet his goal of total abstinence. He reports that his last drink was 6 days ago.

On physical exam Ben has normal vital signs. He is mildly tender in the right upper quadrant of his abdomen. Labs show elevated transaminases (approximately twice the upper limit of normal), with normal albumin, platelets, and PT/INR.

Treatment Planning – Medication and Behavioral Health

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Treatment Planning Considerations

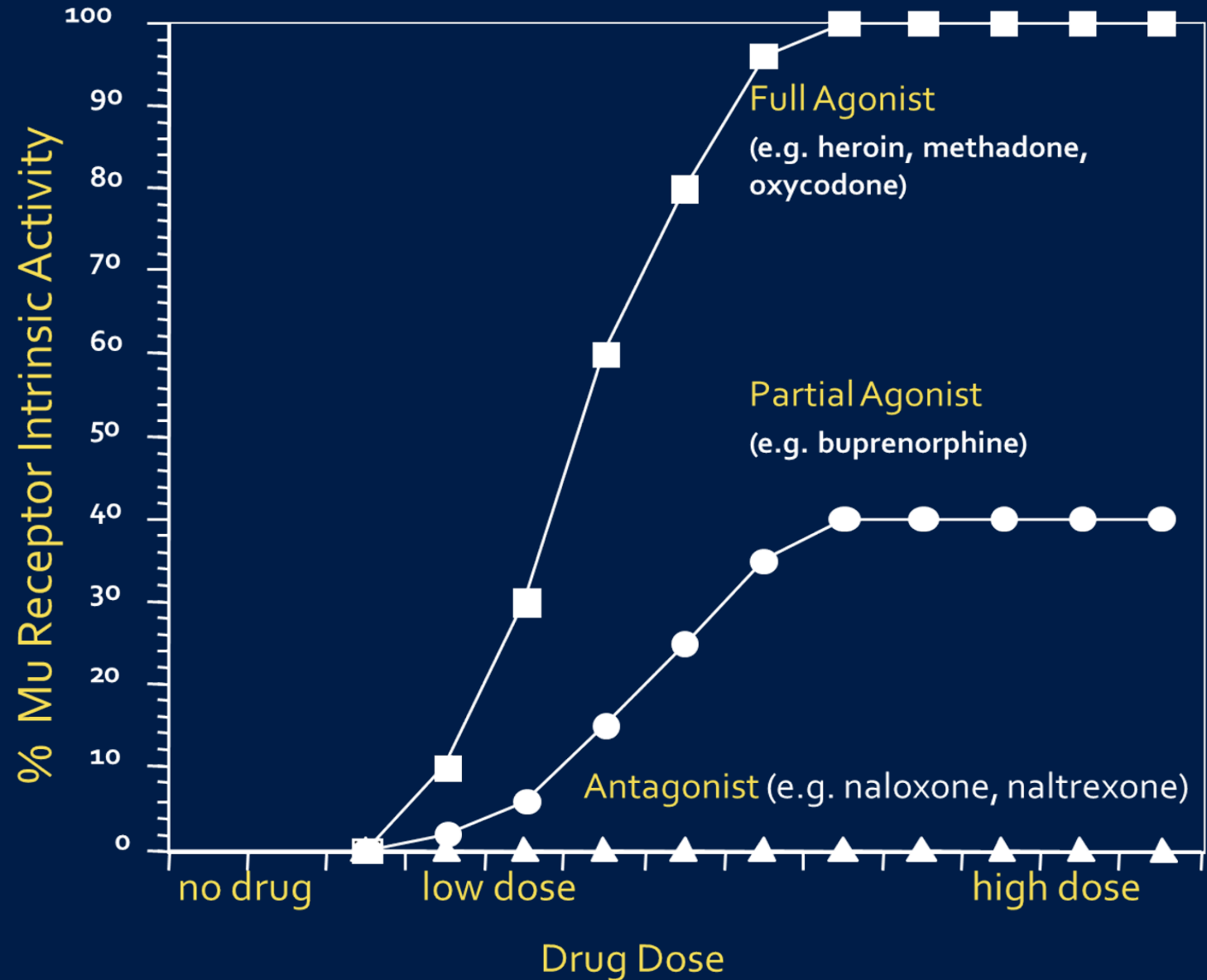
1. What pharmacotherapy options would you discuss with him to help prevent resumed use?

2. What types of behavioral health treatment would you discuss?

Opioid Use Disorder (OUD) Medications

<i>μ Agonists</i>	<i>Route</i>	<i>Requires Withdrawal</i>	<i>Analgesic Properties</i>
Methadone	Oral		✓
Buprenorphine	Transmucosal/ Injectable		✓
<i>μ Antagonists</i>	<i>Route</i>		
Naltrexone	Oral/Injectable	✓	

Opioid Agonists and Antagonists



Treatment Planning – Medication and Behavioral Health

Jesse's Case Information

Jesse is a 30-year-old divorced woman who works in a restaurant. She has developed an opioid use disorder (OUD) after receiving a large quantity of opioid pain pills with several refills after she fractured her clavicle in a soccer game.

Jesse's reason for coming to see you is that she wants help with medications to get control of her OUD and has lost interest in doing things she enjoys and is feeling depressed and hopeless.

Recently, she has started buying pain pills from friends and fears she will lose her job or lose custody of her two children.

She has not had any treatment for her OUD previously, and states that she "doesn't believe in" 12-step programs or a higher power.

On physical exam, she has a mildly elevated heart rate, enlarged pupils, and moist skin. She has no track marks in her antecubital fossae or her neck.

In-office urine drug screening is positive for oxycodone and otherwise negative. HCG test is negative. Metabolic panel, hepatitis testing, and HIV testing are pending.

Treatment Planning – Medication and Behavioral Health

Jesse's Case Information

Jesse is a 30-year-old divorced woman who works in a restaurant. She has developed an opioid use disorder (OUD) after receiving a large quantity of opioid pain pills with several refills after she fractured her clavicle in a soccer game. Jesse's reason for coming to see you is that she wants help with medications to get control of her OUD and has lost interest in doing things she enjoys and is feeling depressed and hopeless. Recently, she has started buying pain pills from friends and fears she will lose her job or lose custody of her two children. She has not had any treatment for her OUD previously, and states that she "doesn't believe in" 12-step programs or a higher power. On physical exam, she has a mildly elevated heart rate, enlarged pupils, and moist skin. She has no track marks in her antecubital fossae or her neck. In-office urine drug screening is positive for oxycodone and otherwise negative. HCG test is negative. Metabolic panel, hepatitis testing, and HIV testing are pending.

Treatment Planning Considerations

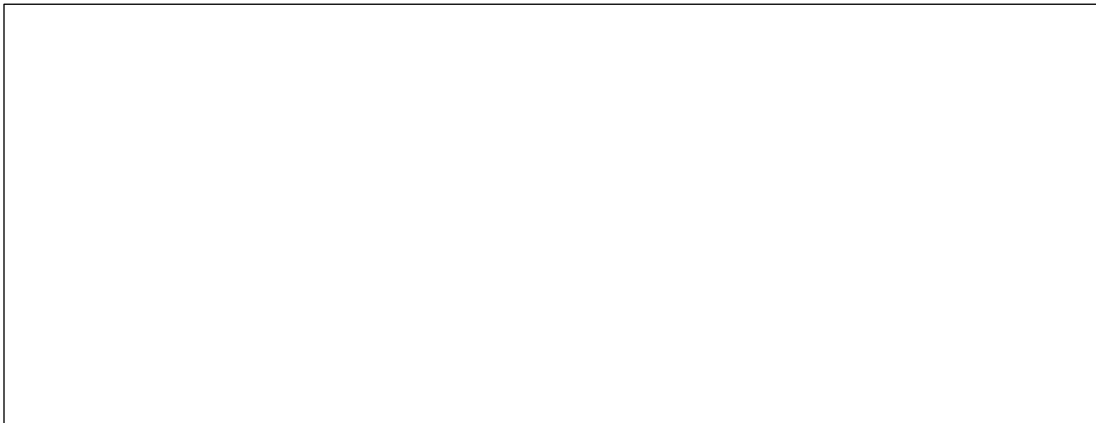
1. What pharmacotherapy options would you discuss with her to help prevent resumed use?

2. What types of behavioral health treatment would you discuss?

3. What community and peer-led supports would you discuss with her?



4. What harm reduction options would you discuss?



Tobacco Use Disorder (TUD) Medications

First Line Medications

<i>Medication</i>	<i>Route</i>	<i>FDA</i>	<i>Mechanism</i>
Nicotine	Various	Y	Nicotine Agonist
Varenicline	Oral	Y	Nicotine Agonist
Bupropion	Oral	Y	Dopamine/NE reuptake inhibitor

Second Line Medications

<i>Medication</i>	<i>Route</i>	<i>FDA</i>	<i>Mechanism</i>
Nortriptyline	Oral	N	NE/serotonin reuptake inhibitor
Clonidine	Oral	N	α -2 adrenergic agonist

Cahill Ket al. Cochrane Database Syst Rev. 2016 May 9;2016(5). PMID: 2715889.

Baker et al. JAMA. 2021;326(15):1485-1493.

Apollonio D, et al. Cochrane Database Syst Rev. 2016 Nov 23;11(11). PMID: 27878808.

Treatment Planning – Medication and Behavioral Health

Harvey's Case Information

Harvey is a 58-year-old man who works as a truck driver and has a 30 pack-year smoking history. He currently smokes 30 cigarettes per day and smokes his first cigarette while sitting on the side of the bed when he wakes up.

He has tried to quit smoking many times using nicotine patches and has also utilized the Quitline. He lacks confidence in his ability to quit but is asking for help because he recently learned that he has mild COPD. Harvey is married and has 3 adult children.

He has mild intermittent depression. His physical exam and labs are unremarkable.

Treatment Planning – Medication and Behavioral Health

Harvey's Case Information

Harvey is a 58-year-old man who works as a truck driver and has a 30 pack-year smoking history. He currently smokes 30 cigarettes per day and smokes his first cigarette while sitting on the side of the bed when he wakes up. He has tried to quit smoking many times using nicotine patches and has also utilized the Quitline. He lacks confidence in his ability to quit but is asking for help because he recently learned that he has mild COPD. Harvey is married and has 3 adult children. He has mild intermittent depression. His physical exam and labs are unremarkable.

Treatment Planning Considerations

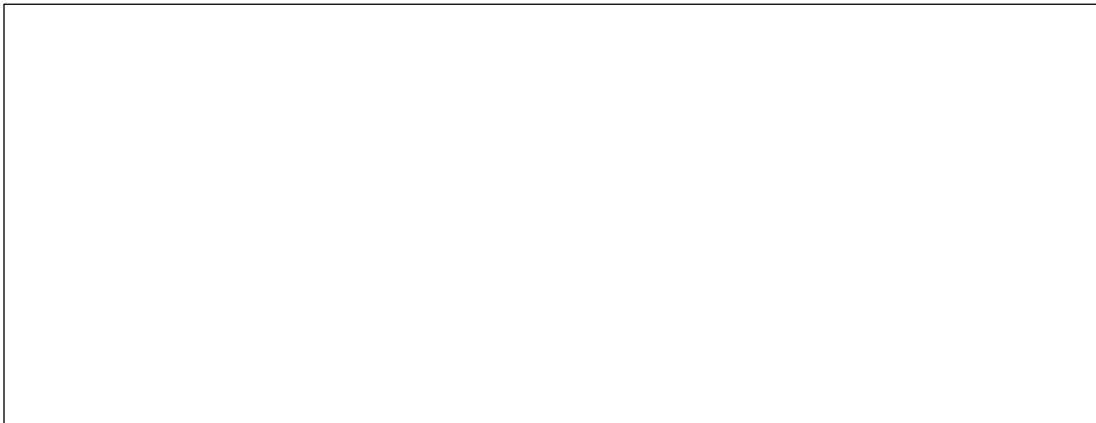
1. What pharmacotherapy options would you discuss with Harvey?

2. What types of behavioral health treatment would you discuss?

3. What community and peer-led supports would you discuss with him?

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4. What harm reduction options would you discuss?

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